'Living better with advanced breast cancer'

(LIBERATE):

Symptom reporting, self-management and signposting support for secondary breast cancer

Kathleen Sian Anne Kane

Submitted in accordance with the requirements for the degree of

Doctor of Philosophy

The University of Leeds

School of Medicine

October 2021

The candidate confirms that the work submitted is her own, except where work which has formed part of jointly authored publications has been included. The contribution of the candidate and the other authors to this work has been explicitly indicated below. The candidate confirms that appropriate credit has been given within the thesis where reference has been made to the work of others.

Publications

Kane K, Kennedy F, Absolom KL, Harley C and Velikova G. Quality of life support in advanced cancer – web and technological interventions: systematic review and narrative synthesis. BMJ Supportive & Palliative Care. Published Online First: 2021 Apr 26.doi: 10.1136/bmjspcare-2020-002820

This published systematic review is reported in chapter 4 of this thesis. I was responsible for planning and carrying out all aspects of the review process, including searching, screening, data extraction, analysis and write up. Co-authors contributed to the conception and design of the review and to the process of screening. I drafted the manuscript and this was critically reviewed by the other authors. All authors reviewed and approved the final version of the manuscript.

This copy has been supplied on the understanding that it is copyright material and that no quotation from the thesis may be published without proper acknowledgement.

© 2022 The University of Leeds and Kathleen Kane

The right of Kathleen Sian Anne Kane to be identified as Author of this work has been asserted by Kathleen Sian Anne Kane in accordance with the Copyright, Designs and Patents Act 1988.

Acknowledgements

This research was carried out within the Patient Centred Outcomes Research (PCOR) group based at Leeds Institute of Medical Research at St James's, University of Leeds, UK. It would not have been possible without the vast amount of support and expertise so generously shared by team members past and present. The direct involvement of supervisory team members in this research is acknowledged throughout the thesis, indicated by their initials (Fiona Kennedy, FK, Galina Velikova, GV, Kate Absolom, KA and Clare Harley, CH), as is the support provided by colleagues in an expert advisory capacity. Andrea Gibson (AG) offered invaluable clinical expertise and practical support throughout the course of this project; Robert Carter (RC) and Jeremy Dwyer (JD) provided ongoing technical and QTool related support, without which the intervention would not have been possible. I am also extremely grateful to Carolyn Morris (CM) for her ongoing guidance and the insights she so kindly offered as the project's Patient Advisor.

I would like to thank the entire PCOR team, who have all helped in some way and have made these past four years so enjoyable. I am extremely lucky to have had the chance to work with such wonderful colleagues. I am so grateful to my fantastic supervisors for giving me the opportunity to undertake this project. I have so much to thank each of them for. Fiona, for your endless support, encouragement and kindness, and for constantly being at the end of an email with positivity and feedback on my never-ending chapters. Galina, for sharing so much of your time and expertise, and for the many hours of clinic list screening. Kate, for welcoming me into PCOR on my very first day and offering so much guidance and reassurance ever since. Clare, for all of your feedback, encouragement and kind words. It is testament to my supervisors that this research continued despite the unfolding pandemic and I will always be grateful for their incredible support.

To my Mum and Dad, I cannot thank you enough for your unwavering support. I would not be where I am without you both. To Steve, for your equally endless support, encouragement, laughs and cups of tea, and for getting me through the highs and lows of write up, lockdowns and everything in between! Thank you for always believing I could do it. To Florence, Ged, Cathy and our amazing Wilf, for the many Zoom calls and FaceTimes when it all seemed impossible. To my Grandad and Nan, for being my biggest supporters, always.

Most importantly, my heartfelt thanks goes to all of the women who so generously shared their time and experiences in support of this research, some of whom sadly did not live to see it reach its completion. I would like to dedicate this thesis to them. I feel privileged to have

shared in their journey and hope that this research goes some way to improving the understanding of SBC and the support available to those living with it. A final, sincere thank you to Breast cancer Now for funding this research (Grant ref: 2016NovPhD818), for their ongoing support throughout its completion and for continuing to advocate for women living with SBC.

Abstract

Introduction

Quality of life (QoL) is a crucial yet poorly addressed concern for women living with incurable secondary breast cancer (SBC). Treatment advancements offer extended survival, yet women face significant side-effects, uncertainty and supportive needs. The internet is increasingly harnessed to provide tailored and readily accessible support, though innovations targeting this growing patient group are lacking.

Aims

- To explore the QoL and supportive needs of women living with SBC.
- To develop and evaluate a tailored online intervention in response.

Methods

(I) Development

A qualitative interview study (n=28 patients, n=7 health/charity professionals) identified diverse supportive needs across shifting disease trajectories. A systematic review of online/technology-assisted interventions (n=35) highlighted the value of interactive health communication applications (IHCAs) and collaboration in self-management. Constructs of self-efficacy and self-care informed programme theory. A proposed intervention encompassing self-management, symptom monitoring and signposting support was finalised through expert consensus.

Results

(II) Evaluation

Feasibility of the intervention was evaluated in both clinically integrated (randomised controlled trial, n=21) and independent-monitoring (online sub-study, n=20) contexts.

Barriers to recruitment such as time burden and health status led to high rates of decline in clinic, with greater uptake in the online setting. Most women used the intervention to independently self-monitor mild-moderate symptoms. Clinical integration was feasible, though health professional engagement was poor. Whilst widely accepted, overall value was limited by insufficient tailoring and higher levels of patient experience further along the trajectory. Self-efficacy represents a potential outcome for future evaluation, though a task-specific measure may be more informative.

Conclusions

An online self-management intervention has the potential to bridge ongoing gaps in support for SBC. Further development must focus on heightening the level of tailoring and specificity in line with individual SBC experiences and key timepoints for support. Innovative research design is needed to overcome barriers to recruitment and encourage health professional engagement.

Table of Contents

Acknowledgements ii
Abstract iv
List of tables xii
List of figures xiii
List of abbreviations xv
Chapter 1: Introduction 17
1.1 Background 17
1.1.1 Cancer & survivorship: dual challenges for global health 17
1.1.2 Survivorship in advanced cancer 17
1.1.3 Secondary breast cancer 18
1.1.4 Treating secondary breast cancer 19
1.1.5 The individual and the SBC experience 22
1.1.6 QoL and supportive needs 23
1.1.7 The patient's perspective 23
1.1.8 The shift towards self-management 24
1.1.9 The internet and 'connected health' 25
1.2 Research rationale 26
1.2.1 Terminology 26
1.3 Aims 26
1.4 Overview of thesis 27
1.4.1 Phase I 27
1.4.2 Phase II 27
Chapter 2: Research design & methodology 29
2.1 Chapter overview 29
2.2 Chapter aims 29
2.3 Project overview 29
2.4 Multiple and mixed methods research 30
2.4.1 Defining mixed versus multiple methods 31
2.4.2 Paradigmatic considerations 34
2.5 LIBERATE: A MMMR approach guided by critical realism 35
2.5.1 Complex methods for complex research 35
2.5.2 Critical realism 36
2.5.3 Principles of realist evaluation 37
2.6 Complex interventions 38
2.6.1 The MRC framework 39

2.6.2 The development phase & intervention theory 40
2.6.3 Feasibility & piloting: Informing intervention evaluation 42
2.7 Reflections 43
2.8 Summary 43
Chapter 3: Exploring quality of life & routes to support in secondary breast cancer - a qualitative interview study 44
3.1 Chapter overview 44
3.2 Chapter aims 44
3.3 Introduction 44
3.3.1 Background 44
3.3.2 Rationale 44
3.3.3 Aims 45
3.4 Methods 45
3.4.1 Design overview 45
3.4.2 Sampling 45
3.4.3 Patient & Public Involvement and study documentation 46
3.4.4 Dual approach to analysis 46
3.4.5 Ethical approval 46
3.4.6 Recruitment strategy: women living with SBC 46
3.4.7 Recruitment strategy: professionals 48
3.4.8 Semi-structured qualitative interviews 48
3.4.9 Thematic analysis 48
3.5 Stage 1 analysis 51
3.6 Stage 1 results 52
3.6.1 Women living with SBC: final sample 52
3.6.2 Health and charity professionals: final sample 54
3.7 Stage 2 analysis 54
3.8 Stage 2 results: Women's perspective 55
3.8.1 Narratives surrounding secondary breast cancer 55
3.8.2 Adjustment 58
3.8.3 Self-awareness 59
3.8.4 Living with incurable cancer 61
3.8.5 Connection to care 64
3.8.6 Thematic overview 67
3.9 Stage 2 results: Health & charity professionals' perspective 68
3.9.1 The key timepoints 68
3.9.2 The individual 69

3.9.3 The ideal model of support 71
3.9.4 Thematic overview 73
3.10 Discussion 74
3.10.1 Bringing together the patient and professional perspective 74
3.10.2 Reflections 77
3.10.3 Summary 77
Chapter 4: A systematic review of online & technology-assisted interventions supporting QoL in advanced cancer 79
4.1 Chapter overview 79
4.2 Chapter aims 79
4.3 Introduction 79
4.3.1 Previous reviews 80
4.4 Aims 81
4.5 Methods 81
4.5.1 Protocol 81
4.5.2 Search strategy 81
4.5.3 Eligibility criteria 82
4.5.4 Study selection 83
4.5.5 Data extraction 84
4.5.6 Risk of bias 84
4.5.7 Data synthesis: a narrative approach 84
4.6 Results 85
4.6.1 Study selection 85
4.6.2 Study characteristics 86
4.6.3 Risk of bias assessment 86
4.6.4 Categorising interventions 101
4.6.5 Intervention features and delivery 103
4.6.6 Exploring efficacy: Quality of life and psychosocial outcomes 107
4.7 Discussion 113
4.8 Reflections 116
4.9 Summary 117
Chapter 5: Intervention theory 118
5.1 Chapter overview 118
5.2 Chapter aims 118
5.3 Introduction 118
5.4 Self-management 119
5.4.1 Concept analysis 119

5.4.2 Self-care vs self-management 120
5.4.3 Self-management behaviours 121
5.5 Middle Range Theory of Self-care of Chronic Illness 122
5.5.1 Underlying processes & proficiency 124
5.5.2 Factors influencing self-care 125
5.6 Self-efficacy & the Social Cognitive Theory 125
5.6.1 Self-efficacy and health behaviour 127
5.6.2 Cancer-specific self-efficacy 127
5.7 Quality of life 128
5.8 Developing a programme theory 129
5.9 Reflections 133
5.10 Summary 133
Chapter 6: Intervention design & development 134
6.1 Chapter overview 134
6.2 Chapter aims 134
Section one: Bringing the evidence together 134
6.3 Intervention design: results of stage 1 qualitative analysis 134
6.3.1 Supportive needs 135
6.3.2 Factors influencing information and support needs 135
6.3.3 Key attitudes, values & support seeking tendencies 137
6.3.4 Routes to support 139
6.3.5 Barriers 142
6.4 Intervention design: theory & the evidence base 142
6.4.1 Applying phase I evidence & theory 142
6.4.2 Drawing on the wider evidence base 143
6.4.3 Applying theory & evidence: guidance for developing health interventions 144
Section two: Finalising the intervention design 152
6.5 Design proposal & expert consensus 152
6.5.1 A modified approach to expert consensus 152
6.5.2 Gathering the expert group 153
Section three: Stages of intervention development 157
6.6 Intervention development 157
6.6.1 Content collation & development 157
6.6.2 Symptom monitoring questionnaire development 161
6.6.3 Website design & development 169
6.7 Reflections 170
6.8 Summary 171

Chapter 7: Planning for feasibility evaluation 172
7.1 Chapter overview 172
7.2 Chapter aims 172
7.3 Usability testing 172
7.3.1 Expert testing 173
7.3.2 User-based usability testing 173
7.3.3 Results of user-based usability testing 177
7.3.4 Reflections 184
7.3.5 Summary 184
7.4 Feasibility evaluation: Design and methods 186
7.4.1 Rationale 186
7.4.2 Aims & objectives 186
7.4.3 Study design 187
7.4.4 Study documents 191
7.4.5 Intervention duration and frequency 191
7.4.6 Selection of outcome measures 192
7.4.7 Study methods 195
7.4.8 Reflections 201
7.4.9 Summary 202
Chapter 8: Feasibility Evaluation (I) - quantitative analysis & results 203
8.1 Chapter overview 203
8.2 Chapter aims 203
8.3 Analysis 203
8.3.1 Endpoints 204
8.3.2 Data validation 208
8.3.3 Statistical analysis 208
8.4 Results 209
8.4.1 Recruitment, follow-up and attrition 209
8.4.2 Withdrawals and non-return of outcome questionnaires 213
8.4.3 Baseline characteristics: all participants 215
8.4.4 Intervention engagement: symptom monitoring questionnaire completion 221
8.4.5 Intervention engagement: LIBERATE website analytics 231
8.4.6 Intervention delivery: clinical process measures 233
8.4.7 Integrity of intervention & study procedures 237
8.4.8 Outcome measures 238
8.5 Preliminary interpretations 246
8.6 Reflections 248

8.7 Summary 248
Chapter 9: Feasibility Evaluation (II) - qualitative perspectives & integration of findings 249
9.1 Chapter overview 249
9.2 Aims 249
9.3 Analysis 249
9.3.1 End of study feedback 249
9.3.2 End of study interviews 249
9.4 Results 250
9.4.1 End of study feedback 250
9.4.2 End of study qualitative interviews 258
9.5 Integration of findings 272
9.5.1 The participant 273
9.5.2 The user 275
9.5.3 The patient 276
9.6 Reflections 279
9.7 Summary 280
Chapter 10: Discussion & recommendations 281
10.1 Chapter overview 281
10.2 Aims addressed 281
10.3 Overview of findings 282
10.3.1 Context 282
10.3.2 Mechanism 283
10.3.3 Outcome 284
10.4 Implications 285
10.4.1 Understanding the SBC experience 285
10.4.2 Future research needs & priorities 287
10.5 Strengths and limitations 289
10.6 Recommendations 291
10.6.1 Future research 291
10.6.2 Further and future intervention development 292
10.7 Conclusion 293
References 295

List of tables

Table 2.1 Approaches to the integration of mixed methods 32
Table 2.2 Key actions for the development of complex interventions 41

Table 3.1 Purposive sampling strategy for recruitment of women living with SBC. 45
Table 3.2 Deductive development of the professionals' coding framework. 52
Table 3.3 Purposive sampling strategy: patients (target and actual recruitment). 53
Table 3.4 Patients' baseline clinical data. 53
Table 3.5 Convenience sample of health and charity professionals. 54

Table 4.1 Example electronic database search strategy 82
Table 4.2 Eligibility criteria 83
Table 4.3 Overview of studies 88
Table 4.4 Online and technology-assisted intervention subtypes. 102
Table 4.5 Overview of QoL outcome measures 108
Table 4.6 Overview of psychosocial outcome measures 109

Table 5.1 Re-enforcing self-efficacy: four key influences 126
Table 5.2 Realist matrix of the proposed mechanisms of action & change. 132

Table 6.1 Designing effective ehealth interventions: core features to consider 148
Table 6.2 LIBERATE intervention proposal 154
Table 6.3 Example of clinically reported symptom (CTCAE) translated for use as a patient reported symptom (PRAE) 167

Table 7.1 Health ITUES adapted for the LIBERATE intervention. 176
Table 7.2 LIBERATE usability assessed using the Health ITUES 178
Table 7.3 Usability feedback, actions and future considerations. 180
Table 7.4 Cross-context study objectives for the LIBERATE feasibility evaluation 187
Table 7.5 Matching study design to the intervention context, features and delivery. 187
Table 7.6 Study participant eligibility criteria 196

Table 8.1 Randomised study arm allocation using minimisation: balance across groups. 212
Table 8.2 Baseline sociodemographic characteristics: comparing RCT and sub-study. 216
Table 8.3 Baseline computer usage characteristics: comparing across studies 217
Table 8.4 Baseline clinical characteristics: comparing across studies 219
Table 8.5 LIBERATE website analytics: number and proportion of unique page views. 232
Table 8.6 Attendances outside of consultation: comparing across study arms. 233
Table 8.7 Contacts outside of consultation: comparing across study arms. 233
Table 8.8 Missing item data across outcome measures. 239
Table 8.9 Pre and post-test FACT-B scores across studies. 239
Table 8.10 Pre and post-test descriptive profiles of EQ-5D-5L scores across studies 242
Table 8.11 Pre and post-test CBI-B total scores across studies 244
Table 8.12 Pre and post-test SEMCD-6 total scores across studies. 245
Table 8.13 Mean change scores across outcome measures for RCT participants. 245
Table 8.14 Estimations of effect size 246

List of figures

Figure 1.1 Overview of thesis 28

Figure 2.1 Overview of the LIBERATE project 30
Figure 2.2 Overview of research design applying a multi-phase MMMR approach 33
Figure 2.3 Key stages of the MRC framework 39

Figure 3.1 Methodological steps for reflexive thematic analysis 51
Figure 3.2 Thematic map: The perspective of women living with SBC 67
Figure 3.3 Thematic map: The perspective of health & charity professionals 73
Figure 3.4 Thematic map: Integrating the patient & professional perspective. 75

Figure 4.1 PRIMSA flow diagram of study identification & selection 85
Figure 4.2 Risk of bias assessment applying the Cochrane Collaboration's tool (RCTs) 87
Figure 4.3 Model of online & technology-assisted intervention delivery. 103

Figure 5.1 The Self-care Spectrum (adapted from the Self-Care Forum) 120
Figure 5.2 The Middle Range Theory of Self-Care of Chronic Illness: Self-care behaviours 123
Figure 5.3 Bandura's Social Cognitive Theory: Reciprocal determinism 126
Figure 5.4 Proposed logic model for the LIBERATE intervention 131

Figure 6.1 Supportive needs of women living with SBC 136
Figure 6.2 Barriers to the access and provision of support in SBC 142
Figure 6.3 The LIBERATE IHCA: Target population-centred, evidence and theory-based approach bridged through expert consensus 156
Figure 6.4 Mapping core areas of supportive need to the LIBERATE intervention 157
Figure 6.5 Example web page from the 'How to read the evidence' section of LIBERATE 159
Figure 6.6 An extract from the collection of case studies, available for users to download 160
Figure 6.7 The established QTool/PROMPT/EPR system 163
Figure 6.8 Example of symptom monitoring questionnaire navigation 163
Figure 6.9 Example of questionnaire item and rating 164
Figure 6.10 Example of self-management advice summary 164
Figure 6.11 Example of users' display of results 165
Figure 6.12 Example of clinicians' display of results 165
Figure 6.13 Key differences between clinically integrated & independent monitoring versions of the symptom monitoring component 169
Figure 6.14 Key design features of the LIBERATE website 170

Figure 7.1 Situating outcome measures in the Context, Mechanism, Outcome realist evaluation framework 193
Figure 7.2 The LIBERATE Feasibility Evaluation: RCT and single arm sub-study. 199

Figure 8. 1 CONSORT diagram of recruitment and study involvement: LIBERATE feasibility RCT & sub-study.....210
Figure 8.2 LIBERATE feasibility RCT: Number and reasons for decline. 211
Figure 8.3 LIBERATE feasibility RCT: Rate of recruitment 211
Figure 8.4 LIBERATE feasibility sub-study: Rate of recruitment.....213
Figure 8.5 Number of symptom monitoring questionnaires completed (RCT).....221
Figure 8.6 Number of symptom monitoring questionnaires completed (sub-study). 222
Figure 8.7 Frequency and type of alerts generated across the 12 week study period 223
Figure 8.8 Proportion of algorithms activated across groups (RCT).....224
Figure 8.9 Proportion of algorithms activated across groups (sub-study).....224
Figure 8.10 Type and frequency of reported symptoms (RCT). 226
Figure 8.11 Severity of reported symptoms (RCT). 227
Figure 8.12 Frequency of reported symptoms (sub-study).....229
Figure 8.13 Severity of symptoms reported (sub-study).....230
Figure 8.14 Swimmer Plot of treatment & disease related events (RCT). 235
Figure 8.15 Kaplan Meier survival estimate for intervention & waiting list control participants 236

Figure 9.1 Reported ease of use of the LIBERATE website (RCT, n=7) 251
Figure 9.2 Reported ease of use of the LIBERATE website (sub-study, n=14). 251
Figure 9.3 Frequency of use (RCT and sub-study).....252
Figure 9.4 Content missing from LIBERATE website (RCT and sub-study) 252
Figure 9.5 Reported usefulness of website components (RCT, n=7). 253
Figure 9.6 Reported usefulness of website components (sub-study, n=14).....253
Figure 9.7 Frequency of symptom monitoring (RCT and sub-study).....254
Figure 9.8 Time taken to complete questionnaires.....254
Figure 9.9 Ease, relevance & usefulness of symptom monitoring (RCT, n=7).....255
Figure 9.10 Ease, relevance & usefulness of symptom monitoring (sub-study, n=14).....255
Figure 9.11 Reported use of symptom results in the consultation setting (RCT, n=7). 256
Figure 9.12 Reported use of symptom results in the consultation setting (sub-study, n=14)…256
Figure 9.13 Perceived value of clinicians reviewing symptom results (RCT and sub-study)……256
Figure 9.14 Time taken to complete study outcome questionnaires (RCT and sub-study). 257
Figure 9.15 Relevance of outcome questionnaires (RCT and sub-study).....257
Figure 9.16 Recommendation of website (RCT and sub-study) 257
Figure 9.17 Thematic map: core themes and surrounding sub-themes 259

List of abbreviations

ADL	Activities of Daily Living
AE	Adverse Event
CBI-B	Cancer Behaviour Inventory – Brief
CNS	Clinical Nurse Specialist
CTCAE	Common Terminology Criteria for Adverse Events
EPOCS	Electronic Patient reported Outcomes from Cancer Survivors
EPR	Electronic Patient Record
ePROMs	electronic Patient Reported Outcome Measures
EQ-5D-5L	EuroQoL Group – 5 dimensions, 5 levels
EQ-VAS	EuroQoL Visual Analogue Scale
ER	Oestrogen receptor
eRAPID	electronic patient self-Reporting of Adverse-events: Patient Information and aDvice
FACT-B	Functional Assessment of Cancer Therapy – Breast
GCM	Generic Choice Model
GP	General Practitioner
HER2	Human Epidermal Growth Receptor Factor 2
HRA	Health Research Authority
HRQOL	Health Related Quality of Life
IHCA	Interactive Health Communication Application
IOM	Institute of Medicine
LIBERATE	Living better with advanced breast cancer
LTHT	Leeds Teaching Hospitals Trust
MAB	Monoclonal Antibodies
MBC	Metastatic Breast Cancer
MMMR	Multiple and Mixed Methods Research
NCI	National Cancer Institute
PBC	Perceived Behavioural Control
PCOR	Patient Centred Outcomes Research Group
PICOS	Population, Intervention, Comparator, Outcome, Study design
PIS	Patient Information Sheet
PPE	Personal Protective Equipment
PPM+	Patient Pathway Manager
PR	Progesterone receptor
PRAE	Patient Reported Adverse Event
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta Analyses
PRO / PROM	Patient Reported Outcome / Patient Reported Outcome Measure
QoL	Quality of Life
RCT	Randomised Controlled Trial
REC	Research Ethics Committee

SBC	Secondary Breast Cancer
SEMCD-6	Self-Efficacy for Measuring Chronic Disease – 6 item scale
SMI	Small Molecule Inhibitor
SMS	Self-management Support
TA	Thematic Analysis
TPB	Theory of Planned Behaviour
TRA	Theory of Reasoned Action
WL	Waiting List

For outcome measures outlined within chapter 4, tables of abbreviations are provided.

Chapter 1: Introduction

1.1 Background

1.1.1 Cancer & survivorship: dual challenges for global health

The global burden of cancer is growing at a rapid rate. In 2020, approximately 19.3 million people were diagnosed with cancer across the world. Over the next 20 years, this is projected to increase by almost 50%, reaching an estimated 28.4 million cases worldwide.[1] Furthermore, the number of people living with and surviving beyond a cancer diagnosis is on the rise. By 2040, there will be approximately 5.3 million cancer survivors in the UK, almost doubling from the estimated 2.9 million in 2020.[2] Such a significant increase can be attributed to ongoing treatment advancements, leading to steady improvements in the rate of cancer survival, as well as rising life expectancy across the world's growing populations.[1, 2]

Whilst this situation is a triumph of clinical and scientific advancements, it is also reflective of a newer, evolving challenge for healthcare systems across the world.[3] By definition, a person is considered to be a cancer survivor from the point of diagnosis, throughout their treatment and beyond.[4] For many, 'beyond' signifies the cessation of active treatment, after which the management of ongoing symptoms, lasting or developing 'late effects' of treatment and psychosocial adjustments in the lives of the individual, and those around them, take precedence. For others, this reflects the ongoing management of disease, which may be controlled to varying extents and for varying amounts of time. Either way, cancer survivorship is an ongoing trajectory which continues to the end of life.[5, 6] The National Cancer Institute (NCI) captures this in their definition of survivorship as extending from diagnosis and treatment 'through the balance of an individual's life', whilst also recognising the impact on family, loved ones and carers.[6, 7] The ongoing and complex needs of the many more people who are surviving with or beyond their cancer therefore places significant demands on healthcare services seeking to adequately support them.[8]

1.1.2 Survivorship in advanced cancer

'Advanced' cancer describes the spread of cancerous cells, either to the tissues or lymph nodes close to the original tumour (stage III), or to a more distant area of the body ('metastatic' or stage IV).[9] Though a cure can rarely be achieved by this point, a range of treatments are able to slow disease progression and control symptoms. As such, more and more patients are living longer with what is referred to as 'incurable yet treatable' cancer.[10, 11] However, this increasingly chronic disease trajectory brings a complex array of supportive care needs experienced over the longer term.[12-14]

Over the past several decades, the field of cancer survivorship research has proliferated, in part sparked by the USA's Institute of Medicine's (IOM) pivotal report '*From cancer patient to cancer survivor: lost in transition*'.[3, 15] In the UK, the National Cancer Survivorship Initiative (led by Macmillan Cancer Support, the Department of Health and other key stakeholders) paved the way for significant progress, aiming to identify and better address the diverse needs of those living with and beyond cancer, and outlining key shifts in culture, care and support which would facilitate this.[16] Yet, whilst major progress has been made in understanding and addressing the needs of cancer survivors, the focus has largely been on those managing the multitude of challenges and late-effects faced in life *after* treatment.[17, 18] In advanced stage disease, to survive is to continue living *with* cancer until it is no longer treatable. Individuals experience many of the issues captured under the more traditional conceptualisation of a 'cancer survivor', whilst also dealing with those of the 'cancer patient'. Late effects of past treatments may develop alongside acute side-effects of current treatment. The psychological challenges of living with cancer and adapting to a changing sense of self are also coupled with the need to come to terms with death and dying.[18, 19] As Park and Rosenstein reflect, advanced cancer patients can become lost in the space between survivorship programmes promoting a move 'beyond' cancer, focused on healthy living and monitoring, and those looking towards advance care planning and end of life needs.[18] Indeed, those living with advanced cancer constitute what Mayer and colleagues refer to as the 'overlooked' survivors.[17] The current challenges and shortfalls in addressing this more nebulous phase of survivorship are evidenced by the many unmet needs of those living with advanced cancer.[20]

1.1.3 Secondary breast cancer

Female breast cancer represents the greatest proportion of the global cancer burden. With 2.3 million cases diagnosed worldwide in 2020 alone, it is the most frequently diagnosed of all cancers and the leading cause of cancer-related death in women.[1] Despite significant steps forward in the treatment of primary breast cancer over the past 20 years, the risk of relapse remains considerable. In approximately 20-30% of cases, cancerous cells from the primary tumour in the breast will spread (or 'metastasize') to other regions of the body, usually the brain, bones, liver or lungs.[21, 22] This is an advanced and incurable stage of disease, known as secondary, metastatic or stage IV breast cancer.[23] Furthermore, in approximately 10% of cases, breast cancer has already progressed to this advanced stage by the time it is diagnosed. This is referred to as 'de novo' secondary breast cancer.[24] The presence and progression of metastases (new sites of cancerous cells) can cause a host of symptoms, depending on where in the body they have travelled to, as well as pain, insomnia, fatigue, depression and declining physical function more generally.[25]

In the UK alone, approximately 35, 000 women are living with secondary breast cancer (SBC).[26] However, this incidence remains an estimation; UK hospital trusts have only recently started routinely recording SBC diagnoses, an oversight which is mirrored across global healthcare settings.[26, 27] Prognosis for these women is equally uncertain. Reports of steadily improving survival rates in certain subtypes of SBC can in part be related to breakthroughs in our biological understanding of tumours, allowing for increasingly targeted, novel therapies, able to prolong life and alleviate symptoms. This has created a shifting and increasingly complex environment for patients and physicians to navigate, with evolving disease trajectories, side effects and toxicities to manage and weigh up.[28, 29] However, median survival remains at 2-3 years post diagnosis and advancements in the SBC setting very much lag behind those seen for early breast cancer.[24, 30, 31] Whilst the 5 year survival rate for primary breast cancer ranges from 86-99%, for those with distant metastases this remains at just 29%.[32]

1.1.4 Treating secondary breast cancer

In SBC, the goals of treatment are therefore to slow the spread of disease, control symptoms and achieve the best possible quality of life (QoL).[33] Some women may respond well to a particular treatment for months or even years, whilst for others the response may be shorter lived. With each failed or diminished response, there are fewer treatment options in reserve and toxicities can accumulate over time.[21] Patients' treatment pathways are therefore complex, often multi-faceted, and very much tailored to the individual and their cancer. Management options are dependent upon a range of factors, including the cancer's molecular and anatomical characteristics, the patient's past treatment history, their level of response and the symptoms which are currently affecting them.[21, 29]

1.1.4.1 Selecting the most appropriate treatment

Breast cancer tumours can be categorised into subtypes relating to the presence or absence of receptor proteins on their cell surfaces. These molecular markers ultimately guide treatment decisions, as they determine which therapies the cancer will respond to.[34]

The human epidermal growth factor receptor 2 (HER2) is a protein, coded for by the HER2 gene, which is present on all breast cells and is involved in normal cellular growth and repair. An estimated 15-20% of patients diagnosed with breast cancer have an excess or 'overexpression' of this protein, causing uncontrolled growth and division of cells. The resulting breast tumours are therefore referred to as HER2+ and are associated with more aggressive disease progression and poorer prognosis.[34] However, the excess HER2 receptors are an effective target for treatment and have been the focus of major recent breakthroughs, leading to dramatically improved survival for this subgroup of patients.[29, 35]

Normal breast cells also have receptors on their surfaces which respond to the female hormones oestrogen (ER) and progesterone (PR). When present on cancerous breast cells, these receptors allow the hormones to stimulate growth. This occurs in approximately 70% of cases and is referred to as hormone-sensitive or hormone receptor positive breast cancer (HR+ or ER/PR+).[36] They carry a better prognosis than hormone receptor negative cancers since they tend to be less aggressive and there are more treatment options available.[37] Where both receptors (ER, PR) are absent, and the HER2 protein is not over-expressed, the breast cancer is referred to as 'triple negative'. The absence of these potential treatment targets (occurring in an estimated 15% of cases) means that viable therapeutic options are significantly more restricted. This, combined with the aggressive nature of triple negative breast cancer, means that prognosis is usually poor.[37, 38] Whilst emerging treatments offer the potential for improved disease control in this subgroup, survival remains limited.[38]

1.1.4.2 Treatment options

Pharmacological treatments for SBC can be broadly categorised into three groups: chemotherapy, hormone or endocrine therapy and targeted or biological therapies. The needs and experiences of women treated within and across each of these groups of treatments will be distinct. The latter encompasses many of the recent treatment advances which are steadily changing the landscape of SBC management.

(i) Chemotherapy

Chemotherapy is a family of anti-cancer drugs which work in different ways to destroy rapidly dividing cancer cells. Because they are delivered to the whole body (either directly into the bloodstream or taken in tablet form), they also affect normal cells, which may lead to a wide range of side-effects.[21, 33] A patient's response to treatment must, therefore, be significant enough to outweigh the risk of side-effects, toxicity and (where delivered intravenously and therefore requiring hospital attendance) the inconvenience for patients. Side-effects can include nausea and vomiting, diarrhoea, mouth ulcers, soreness of the hands and feet, loss of hair and risk of infection.[39] Patients are therefore regularly reviewed by their oncologist and ongoing self-monitoring for signs of toxicity is vital. In the SBC setting, chemotherapy may be prescribed alone or in combination with other treatments, at varying doses and regimens, to alleviate symptoms and limit disease progression. However, response to treatment (or 'chemosensitivity') is frequently short-lived.[40]

(ii) Hormone or endocrine therapy

Hormone or endocrine therapies work by targeting the hormone receptors, meaning this therapeutic avenue is open only to those with hormone-responsive (ER+/PR+) breast cancers.[41]

They may be given alone or alongside other treatments and act to reduce the level of oestrogen in the body, preventing it from stimulating cancer growth. The choice of drug largely depends on whether the woman is pre or post-menopausal, since some target ovarian oestrogen (produced prior to menopause) whilst others block oestrogen production that occurs elsewhere in the body (targeted post menopause). Their use can delay the need for toxic chemotherapy, and patients take these medications as tablets at home or as an injection in clinic.[21, 33] They are regularly reviewed, though less frequently when responding well to treatment and managing side-effects. For some women, however, side-effects mimicking menopausal symptoms (such as hot flushes, night sweats and aching joints) may be extremely debilitating and difficult to manage, risking poor compliance.[33, 42]

(iii) Targeted & biological therapies

The advent of targeted therapies has transformed the landscape of cancer treatment and paved the way for increasingly personalised medicine, allowing patients to receive treatment which targets their specific cancer. Furthermore, in SBC, they offer additional and much needed treatment options where women have become resistant to other lines of therapy.[29, 43] These novel drugs control the spread of cancer by blocking specific pathways and cellular processes which allow cancerous cells to proliferate.[43] Monoclonal antibodies (MABs) are one group which work by targeting specific proteins, such as HER2. They are harnessed in a number of ways in cancer treatment; some block the cellular signalling which causes cancer cells to divide whilst others bind to the cancer cells to assist the immune system in locating them.[44] Another form, known as 'conjugated' MABs, act as vehicles, carrying drugs or radioactive substances (radiotherapy) directly to the cancer cells.[43, 44] Small molecule inhibitors (SMIs) are an emerging subgroup of targeted treatments which interfere with specific small molecules, halting disease progression by causing cellular injury and programmed cell death. They are much more targeted than the larger macromolecules (such as MABs) and therefore lead to fewer side-effects. SMIs are also easier to administer, since they are usually taken orally as opposed to being injected.[45, 46] An even more recent advancement is the use of immunotherapy in SBC. Similar to the targeted therapies, these drugs work by targeting specific proteins on the breast cancer cells (so called 'checkpoints') which allows the body's immune system to locate and destroy them.[47] Though targeted therapies and immunotherapies lead to much fewer side-effects than systemic treatments (chemotherapy and hormone therapy), the potential for serious toxicity (e.g. problems relating to the lungs, heart, liver and blood clotting) means that women will be seen in clinic frequently.[47, 48]

(iv) Symptomatic treatment

For some women, diminished efficacy or increased side-effect burden may mean that the focus of their management is on improving symptoms, as opposed to slowing the spread of cancer. Others may have planned breaks to allow time for recovery between cycles of treatment, where side-effect management becomes the focus.[33] For example, anti-emetics may be given to treat nausea and a course of radiotherapy may be prescribed to relieve pain. Similarly, a type of drug known as a bisphosphonate is prescribed in women with bone metastases to lessen the likelihood of fractures and to control pain.[25]

1.1.5 The individual and the SBC experience

Whilst the repertoire of treatments for SBC has clearly expanded, with multiple new drugs made available in recent years, this does not directly translate to improved prognosis for all women living with SBC.[27] Though it is increasingly likened to a chronic disease, greater survival has largely been confined to the specific subtypes targeted by treatment advancements (hormone positive and HER2 positive tumours).[49-51] Indeed, as well as tumour subtype, a vast array of factors influence women's response to treatment and, as a result, their prognosis. This includes a woman's age, ethnicity, functional ability (referred to as 'performance status'), the number and location of their metastases, previous treatments (treatment 'exposure') and the amount of time between primary breast cancer and the diagnosis of metastasis ('metastasis free interval').[52] Just as response to treatment varies, so too does the nature of the disease in terms of how it manifests and, ultimately, progresses. Collectively, this results in great diversity in how SBC is experienced.[53, 54]

Kida et al emphasise the heterogeneity of SBC, describing distinct patterns of disease progression which patients may experience across varying trajectories.[53] The chronic disease-like trajectory is captured in what they refer to as the 'smouldering' pattern of SBC, characterised by slow progression, prolonged periods of symptom control and survival exceeding 5-10 years post diagnosis. The 'gradual' trajectory follows a pattern of gradually progressive symptoms and disease; the rate of disease progression increases over time. In contrast, patients experiencing SBC across a 'rapid' trajectory have progressive disease from the point of diagnosis. Symptoms are multiple and severe and prognosis may only be several months. Patients with 'de novo poor condition' experience this rapid progression over an even shorter trajectory and their health has usually already significantly deteriorated at diagnosis. Most often, these patterns of progression fluctuate between 'acute' and 'stable' phases. In an acute phase, a patient will experience a high burden of frequent or changing symptoms, whilst in a stable phase, symptoms are well-managed and of a comparatively low burden.[53]

1.1.6 QoL and supportive needs

Central to all of these varying survivorship experiences is the need for quality of life (QoL) to be both prioritised and maintained from diagnosis to the end of life.[24] QoL is a multi-dimensional construct which seeks to capture an individual's own appraisal of their well-being.[55] Many overlapping definitions exist yet, in essence, they all refer to the subjective evaluation of functioning across many interrelated domains: physical, psychological, disease and treatment related, social, cognitive, sexual and spiritual.[55, 56]

Despite significant steps forward in treatment and, in some cases, prognosis, QoL for women living with SBC has improved relatively little over the past decade.[54, 57, 58] Gains made in available therapeutic options, improved response to treatment and increased survival often come at the price of toxicity related side-effects and challenges to normal daily living.[24] Persistent pain, fatigue, nausea, headaches and insomnia are some of the day-to-day realities for many patients, often experienced alongside a host of treatment related side-effects, as well as the added psychological implications of prognostic uncertainty.[14, 59, 60] Yet frequently these remain poorly controlled and may not routinely be discussed, impacting upon patients' QoL.[61, 62] Wider-reaching, psychosocial concerns relating to work, finances, family and relationships are also hugely significant and can have a major impact on women's social and emotional well-being. Though increasingly recognised, many of the identified psychosocial and supportive needs of women living with SBC remain unmet.[58, 63-65] It comes as no surprise, therefore, that 80% of SBC patients surveyed in the UK identified QoL as the area most in need of prioritisation and improvement.[63, 66]

1.1.7 The patient's perspective

Whilst the success of a treatment can be gauged objectively through clinical markers, the patient's subjective experience must be harnessed when looking to assess their QoL. The use of patient reported outcomes (PROs) is key to this endeavour.[67] By definition, a PRO is an assessment of health status from the patients' perspective, which is made without the interpretation or input of a health professional or anyone else.[68] A patient reported outcome measure (PROM) is a self-completed questionnaire or tool designed to capture this assessment.[69] The use of PROMs has evolved in recent years, in both clinical trials and in clinical practice, reflecting a shift in focus from survival benefit alone to the impact of cancer and treatment on QoL.[69, 70] In SBC, capturing an accurate assessment of QoL is crucial, not only to ascertain whether women's supportive needs are being met, but also to recognise where the burden of treatment may far outweigh the potential benefit.[71] The use of PROMs also supports healthcare professionals to understand the impact of side-effects on patients' QoL and to therefore make more tailored management decisions. In this way, shared

communication and collaborative management are fostered.[72, 73] In fact, the routine use of PROMs in clinical practice has been proven to result in improved QoL and emotional well-being for patients.[73]

1.1.8 The shift towards self-management

Increasingly widespread use of PROMs has also evolved in line with a shift in focus towards supporting patients' self-management of cancer beyond the clinical setting.[74]

Whilst oncologists continue to review patients falling into the identified treatment groups with varying frequency, they may not be best placed to identify longer-term issues and supportive needs as treatment related discussions may take precedence. Clinical Nurse Specialists (CNSs, who may also be referred to as breast care nurses), though ideally placed for this role, are often in short supply. The role of GPs in the routine follow-up of patients with cancer, in contrast to their involvement in specialist referral and later palliative stages, is ill-defined. [75-77] Cumulatively, this means that clinical and supportive management of women with SBC, just as the trajectory of the disease itself, can vary significantly. This, combined with the potential for some treatments to be largely delivered away from the healthcare setting, means that the onus is increasingly on the patient (who may or may not have the support of family and wider social networks) to monitor and manage their cancer at home, know when to seek help, and cope with the wider, ongoing psychosocial impacts.[74, 78]

To do so, adequate support and resources for self-management are essential. However, self-management is much more firmly established across other chronic diseases such as diabetes, hypertension and arthritis; there is a breadth of evidence for its efficacy in lowering symptom burden, healthcare utilisation and costs, and improving patients' QoL.[79, 80] Self-management support (SMS) for cancer patients, whilst evolving, lags behind.[74, 80] SMS refers to education and supportive interventions, generally delivered or facilitated by healthcare professionals, which aim to improve patients' confidence and skills in the management of a health condition. This usually encompasses ongoing assessment of issues, review of progress, goal setting and support to problem-solve.[74, 81, 82] Calling for improved SMS in cancer, Howell et al highlight strong evidence for its efficacy in addressing a range of physical and psychosocial needs and improving QoL.[74, 83-85] Given these issues will be experienced across an extended trajectory in advanced cancer, whether cyclical or unremitting, the role for SMS is perhaps even more significant.[86] However, the burden of face-to-face delivery of SMS is too great for over-stretched services managing an ever-increasing population of cancer survivors.[87] Just as the internet and technology has supported more widespread use of PROMs, the potential for online and remote delivery of SMS is therefore increasingly being harnessed.[88-90]

1.1.9 The internet and 'connected health'

In today's society, internet use is becoming ever more widespread. In 2020, 92% of adults in the UK reported recent online activity.[91] It is no surprise, therefore, that online sources of health-related information and support are becoming increasingly familiar, accepted and, indeed, sought after.[92, 93] As well as representing a more cost-effective and efficient alternative to resource intensive models of face-to-face follow up and support, the internet is a more widely accessible, convenient and largely anonymous, safe space. As such, it is the chosen source of health information and support for many patients.[94-96] Most recently, the COVID-19 pandemic intensified existing barriers and constraints to the delivery of adequate follow up and support, precipitating an even greater shift towards the internet and technology.[97-99]

Looking to the context of cancer, the internet has steadily grown to become a vital source of information and support for survivors.[95] Indeed, evidence is accumulating for online self-management interventions able to address the significant supportive needs of patients living with cancer in the longer-term.[100-102] When emphasising the need for improved access to information and supportive services, the Metastatic Breast Cancer Working Advocacy Group identified the internet as a key platform.[103] A breadth of recent advancements have led to the development of systems for remote symptom monitoring, harnessing the internet as a platform for the collection of electronic PROMs (ePROMs) and the delivery of increasingly tailored SMS. So called 'connected' health (the integration of technology into the care pathway) has evolved alongside this, allowing patients to be closely yet remotely monitored, with clinicians able to review their symptoms and support their management from afar.[104] Trials of such systems (remote symptom monitoring +/- varying degrees of SMS) have evidenced a range of positive results, from greater control of symptoms, less symptom related distress and improved physical well-being, to reduced contact with healthcare services and prolonged survival.[105-109] The eRAPID complex intervention ('Electronic patient self-Reporting of Adverse events: Patient Information and aDvice'), developed and trialled within the Patient Centred Outcomes Research group (PCOR) at the University of Leeds, is a pivotal example of this growing area of research. This electronic platform allows patients to report symptoms, with pre-defined algorithms generating alerts to clinicians when medical input is urgently required. A range of information, gathered on one website, is combined with symptom-responsive, tailored self-management advice. Subsequent integration with the electronic patient record (EPR) in Leeds allowed for real-time assessment of and response to ePROMs by clinicians.[108, 110] This has paved the way for greater consideration and communication of QoL in everyday oncology practice.[73, 111-113] The guiding role of eRAPID in the current research will be explored in greater detail in subsequent chapters.

1.2 Research rationale

This research, funded by Breast Cancer Now, seeks to bridge the widely identified gaps in the availability of information and support for women with SBC, through the development and evaluation of an online supportive intervention. In doing so, it will harness the growing body of evidence for both internet-based self-management of long-term conditions and the use of electronic symptom monitoring as a means of better assessing and supporting patients' QoL.[73, 112, 114, 115] Successes in the implementation of ePROM monitoring combined with online self-management will be built upon, expanding and tailoring this approach to address the unmet supportive needs and QoL concerns of some of the 35, 000 women living with SBC across the UK.[26] This alternative route to support could also offer a potential practical and cost-effective solution for health services needing to manage increasing numbers of women living longer with SBC.[87]

1.2.1 Terminology

A lack of understanding and awareness of SBC is often compounded by confusion relating to differing terminology. Whilst 'metastatic breast cancer' (MBC) is more commonly accepted across the scientific and clinical literature, throughout this thesis, the term 'secondary breast cancer' (SBC) will be applied. This mirrors the terminology used by Breast Cancer Now and is intended to reflect the patient-centred focus of this research. Within their 2019 'Unsurvivors' campaign, Breast Cancer Now surveyed over 2000 women living with SBC and found that 'secondary' was the preferred terminology for the highest proportion of women (40%).[26]

1.3 Aims

Overall, this research sought to support women in *'Living better with advanced breast cancer'.* The aims of this this thesis are therefore to:

1. Explore the issues affecting QoL in women living with SBC.
2. Outline the development of an online complex intervention designed to address the supportive needs (and improve the QoL) of women living with SBC.
3. Evaluate the feasibility and acceptability of this online intervention across two contexts:
   - Clinically integrated: self-management activities directly supported through clinician involvement and close ties to the clinical setting.
   - Independent self-monitoring: guided self-management activities conducted independently in the community.

Though ultimately guided by evidence, theory and the patient perspective, in the earliest stages of the research, it was anticipated that the LIBERATE intervention would combine:

- **Collection of self-reported symptoms and side-effects**
- **Tailored self-management advice**
- **Information & signposting to both local and national support services and resources**

1.4 Overview of thesis

Figure 1.1 Provides an overview of the LIBERATE research aims, associated research activities and the corresponding thesis chapters in which they are outlined.

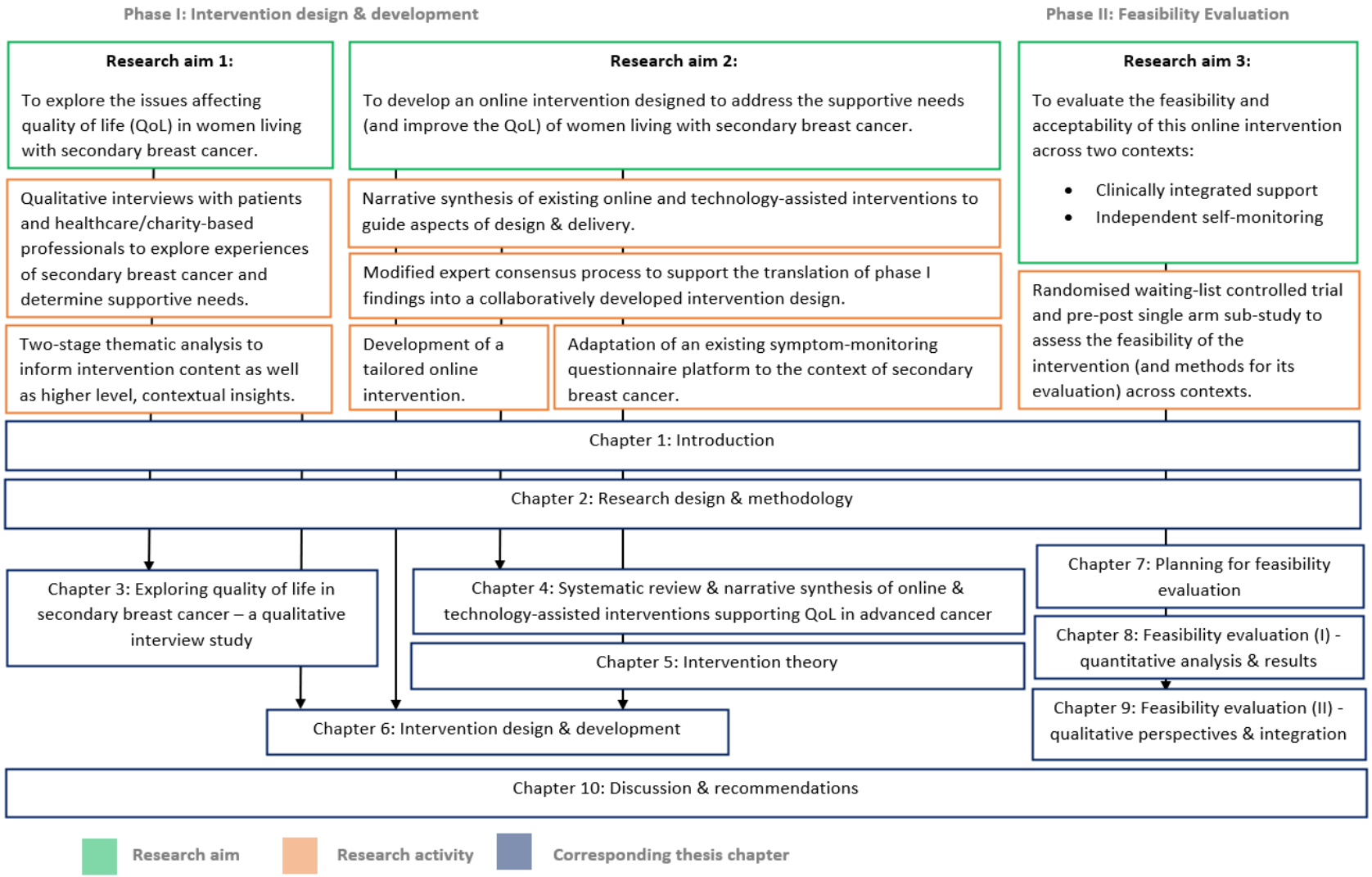
1.4.1 Phase I

Chapter 2 outlines the paradigmatic and methodological decisions which shape the LIBERATE research, grounding these in the context of complex intervention development and evaluation, and introducing the foundational work of the eRAPID programme of research. Chapters 3 and 4 outline the dual strands of research conducted as part of phase I, seeking to understand both the lived experiences (a qualitative interview study, chapter 3) and the current evidence base (a systematic review of online and technology assisted interventions in advanced cancer, chapter 4) which went on to guide the development of an online intervention tailored to context of SBC. Having gathered both the evidence and the person-based perspective, chapter 5 looks to integrate theory in the development of the LIBERATE intervention. Guided by principles of realistic evaluation, a programme theory encompassing the constructs of both self-care and self-efficacy is outlined. Taking these findings forwards, chapter 6 details their translation into the design and development of the LIBERATE intervention, following a target population-centred, evidence and theory-based approach.

1.4.2 Phase II

Moving into phase II, chapter 7 outlines the design of a feasibility evaluation which takes a dual approach, encompassing a randomised controlled trial conducted in the clinical context and a single arm sub-study conducted via online channels. Chapters 8 and 9 detail the range of results gathered across these settings, applying mixed methods analysis. Finally, chapter 10 provides an overview of the research findings and implications, setting out recommendations for future further development and evaluation of online supportive interventions in the context of LIBERATE and SBC more widely.

Figure 1.1 Overview of thesis



Chapter 2: Research design & methodology

2.1 Chapter overview

This chapter will describe the core methodology, providing an overview of the two key phases of research and discussing the context and framework which will underpin the development and evaluation of a complex intervention.

Each subsequent chapter will explore the methods applied as part an overall multiple and mixed methods research (MMMR) approach in greater detail.

2.2 Chapter aims

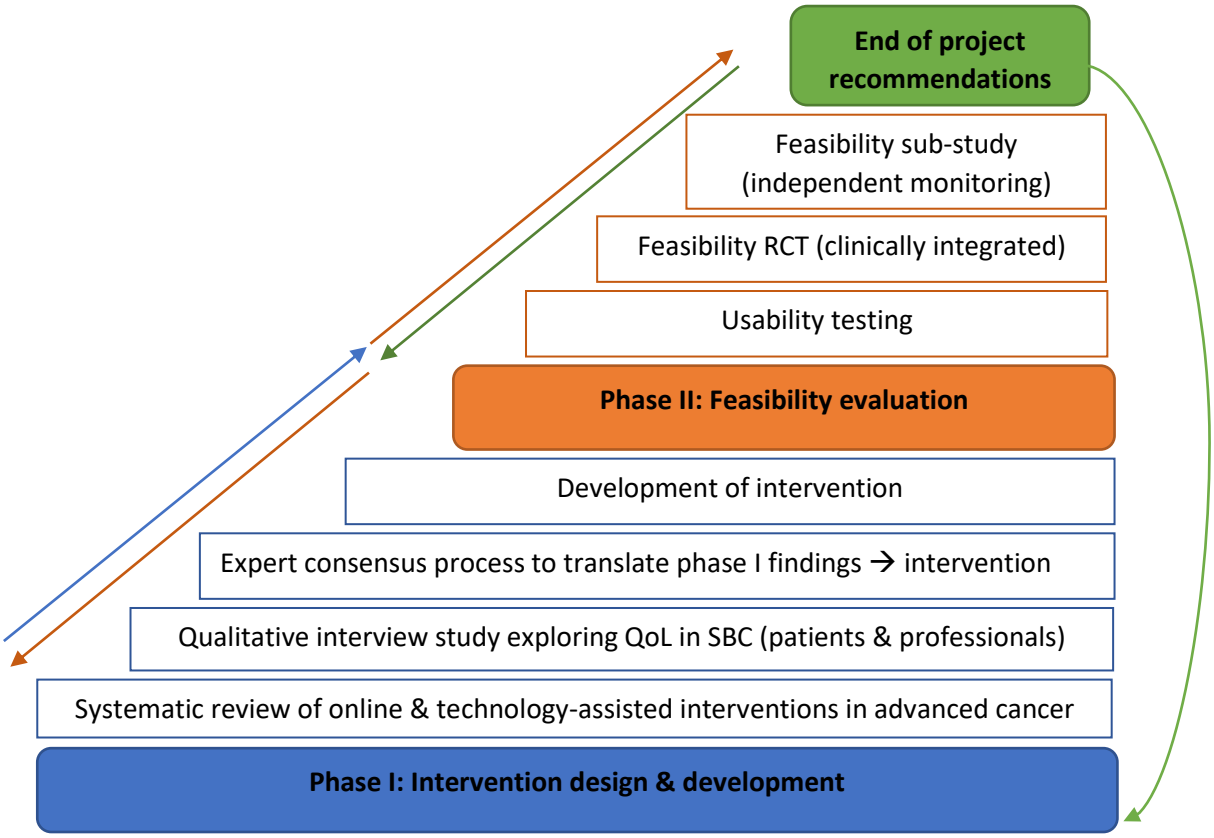
- To provide an overview of the design and context of the LIBERATE project.
- To explore its philosophical underpinnings & core methodological approach.

2.3 Project overview

The LIBERATE research project is composed of two distinct phases, guided by the Medical Research Council's (MRC) Framework for Developing and Evaluating Complex Interventions.[116, 117] In brief, these are interventions comprising multiple, interacting elements.[116] Their defining features and application to health research will be discussed in greater detail throughout this chapter. In the context of LIBERATE, a range of evidence gathered in phase I guided the design and development of a complex intervention, the feasibility of which was evaluated within phase II. Whilst phase I sought to understand and develop solutions to address the issues and supportive needs which impact upon QoL in SBC, phase II looked to lay the groundwork for rigorous evaluation and offer recommendations for potential future implementation of the proposed intervention across the clinical and community setting.

This multi-stage, multi-phase project required similarly diverse research methods, situated within a philosophical framework which was able to accommodate such complexity. Each of the two phases comprised a number of key research activities, summarised in Figure 2.1. As shown by the multi-directional arrows, it was anticipated that the various stages would iteratively inform one another.

Figure 2.1 Overview of the LIBERATE project



2.4 Multiple and mixed methods research

Across phase I intervention development, a range of qualitative methods were applied with the collective aim of generating knowledge and understanding surrounding the lived-experiences and supportive needs encountered in SBC (and advanced cancer more widely). However, quantitative analytic methods were also pivotal in informing the evaluation of this intervention across phase II, supported by supplementary qualitative insights.

Collectively, the research was conducted using multiple and mixed methods research (MMMR) inquiry. This approach has increasingly been applied across diverse fields of health research over the past several decades, in order to answer multi-faceted research questions.[118] It has therefore lent itself well to the development and evaluation of complex health interventions.[119]

With growing acceptance of qualitative methods throughout the 1980s and beyond came a surge in research applying both qualitative and quantitative data synergistically.[120] From this, the rapidly growing field of MMMR emerged. Yet, in the decades since, confusion and controversy remain.[121] Confusion stems from differing opinions, applications and iterations of 'mixed methods' and 'multiple methods', whilst controversy relates to what some see as the clashing epistemological stances of the once distinct qualitative and quantitative paradigms.[118]

To justify and provide further context to the research design and methodological decisions central to the LIBERATE project, both of these aspects will be explored further.

2.4.1 Defining mixed versus multiple methods

Put simply, a 'mixed methods' approach involves the collection, analysis and interpretation of both qualitative and quantitative data within a single or multi-phase study.[122] Proponents often stipulate that the hallmark of a true mixed methods approach is the successful integration of divergent methods throughout the research process.[118, 123] Some are keen to distinguish this from a 'multi-methods' approach, whereby qualitative and quantitative methods may be used in parallel, or sequentially, but their integration does not occur until the concluding phases.[121]

Such subtleties have been captured in the emergence of increasingly distinct definitions and the growing acceptance of these separate yet closely related approaches.[118] Further clarification is given in reference to the type of data; whilst *mixed* methods involves the combination of qualitative and quantitative data, *multi*-methods research may apply multiple forms of qualitative methods (e.g. interviews, case studies, ethnographic studies etc.) to generate a range of qualitative data, or multiple forms of quantitative methods (e.g. questionnaires/surveys, experimental research etc.), leading to various quantitative data sets.[124] In other words, whilst a mixed-methods study must, by definition, involve qualitative and quantitative research, multi-methods research encompasses more diverse methodological combinations.[125] Given their overall shared interest in applying diverse methods to achieve research goals, these approaches are increasingly collectively referred to as Multiple and Mixed Methods Research (MMMR).[125]

Looking to LIBERATE, a combination of approaches falling under MMMR were applied (see Figure 2.2). This research project set out to address the identified research aims using all available, relevant methods, allowing for methodological rigour in both understanding SBC and in evaluating an intervention developed in response. More traditionally, distinct research methods are applied under the dichotomy of either Qualitative or Quantitative research designs. Both have inherent strengths and limitations, as well as key features which align with different research goals.[126] Where the aim is to explore and to understand particular problems or phenomena, and the meanings assigned by particular groups and individuals, qualitative research facilitates an inductive line of inquiry. For more objective research goals, quantitative research can be applied to test and validate hypotheses deductively, leading to findings which may be generalised (where samples are of a sufficient size) and which are independent of the researcher.[126, 127] At the heart of MMMR approaches is the goal to build on the strengths of

both qualitative and quantitative research whilst balancing out the limitations inherent to each. Whether a multiple or mixed methods design, the use of diverse methods to gather diverse data can allow researchers to answer questions in a way that is both exploratory and confirmatory.[128] Furthermore, it is argued that this wider-reaching approach allows us to answer research questions more comprehensively and more completely than any single method alone.[129]

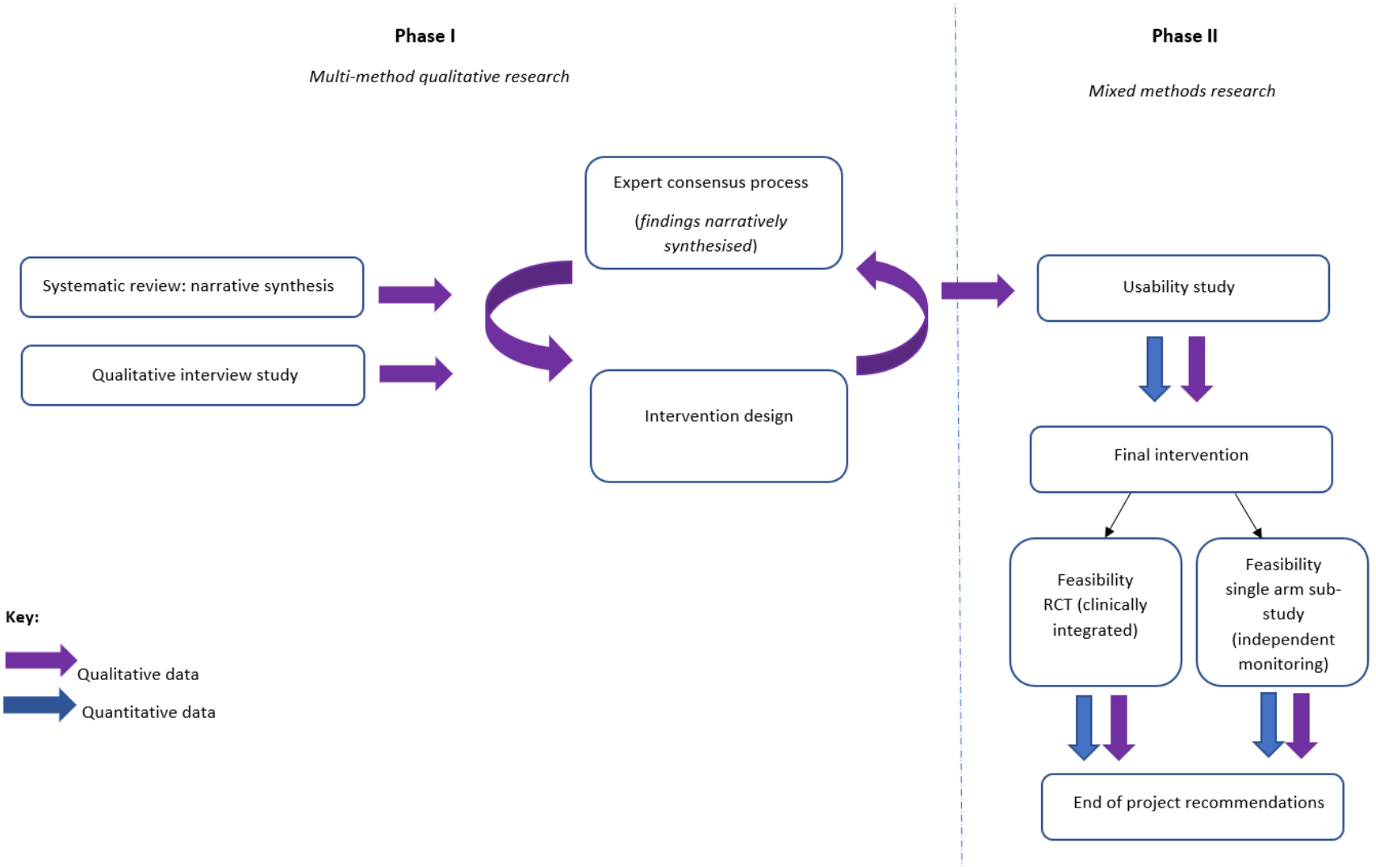
Given the crucial importance of integration in mixed methods in particular, a wealth of literature has sought to define and rationalise different approaches, allowing for a more refined and study-specific methodological rationale.[123, 130] Several of these approaches are outlined in Table 2.1 below.

Table 2.1 Approaches to the integration of mixed methods[129, 130]

Integrative approaches for mixed methods research	
Complementarity	The use of one method to explain and further illustrate the results of another.
Development	The use of one method to build on or inform the use of another.
Initiation	The use of another method to look at aspects of the research question not yet explored, to offer new insight and perspective.
Expansion	The use of a different research methods to examine different aspects of a research question from the offset.
Triangulation	Applying both methods to support and substantiate findings.

Within this thesis, the integration of mixed methods at key stages of phase II will be outlined. A complementarity approach was applied to qualitative and quantitative data collected as part of user-based usability testing. Collectively, these data sets informed the final intervention refinement. Following subsequent feasibility evaluation, statistical data relating to intervention use and other trial data (e.g. attrition, completion rates etc.) was triangulated with qualitative inquiry, in the form of both textual feedback and interview data, to allow the reasons and the context behind such findings to be explored. MMMR approaches also encourage an element of flexibility, giving researchers the freedom to adapt and respond to the unfolding research context. The Oxford Handbook of MMMR refers to this as 'prepared contingency'; in other words, maintaining rigour and quality in the planning and application of diverse methods, whilst allowing for some aspects of design to be informed by the emerging data.[125] This principle was applied to the research at hand, with subsequent stages evolving in line with the data and findings of the previous ones. The intervention design and development, for example, was shaped by phase I findings, and in turn influenced aspects of the phase II feasibility evaluation.[131]

Figure 2.2 Overview of research design applying a multi-phase MMMR approach



2.4.2 Paradigmatic considerations

Throughout this research, 'paradigm' is used as a collective term, encompassing ontology, epistemology, methodology and methods.[132] Collectively, these various paradigmatic 'ingredients' represent the foundations of social and scientific research. Ontology is the study of reality, being and existence in the social world. It is through ontology that we explore what we know about the nature of reality.[132, 133] Epistemology, on the other hand, questions, '*what do we know*?' and '*how do we know it?*' In other words, the study of truth and knowledge, and how these are generated, shared and communicated. Applying this thinking, a methodology is a strategy for acquiring knowledge whilst the methods are the specific tools used to carry out this strategy.[127, 132, 133] Kuhn brought these concepts together, defining a paradigm as a set of shared beliefs which guide the questions researchers ask and the ways in which they set about answering them.[134] Numerous different research paradigms exist, each with their own underpinning philosophical assumptions and methodological traditions. The ontological and epistemological viewpoints associated with each paradigm govern its assumptions relating to knowledge and reality, in turn guiding the methodology and methods which are applied when conducting research. Qualitative research is founded in the interpretivist paradigm, for example, whilst quantitative research is traditionally conducted within the positivist paradigm.[127]

For positivists, research is undertaken to prove or disprove theory-driven hypotheses. The researcher is external to the research process, able to objectively gather data and observe causal relationships, adding to knowledge about the social and scientific laws which govern reality. The positivist paradigm therefore has long-established roots in the natural sciences; it was a driving force in scientific enquiry throughout the nineteenth and twentieth centuries.[127, 132] In contrast, interpretivists reject this notion of reality being 'discoverable', instead proposing that reality is socially constructed and grounded in social context. In doing so, interpretivism aligns with the ontological position of relativism. Research about the nature of this social reality is explorative and subjective; there is no universal truth governed by laws, rather there is meaning constructed by individuals and driven by experience, culture and values. The researcher and their own perceptions and interpretations are inherent to the research process.[127, 132]

These long-held distinctions and traditions have fuelled what, throughout the 1970s and 80s, were described as 'paradigmatic wars', as the emerging mixed methods movement attempted to bring together and reconcile the differences within a single, cohesive paradigm.[124] So called 'purists' from both sides of the positivist versus interpretivist divide have long refuted such efforts, rejecting mixed methods on the basis of what they felt to be the absolute

incompatibility of the historically distinct qualitative and quantitative paradigms.[135, 136] However, an expansive following in MMMR have laid the foundations for a number of alternative paradigms, able to justify and embrace the application of qualitative and quantitative methods.

2.5 LIBERATE: A MMMR approach guided by critical realism

2.5.1 Complex methods for complex research

In setting the scene for this research, and justifying its MMMR approach, it is important to consider the complexity of its nature and scope. Its concern with the psychosocial well-being of women being treated for cancer grounds it firmly within the field of applied, clinical psychology. Yet this research extends beyond the reach of psychological theory and clinical practice, into the realms of complex intervention evaluation (arguably, a field in its own right), encompassing complex systems science, complex healthcare systems and health informatics. Understandably, these multiple 'lenses', through which the research questions are viewed, bring great epistemological diversity and divergent methodological traditions. In addition, the complexity of the intervention itself, comprising multiple components, targeting women across multiple settings and resulting in multiple measurable outcomes, called for methods as complex as the research focus and context to which they are applied.

In 1985, Cook advocated for what he termed 'critical multiplism', referring to the need for research questions to be viewed from a range of different perspectives, encompassing diverse methods and their varying biases.[137] This followed an earlier call for researchers in the field of programme evaluation to free themselves of the methodological constraints and notions of incompatibility entrenched in the traditional paradigms.[138] Decades later, Johnson, Onwuegbuzie and Turner observed that this approach had been embraced within evaluation research to a far greater extent than other fields (psychology, for example), due to its inherent complexity and the need for practical and multi-faceted approaches.[121]

Indeed, Breen and Jones describe the historic pull of positivism throughout the field of psychology, with researchers looking to establish its 'legitimacy' by mirroring the objectivity and generalisability of the natural sciences.[139] Quantitative methods and experimental research design have therefore traditionally been favoured. Yet, there is increasing awareness of the need for what is described as methodological pluralism, whereby methods within and beyond the reach of a positivist epistemology are embraced to better understand the complexity of social and psychological research and phenomena.[139] Such phenomena are often interwoven into the complex systems and settings of complex interventions which, as highlighted, have been a long-established and widely accepted focus of mixed methods

research. Quantitative researchers must hypothesise what is to be measured, yet complex interventions often lead to unanticipated changes to the system in which they are implemented. Methods must therefore be reactive to emerging outcomes; pluralism as opposed to positivism equips researchers with the necessary diversity of tools and flexibility in approach.[140, 141] The various facets of complexity at the very foundation of this research therefore advocate a MMMR approach.

2.5.2 Critical realism

Critical realism represents the major philosophical influence throughout this research, guiding a realistic evaluation of a complex intervention.

Following much debate of positivism and interpretivism throughout the mid-late twentieth century, realism emerged as an alternative viewpoint.[142-144] This fresh philosophical perspective explained science in a way which disposed of the traditional epistemological assumptions, focusing instead on the mechanics of explanation and causation.[142] Ultimately, philosophical realism was defined by Phillips (1987) as the view that, 'objects or entities exist independently of our perceptions of them, or the theories we have about them.'[145] (p. 205)

Over many decades, social scientists have paved the way for realist principles to extend beyond the natural sciences and into studies of society.[142] Roy Bhaskar's pivotal writings on critical realism brought together philosophies of science and social science, seeking to differentiate social reality into what is real, what is actual and what is observable (i.e. empirical).[142, 146] According to critical realism, there is a reality which exists independently of our knowledge and interpretations of it; this 'real world' exists in structures and mechanisms which cannot be observed.[142] It is the unobservable mechanisms (the 'real') which cause actual events, leading to observable experiences. Thus, it is through the observable domain of reality that we are able to understand the social world.[142, 146]

In this way, critical realists walk a middle-ground, accepting that the law-finding pursuits of the natural sciences cannot be mirrored in studies of society, yet rejecting the interpretivists' reduction of social science purely to the interpretation of meaning.[142] In other words, critical realism embraces both interpretive understanding and causal explanation as having a place in the social sciences.[142]

Key to these principles is the idea of causal mechanisms and the basic formula which underlies much of realism:[143] (p. xv)

Mechanism + Context = Outcome

Ideas relating to causality are a central ontological consideration of any paradigm. Critical realism rejects the notion that causation relates to a simple, law-driven model of a singular cause leading to a singular effect, governed by known regularities.[147] In fact, as has been extensively discussed amongst critical realists, there are many causal mechanisms or processes at play within a world which comprises an open, complex and dynamic system. This system is made up of objects, relations and structures, all interacting across different contexts.[148, 149] In other words, the relationship between a causal process and its resulting effects very much depends upon the context in which the process is activated.[143] Maxwell and colleagues emphasise that this goes beyond the proposition that causal processes will vary between contexts. Much more than this, context is *directly involved* in the causal process.[150] For realist social scientists, this 'context' encompasses individuals' beliefs, interpretations and intentions, all of which are inextricably linked in the mechanisms of causation.[151]

Given such underlying complexity, this throws into question how these causal processes can be 'controlled' for in an experimental sense.[150] Shadish, Cook and Campbell clearly delineate between what they refer to as 'causal description' and 'causal explanation', when defending the place of experimental research. The former refers to a cause-effect which can clearly be observed and described, such as the effect of an intervention or treatment being modified. Here, experimental approaches excel. Causal explanation, however, refers to the underlying mechanisms and contextual factors in which the cause-effect relationship is embedded.[152] Shadish and colleagues argue that, whilst experimental methods are less adept at illuminating causal explanations, they could be better designed and more effectively conducted to achieve a more successful balance between the two.[147, 152]

2.5.3 Principles of realist evaluation

Across fields of research, the RCT is seen as the strongest evidence basis for demonstrating causality.[153] However, for some realists, their experimental designs focus too heavily on the description of causality, to the neglect of causal explanation. This approach to evaluation can be seen as overly simplified, especially where complex interventions are involved.[154]

Applying these discussions to the research at hand, realist evaluation is centred upon the evaluation of complex interventions within complex settings. Pawson describes the aim of a realist evaluation as being to determine how a programme or intervention works, for whom, in what specific circumstances and over what timeframe.[155] It applies realism's philosophical and conceptual thinking to research practice. This was the ultimate aim of phase II of this research. In fact, Fletcher and colleagues specifically advocate for the use of realistic evaluation principles across all phases of the MRC framework, arguing that complex causal mechanisms,

so crucial to considerations of intervention feasibility and efficacy, will be more fully understood.[154]

In applying realistic principles, an evaluation is designed in a way that seeks to develop, test and refine theory relating to the mechanisms and contexts which interact to lead to (social) outcomes.[154, 155] For the research at hand, this may relate to how the intervention components interact with each other, how the user interacts with the intervention (driven by factors such as their values and beliefs) and how the intervention, the user and underlying causal processes interact with their context across an open system. In realist evaluation terms, this is described as a 'Context-Mechanism-Outcome configuration' (CMO) and is one example of a middle-range theory (which will be further explored in chapter 5).[155] Despite its positivist origins, experimental design in the social sciences is in fact strongly supported by critical realism.[149] Together, these are core methodological pillars of a realist evaluation and can be applied to explain how an intervention interacts with its context to produce outcomes, accounting for complex underlying social processes.[154, 156]

2.6 Complex interventions

As outlined earlier, a complex intervention is defined as an intervention composed of multiple interacting or interdependent elements. They may require the adoption of new behaviours (by those delivering the intervention and/or those receiving it), target a range of individuals or populations, offer varying levels of tailoring or flexibility, and lead to a number of different outcomes.[117, 157] Their multi-faceted nature means that they are frequently developed and implemented with the aim of tackling complex health challenges across multi-disciplinary settings.[116, 158] Elements of complexity also extend beyond the design of the intervention itself, encompassing the context in which it is implemented and the underlying causal pathway(s) which lead to measurable outcomes.[116, 159] Indeed, rather than being of a 'standard' design, interventions may take on different forms in different contexts.[160]

As discussed in chapter 1, the eRAPID complex intervention represents a key, guiding example from which the LIBERATE research developed. This online symptom monitoring and self-management intervention encompassed numerous interacting components:[161]

1. Online symptom monitoring questionnaires with established severity levels.
2. An electronic platform to host these questionnaires, with infrastructure for integration into the Electronic Patient Record (EPR).
3. Automated, tailored self-management advice.
4. Clinician review and follow up of patients' reported symptoms.

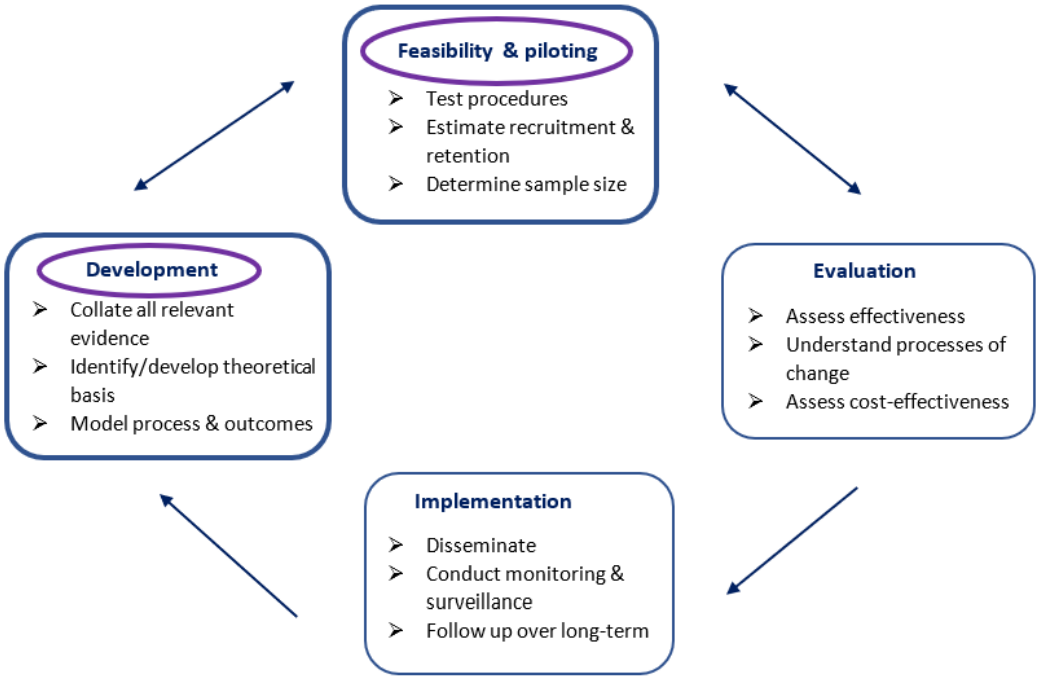
5. A website with patient information and advice, specifically related to self-reported symptoms.

The proposed initial outline for a multi-component online intervention (guided by eRAPID content and findings) met the broad definition of a complex intervention through interacting functions for symptom-monitoring and self-management in SBC, tailored to patients across clinical and community settings.[116] The evolution and development of the LIBERATE complex intervention will be explored in greater detail throughout the thesis.

2.6.1 The MRC framework

The Medical Research Council's (MRC) framework for developing and evaluating complex interventions is central to the research methodology and project as a whole. Four key phases are stipulated: development, feasibility & piloting, evaluation, and implementation.[116, 117] A range of research methods were therefore be applied within the 'development' and 'feasibility & piloting' phases of the MRC framework (highlighted in Figure 2.3 below), to address the identified research objectives.

Figure 2.3 Key stages of the MRC framework[116, 117]



Originally published in 2000,[162] this framework was later updated to account for experiential evidence gathered since its inception and to respond to calls for greater emphasis on the early developmental and piloting stages.[116, 117] Resulting renewed focus on these two pivotal stages is the basis upon which the LIBERATE project was designed.

The process of intervention development through to implementation (Figure 2.3) also evolved from a linear model, based on phases of drug development, to the cyclical model outlined above. The arrows make it clear that there is likely to be iterative, back and forth movement between the stages in order to develop and assess the feasibility of an intervention in a way which is both systematic and responsive to the evidence gathered.[117]

2.6.2 The development phase & intervention theory

Further guidance was published in 2019, recognising a need for more clarity and consensus on the development phase in particular.[158] O'Cathain and colleagues sought to specifically outline the actions health researchers must take in order to move from ideas, evidence and theory to interventions which are ready to be evaluated in a pilot or feasibility setting.[158] These key actions (outlined in Table 2.2) helped to further shape the proposed research design and objectives, as detailed in the corresponding thesis chapters.

Amongst these key developmental actions is the identification and application of core underlying theory, with the intention of explaining *how* the intervention will work. Indeed, MRC guidelines cite the need for a 'coherent theoretical basis'.[116] This is to ensure that the resulting intervention is best placed to effectively address the health challenge under focus, ultimately leading to its implementation in the real-life setting. Many interventions in the broader field of chronic illness draw upon theories relating to behaviour change. Those supporting patients with diabetes, for example, are often designed around key modifiable behaviours, such as diet and exercise. These are then targeted using 'techniques' or intervention components designed to modify such behaviours and bring about positive, enduring change.[163] However, as will be discussed in chapter 5, the link between behaviour change and the ongoing self-management of SBC is not so clearly delineated. The end-goal of the proposed intervention was not necessarily to promote a change of behaviour evidenced to lead to a positive health outcome. Instead, it intended to support women to develop their skills and confidence in performing the self-management behaviours which are integral to their disease trajectory. Importantly, it is acknowledged that selection of theory a priori can in fact prove to be counter-productive to intervention development since, with iterative progression through the development phase, it may not fit as originally intended.[158] Whilst this by no means dismisses the importance of a well-established theoretical grounding, it did support the decision to draw on theory throughout the development process, and to review its relevance iteratively and in parallel with the other strands of development.[158]

Table 2.2 Key actions for the development of complex interventions[158]

Action	Steps planned to address action	Chapter outlining action
1. Plan the development process.	Multi-stage development process guided by the MRC framework and underlying methodological rationale. Key research activities grounded in current evidence bases for SBC and complex interventions.	Chapter 1 (Introduction) Chapter 2 (Research design & methodology)
2. Involve stakeholders *(including those who will deliver, use and benefit from the intervention).*	Conducting the phase I qualitative interview study of patients and health & charity professionals, involving these 'stakeholders' in the early and pivotal stages of research.	Chapter 3 (Exploring QoL and routes to support in secondary breast cancer: A qualitative interview study)
3. Bring together a team and establish a decision-making process.	Consulting with an expert consensus group to aid collaboration in the translation of phase I findings.	Chapter 6 (Intervention design & development)
4. Review published research evidence.	Conducting a systematic review of online and technology assisted interventions in the context of advanced cancer to guide aspects of design and delivery.	Chapter 4 (Systematic review)
5. Draw on existing theories.	Exploring relevant theories guided by phase I findings and the wider literature. This theoretical overview informed the underlying programme theory, the relevance and applicability of which was then reviewed during the feasibility evaluation.	Chapter 5 (Intervention theory)
6. Articulate programme theory.		
7. Undertake primary data collection.	Conducting the phase 1 qualitative interview study, providing data to inform the intervention design.	Chapter 3 (Exploring QoL and routes to support in secondary breast cancer: A qualitative interview study)
8. Understand context.	Developing a strong knowledge and evidence base in fields of SBC and self-management interventions throughout phase I. Adding to this an understanding of the lived experiences of women to give a full and informed context.	All phase I chapters
9. Pay attention to future implementation of intervention in 'real world' setting.	Ensuring intervention design & development was informed by available resources, practical considerations and intended contexts.	Chapter 5 (Intervention theory) and Chapter 6 (Intervention design & development)
10. Design and refine the intervention.	Presenting the initial proposed design to an expert consensus	Chapter 6 (Intervention design & development)

	group and reviewing/refining on the basis of feedback.	
11. End the development phase.	Reviewing all phase I findings to ensure that these were reflected in final intervention. Progression to user-based usability testing & feasibility evaluation followed satisfactory run-through testing.	Reflections on phase I research.

2.6.3 Feasibility & piloting: Informing intervention evaluation

Petticrew argues that the most important consideration for researchers is not, '*is the intervention simple or complex?*' but rather, '*does the intervention warrant a simple or complex approach to evaluation?*'[164] 'Simplicity' denotes a direct, linear pathway from intervention to outcome. Yet the existence of such simplicity, even in interventions so often thought of as 'simple' (e.g. the administration of a drug in a clinical trial) is contested.[165] When intervention outcomes are derived through non-linear processes, as is so often the case where multiple, interacting components, diverse populations and varying contexts are involved, complexity in evaluation is also needed in order to fully explore the intervention and the system in which it is embedded.[164] For the impact of a complex intervention to be successfully evaluated, initial feasibility considerations (of both the intervention itself and the trial design) are therefore crucial.[166]

As such, both the developmental and the evaluation phases of this project considered the LIBERATE intervention across several contexts:

- Within a clinically integrated setting, with intervention delivery linked to care.
- Within the community setting, with the intervention accessed independently of participants' usual care, in an 'independent monitoring' capacity.

In performing feasibility testing of the proposed intervention across these settings (outlined in greater detail in chapter 7), crucial aspects of the evaluation itself were trialled and refined, ensuring that its methods and results were able to capture and holistically explain this intervention complexity.

Exploration of underlying theory and the development of programme theory (chapter 5) highlighted as key actions to be performed within the development phase, also supported the conduct and interpretation of this multi-strand feasibility evaluation.

2.7 Reflections

The in-depth exploration of the outlined methodological approach and philosophical assumptions guided and strengthened the application of the MRC's framework across developmental and evaluation phases. However, though the direction and bounds of this research were clearly defined from the outset, the iterative nature of the framework also demands an element of flexibility, allowing methods to be applied in response to emerging findings. Clearly, a balance needed to be struck. Discussing their use of mixed methods across multiple phases of complex health research, Strudsholm and colleagues emphasise the importance of what they describe as 'methodological congruence'.[119] In other words, the compatibility and appropriateness of the methods chosen when following a MMMR line of inquiry, and the extent to which they are in keeping with the underlying theory and assumptions. The transparency of such decisions, and the steps taken in making them, will therefore be outlined within each of the chapters outlining the various research activities.

2.8 Summary

This chapter has described the overarching design and methodology of the LIBERATE research, justifying these decisions in the context of the research aims and underlying philosophical assumptions. Taking an overarching critical realist perspective, and following an overall MMMR approach, subsequent chapters will now explore the methods chosen to shape the design and evaluation of a complex intervention.

Chapter 3: Exploring quality of life & routes to support in secondary breast cancer - a qualitative interview study

3.1 Chapter overview

This chapter will present the methods and results of a qualitative interview study, which represents a core component of phase I research. It will explore, from a range of perspectives, the QoL and supportive needs of women living with SBC. Furthermore, it will outline how these qualitative insights were taken forwards alongside other phase I findings, supporting the development of a theoretical basis, and collectively shaping a tailored, online supportive intervention.

3.2 Chapter aims

- To outline the rationale and methods for a qualitative interview study.
- To explore the perspectives of two key groups: women living with SBC and a range of professionals involved in their care and support.
- To integrate the findings from these groups and discuss how they guided the next phase of research.

3.3 Introduction

3.3.1 Background

As highlighted in chapter 1, despite widespread consensus of the significance of QoL for women living with SBC, and the pressing need for further research in this area, gaps in our understanding are still evident. Indeed, for the past several decades, research has alerted us to a breadth of unmet supportive needs, with women's QoL slow to improve compared to the rapidly advancing treatment landscape.[57, 58, 61] More recently, studies have confirmed the extent and diversity of supportive needs across a heterogenous disease trajectory, with the internet representing a potentially viable mode of support delivery.[54, 167, 168] Crucially, however, qualitative studies have lacked insight into SBC in the UK context.[167, 169-172]

3.3.2 Rationale

As the management and trajectory of SBC continues to evolve, so too are women's experiences of living with it. Yet research exploring their QoL lags behind continuing therapeutic advancements. Furthermore, given the ongoing identification of unmet needs, barriers to support, and diminished QoL for these women, research must now focus on how best to address these issues in the context of current treatment and resources.

An up to date perspective of women's QoL and their needs, preferences and tendencies for support is therefore warranted, to bridge longstanding gaps and to directly inform the development of supportive interventions for women living with SBC in the UK context.

3.3.3 Aims

This study formed a core element of phase I research. Overall, it aimed to:

- Identify the informational and supportive needs of women living with SBC, as well as their preferences and support seeking tendencies, in order to inform the scope and content of a tailored intervention.
- Explore the lived experiences of this growing group of women, fostering a broader understanding of their QoL.

3.4 Methods

3.4.1 Design overview

This study sought to explore QoL in SBC through in-depth, semi-structured interviews with two key groups:

- Women living with SBC
- Health and charity professionals involved in their care and support

3.4.2 Sampling

Purposive sampling is used to identify participants who have key characteristics central to the research question.[173] Variation is captured by identifying participants within numerous sub-samples or strata (known as 'stratified purposive' sampling), each of which can be compared across the sample as a whole.[174, 175] Having identified the significant diversity across this patient group during early background research, stratified purposive sampling aimed to include 30 women from a range of different age groups, on a breadth of different treatments, and at varying timepoints since diagnosis (Table 3.1).

Table 3.1 Purposive sampling strategy for recruitment of women living with SBC

		Treatment status			
		Chemotherapy	*Targeted therapy +/- hormone therapy**	*No active treatment*	**Total** (target)
Age	≤ 40	3	4	3	10
	41 – 59	3	4	3	10
	≥ 60	3	4	3	10
	Target total	9	12	9	**30**

**These treatments formed a collective group since they are often delivered in combination.*

Convenience sampling refers to the identification of participants in accordance with ease, access and availability as opposed to a pre-defined strategy.[175] For health and charity professionals, convenience sampling was performed, applying a pragmatic approach to identify approximately 10 participants across a breadth of different roles.

3.4.3 Patient & Public Involvement and study documentation

The project's Patient Advisor was involved throughout the design of the study protocol and associated study documentation. The Independent Cancer Patients' Voice (ICPV) patient advocate group were also consulted and their expertise helped to shape the content and delivery of a number of the study documents (e.g. patient participants' PIS, consent form, invite letter and general topic guide).

Core recruitment materials (Participant Information Sheets and consent forms) are available to view on the LIBERATE section of the Patient Centred Outcomes Research group's website. (https://pcor.org.uk/liberate-living-better-with-advanced-breast-cancer-symptom-monitoring-self-management-and-sign-posting-support-for-women-living-with-secondary-breast-cancer/)

3.4.4 Dual approach to analysis

In order to meet the dual aims of this study, the data was analysed and interpreted across two stages.

Stage 1. Pragmatic, descriptive: identifying supportive needs salient to intervention design.

During the initial stages of thematic analysis, a detailed coding framework for each of the two datasets was constructed. Key qualitative data was extracted at the level of the codes to directly inform the design and content of the proposed intervention.

Stage 2. Thematic, explorative: seeking to understand broader experiences and QoL.

Following on from this, an in-depth thematic analysis explored women's lived experiences and the context(s) in which the intervention will be embedded.

3.4.5 Ethical approval

The study was granted NHS ethical approval by the South Yorkshire Research Ethics Committee (REC) and the Health Research Authority (HRA). Local level ethical approval was also obtained from the LTHT Research & Innovation department.

3.4.6 Recruitment strategy: women living with SBC

The purposive sampling framework (Table 3.1) was applied across two settings (clinic-based and online), in accordance with the eligibility criteria outlined below.

3.4.6.1 Eligibility criteria

- Women with a diagnosis of SBC (clinically confirmed or self-reported).
- Undergoing any form of cancer treatment OR not on current active cancer treatment (e.g. having a break from treatment or receiving symptomatic treatment only).
- Not displaying symptoms indicative of psychopathology.
- Able to read and understand English.
- Able and willing to take part, following informed consent.

3.4.6.2 Clinic based recruitment

Patients were recruited from onsite oncology outpatient clinics (based in St James's University Hospital, Leeds). A member of the clinical team screened clinic lists to identify eligible patients and sought permission for the researcher to approach them. Those expressing an interest were given the participant information sheet (PIS) and the researcher explained the study in further detail, answering any questions which arose. The patient had the option of consenting at that point or following up with the researcher at a later date (via telephone or email), once they had further considered the study information.

3.4.6.3 Online recruitment

Alongside clinic-based recruitment, an online recruitment strategy was also developed through established relationships with Breast Cancer Now and Breast Cancer Haven (Yorkshire). These charities shared the study information with their service users via online channels, including email lists, online bulletins, support groups and social media platforms. Women interested in participating were directed to contact the researcher. Following an expression of interest, an invite and PIS were provided via email.

Care was taken to ensure that women's self-reported diagnosis was confirmed using an eligibility checklist during an initial discussion. The PIS also provided a clear definition of SBC, distinguishing it from a primary breast cancer recurrence.

3.4.6.4 Follow-up and consent

Potential participants from both recruitment settings were followed up by email or telephone. Women who had not been in contact after one week were sent a single email reminder or approached at their next clinic appointment. For those willing to participate, an appointment was arranged (in person or via telephone) with the researcher for further discussion and to obtain informed, written consent. Where consent was given verbally via telephone, this was audio-recorded and documented as such.

3.4.7 Recruitment strategy: professionals

The perspective of those involved in delivering care and support to women living with SBC was also sought. Eligible professionals were identified through the multidisciplinary breast oncology team at St James' University Hospital and with managers at Breast Cancer Care, Sheffield (prior to its merge with Breast Cancer Now). Convenience sampling methods were applied, aiming to recruit a diverse sample of oncologists, Clinical Nurse Specialists (CNSs) and charitable professionals. An invite and information sheet, detailing the study and their involvement, was provided via email.

3.4.7.1 Eligibility criteria

- Working in a role involving the care and/or support of women living with SBC.
- Able and willing to take part, following informed consent.

3.4.7.2 Follow-up and consent

For those who expressed an interest, arrangements for completing informed consent and scheduling the interview were made via email. Again, consent was obtained either in writing or over the telephone, depending on the participant's preference and location.

3.4.8 Semi-structured qualitative interviews

Interviews were arranged in line with preferences and availability of participants, conducted either in person, over the telephone or via video-conferencing software (Skype).

Semi-structured interviewing techniques were chosen, to allow for an exploratory, responsive approach to data collection, recognising the likely variation in women's lived experiences. Whilst structured interviews, which apply more defined, questionnaire-like topic guides, allow for more standardised data collection, unforeseen discussion points or elaborations may otherwise be missed.[175, 176] A more inductive approach, allowing for participant-led discussion, was therefore favoured. As such, a broad interview schedule was developed for each group, exploring key topics whilst also allowing for flexibility in discussion and unanticipated insights. These topics were guided by the study's aims and the wider literature, which identified core gaps in the knowledge and understanding of the SBC experience. Excerpts of the interview schedules are included below.

3.4.9 Thematic analysis

Reflexive thematic analysis (TA) was the chosen analytic approach, as outlined by Braun and Clarke.[177] Unlike analytic approaches which are firmly grounded in theory, TA transcends theoretical frameworks, allowing researchers to shape and apply this analytic tool in accordance with their project and perspectives.[178] This flexible approach to analysis was

chosen to suit the complexity of the research context, the researchers' experience and the diverse and evolving theoretical grounding. From a critical realist perspective, TA allows for the identification of themes and patterns to uncover the meaning individuals assign to their experiences, as well as the social context in which these are embedded, and to consider how these have been shaped by the unobservable 'real' domain.[177, 178]

Topics included in women's interview schedule

1. **Past: 'cancer story' - experience of initial diagnosis & beyond, e.g.**

- Diagnoses: primary and secondary
- Symptoms
- Experiences of treatments & side-effects
- Trade-off between side-effects and survival

2. **Present: day-to-day experiences of SBC +/- treatment, e.g.**

- Key issues impacting their QOL/unmet needs
  - Physical/functional/sleep
  - Psychosocial/emotional/relationships
  - Experience of family coping with their condition
  - Legal/financial
  - Spiritual/finding hope
  - Challenges of living well with secondary disease
- Current treatment and appointment schedule
- Symptom management
  - Self-management versus health professional input

3. **Comparison between experiences of primary breast cancer & SBC, e.g.**

- Symptom experiences
- Women's own reactions & the reactions of others
- Available support

4. **Information and support seeking in SBC, e.g.**

- Tendency for information seeking
- Sources of information, availability & suitability
- Role of healthcare professionals: CNS and oncologists
- Other services accessed/other sources of support e.g. Macmillan, hospices

5. **Online versus offline support, e.g.**

- Experiences of online and offline sources of support
- Frequency of use/access
- Thoughts on value of online vs offline sources of support in SBC

Topics included in professionals' interview schedule

1. **Experience of patients' care and support needs in SBC, e.g.**

- Key issues impacting QOL/unmet needs
  - Physical/functional
  - Psychosocial/emotional/relationships
  - Families' response to/coping with loved one's condition
  - Legal and financial
- Comparisons with primary breast cancer

2. **Symptom management & disease progression, e.g.**

- Challenges unique to secondary breast cancer
- Experiences of different illness trajectories

3. **Treatment decisions, e.g.**

- Thoughts on/experiences of patient involvement
- Information surrounding diagnosis and treatment
- Trade-off between side-effects and 'progression-free survival'

4. **Multi-disciplinary management of SBC, e.g.**

- Collaboration/liaison with other health professionals, services, charities etc.
- Thoughts on patient self-management and information seeking

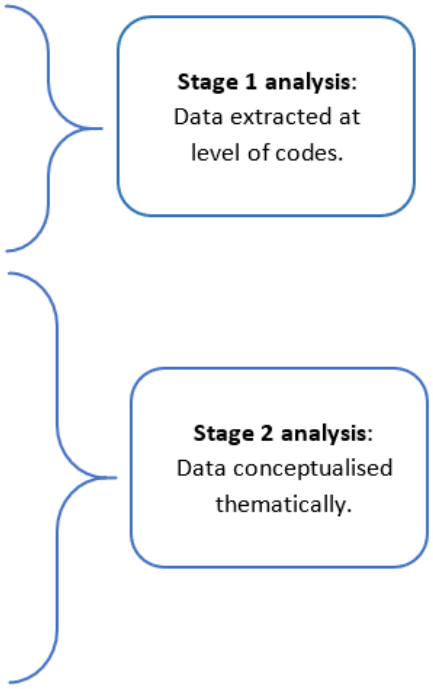
5. **Supportive resources/services in SBC, e.g.**

- Examples regularly encountered/referrals regularly made
- Offline support versus online support
  - Examples
  - Thoughts on availability & usefulness in patients with SBC
  - Barriers to access
- Thoughts on improvements/additions to existing services and resources needed

This flexibility, however, also risks inconsistency in approach, fuelling concerns as to the rigour and reproducibility of thematic analysis. This concern has been heightened by a lack of clear guidance as to how TA should be conducted.[178] In response, Braun and Clarke, and later Nowell and colleagues, outlined a clear step-by-step method to permit a flexible yet replicable approach.[178, 179] These steps were followed to ensure that the identification and interpretation of codes and themes was process-driven and meaningful, and that all analytic stages and decisions were documented within a clear audit trail.[179]

Figure 3.1 Methodological steps for reflexive thematic analysis [177, 178]

Methodological steps for thematic analysis	
1. Data familiarisation	Familiarising oneself with the data through transcription of recordings and in-depth reading of transcripts.
2. Generating codes	Identifying interesting/key features across the data set and assigning codes to describe these features. Collating codes in a systematic way to give a descriptive overview of the data.
3. Developing themes	Gathering codes from across the entire data set and grouping together to form potential themes.
4. Reviewing identified themes	Reviewing themes in line with the coded extracts and with the overall data set. Generation of a thematic map.
5. Defining themes	Continued analysis to further define and refine themes, identifying how they fit together within the overall analysis.
6. Writing up research	Writing up results of analysis in line with the research question(s) and wider literature, using coded extracts of data to illustrate themes and their interrelation.



3.5 Stage 1 analysis

Aim: to identify the informational and supportive needs salient to intervention design.

All interviews were transcribed verbatim by the researcher and transcripts subsequently read and re-read, aiding in the process of familiarisation. Through generating and assigning descriptive codes, the data was then segmented and organised, with sections grouped together under the same or similar codes using categories and sub-categories. The two data sets (women living with SBC and professionals) were coded and analysed separately, with the development and application of separate coding frameworks. For the women living with SBC, the framework was purely inductive, developed and refined iteratively throughout the process of data familiarisation and coding.

For the professionals, elements of a combined inductive and deductive approach to thematic analysis, described by Fereday and Muir-Cochrane, were applied.[180] The Generic Choice Model (GCM) guided the structure of the coding framework and its main categories a priori (Table 3.2).[181] This model, devised by the UK's Department of Health and later adapted to the context of chronic cancer,[13] outlines the key tenets of care and support for patients living with long-term conditions. Throughout the process of coding, this framework was then further developed, with additional codes derived inductively from the data set. This combined

approach was applied since the researcher's prior knowledge of the GCM was likely to influence the sorting and description of data. Double coding of a selection of transcripts (20%) and sense-checking of the coding frameworks and developing themes was performed by a second researcher (FK). This confirmed a high level of intercoder agreement. This process was undertaken as part of a rigorous, methodological and reflexive thematic analysis, ensuring that the flexibility and freedom of the chosen approach did not compromise validity.[178, 179]

Table 3.2 Deductive development of the professionals' coding framework

Element of GCM	Researcher's interpretation for coding framework
1. Clinical services	Role of clinical services and health professionals in patients' diagnosis, treatment, monitoring and support. Managing appointments, in terms of both logistics and the underlying interactions.
2. Self-care and self-management	Symptoms and side-effects encountered and dealt with by health professionals and their experience of patients' self-management and coping.
3. Needs for independent living	Professionals' experience of the impact of disease on patients' ability to perform activities of daily living (ADLs) and their supportive needs relating to daily living.
4. Work, finances and benefits	Professionals' experience of the impact of disease on work and finances and associated supportive needs (availability of and access to services).
5. Psychological experiences	Psychological impact of diagnosis and ongoing disease for patient and for others (family, friends work colleagues etc.); need for and availability of psychological support.
6. Support pathways	Sources of support and services encountered and referred towards, access to support, appropriateness of support and barriers identified. Professionals' attitudes towards available support and thoughts on gaps in current support and patients' unmet supportive needs.

Data was extracted at the level of the codes to directly inform the design of the proposed intervention, providing in-depth detail of women's needs and preferences for information and support, prior to the identification of broader, over-arching themes in stage 2.

3.6 Stage 1 results

3.6.1 Women living with SBC: final sample

In total, 28 women living with SBC were recruited across online and clinical settings. It became apparent that several of the groups specified within the purposive sampling frame were more difficult to recruit to (Table 3.3); specifically, those aged 40 and under and women who were not currently on active cancer treatment. In appreciation of this, a flexible approach to recruitment was taken, with patients over-recruited to some of the better represented age and treatment groups, to account for smaller numbers in others. Recruitment ceased when

data saturation was felt to have been reached. This was defined as the point at which no new ideas or areas of discussion were being identified during transcription and analysis.[182]

Table 3.3 Purposive sampling strategy: patients (target and actual recruitment)

	Treatment status			
	Chemotherapy	*Targeted +/- hormonal therapy*	*No active treatment*	**Total** Actual (target)
Age ≤ 40	1 (3)	2 (4)	0 (3)	3 (10)
41 – 59	5 (3)	8 (4)	1 (3)	14 (10)
≥ 60	4 (3)	6 (4)	1 (3)	11 (10)
Total Actual (target)	10 (9)	16 (12)	2 (9)	**28 (30)**

The average age amongst the women recruited was 56.3 years (Table 3.4), though the sample captured both younger and older age groups. Similarly, whilst the mean number of years since SBC diagnosis was 3.3, this varied between 0-15 years. The majority of women had experienced primary breast cancer (71.4%) and were being treated with hormone and/or targeted therapy (57.1%). Most had multiple sites of metastases (60.7%), with the bones (75%) the most frequent.

Table 3.4 Patients' baseline clinical data

Participants (n=28)		
Age, in years		
Mean (SD)	56.3 (11.6)	
Range	28-78	
Years since SBC diagnosis		
Mean (SD)	3.3 (3.4)	
Range	0-15	
Diagnostic history	**n**	**%**
Preceding primary diagnosis	20	71.4
DCIS	6	21.4
De novo	2	7.1
Current treatment		
Chemotherapy	10	35.7
Hormone +/- targeted therapy	16	57.1
No active treatment	2	7.1
Extent of metastasis		
Single site	11	39.3
Multiple sites (≥ 2)	17	60.7
Site(s) of metastasis		
Bone	21	75.0
Liver	11	39.3

Lungs	6	21.4
Brain	4	14.3
Lymphatics	4	14.3
Other	3	10.7

3.6.2 Health and charity professionals: final sample

In total, 7 professionals were recruited, encompassing a variety of healthcare and charitable roles (Table 3.5). Recruitment was halted at this figure due to research time constraints, as it was felt that additional time to recruit further participants would not result in significant further findings.

Table 3.5 Convenience sample of health and charity professionals

Role	Number recruited
Consultant Oncologist	1
Clinical Nurse Specialist (secondary breast cancer)	3
Clinical Nurse Specialist (primary & secondary breast cancer)	1
Charity professional – Clinical Nurse Specialist	1
Charity professional – Other	1
Total	**7**

The findings elicited at this first descriptive stage of analysis directly informed the content and design of the intervention. These are outlined in detail in chapter 6.

3.7 Stage 2 analysis

Aim: to explore the lived experiences of women with SBC and gain insight into their supportive needs and QoL.

Following the methodological steps for reflexive thematic analysis (Figure 3.1), all coded data was analysed for themes in stage 2. Whereas a code describes a singular idea or feature, a theme is multi-faceted and over-arching; it brings together and organises different ideas and features within the data, allowing the researcher to progress to observe patterns and meaningful concepts.[183] Though aspects of coding combined both data and theory driven approaches, subsequent stages were performed inductively (in other words, guided by the content of the data itself, rather than any theoretical assumptions).[180] Whilst a purely inductive approach is difficult to ensure, themes were conceptualised from and grounded within the data as far as possible. In this way, the second stage of analysis sought to view the data with a wider lens, expanding on stage 1 findings by contextualising them within broader lived experiences.

3.8 Stage 2 results: Women's perspective

Five core themes were identified across the women's experiences (Figure 3.2).

3.8.1 Narratives surrounding secondary breast cancer

Across diverse lived experiences, a range of intersecting narratives were apparent, spanning those personal to the participants and those they encountered more widely, amongst family, friends and on a societal level. It is through these narratives that women shared and made sense of their own diagnosis.

3.8.1.1 Preceding cancer experience

Women's preceding experiences of cancer (or, for some, their lack of 'cancer experience') contextualised their personal narratives of SBC. They reflected on previous treatment as they shared and tried to rationalise their journey to SBC diagnosis. Messages around earlier stage disease were also a focus, encompassing transiency, cure, optimism and finality.

> *"… chemotherapy, FEC-T, was the plan, and then followed by surgery, followed by radiotherapy and… that should have been it." (pt01, previous primary BC diagnosis)*

> *"…with hindsight, I probably should have pushed for chemotherapy at that stage but, you know, I was being told DCIS, 100% cure rate, you'll be absolutely fine, no problem…" (pt08, previous DCIS diagnosis).*

For those who experienced primary breast cancer, commonalities were evident in diagnostic and treatment pathways. Treatment was for a defined period of time and women generally felt well supported, frequently referring to an allocated Clinical Nurse Specialist (CNS). For several women, it was the point at which this transient treatment period ended that they felt most in need of, yet without, support.

> *"I always remember thinking after, you know, after the finish of all the treatments initially, I sort of thought I'd have like a round up sort of meeting with the consultant to say, 'oh right, we've done all of these things and this is what to expect next', but they never did… so therefore I never had the opportunity to say, oh well what should I look out for?" (pt14)*

3.8.1.2 Journey to diagnosis

In contrast to the similarities shared across experiences of earlier stage breast cancer, women described vastly differing, often more convoluted journeys to SBC diagnosis. Symptoms were diverse and frequently unrecognised by women or by health professionals, often attributed to other causes. For some, this led to delays and extended periods of uncertainty.

> *"Breathlessness and difficulty maintaining my voice… so they treated me for worsening asthma, so I was constantly taking inhalers and I have got a history of chest infections and pneumonia, so it was considered it was just my old problems emerging…" (pt12)*

"But it didn't even occur to me that the cancer had gone into my bones to be honest. I just went back to the doctors saying, 'I've got pains in my legs and I can't believe I'm so unfit, what can I do about it?'" (pt16)

3.8.1.3 Coming to terms with diagnosis

The shock and unexpectedness was perhaps most profound for those diagnosed as 'de novo', coming to terms with their SBC diagnosis without any previous experience of breast cancer.

" … it wasn't too bad because we just thought, we'll get through this, but at the back of my mind I was a bit concerned about the bone, I had a lot of bone pain in my ribs and things like this… but when the scans came back, yeah, that was quite devastating. Everyone was upset then because to be told that it wasn't curable, I felt that I'd been given a death sentence. That's, you know, that's how devastated we felt." (pt01)

Whilst some sought positives when processing their diagnosis, others found it more difficult to accept.

"…and then I think it was in the September that year they found it in my bones, so they knew where it was then…so I suppose that was a positive because it meant they could treat it, yeah." *(pt33)*

"It was just short of 4 years, well I thought I had done it! I thought it was finished and I'd kept myself well, I had, I mean I'm fit and well and I ate well and I exercise, I still do now, so it was a bit of a shock. Yeah, because I've got like my little boy, and it's just like… God! Like anybody would feel, not 'why me?' but (pauses) why have I got to go through this again?" (pt35)

3.8.1.4 Understanding and awareness

For most women, awareness of SBC prior to diagnosis was lacking or absent; some were completely unaware whereas others considered it to be rare or unlikely to happen to them.

"I had the notion, and I think a lot of people did as well, that if you have primary and you go through the surgery, chemo, radiotherapy options, whichever combination and order that that's in, then, then that's it done. That's it gone." (pt01)

Understanding and awareness of SBC amongst others appeared to be overwhelmingly lacking or limited, often related to poor understanding of the disease trajectory and complexities of the prognosis. Discussions surrounding the awareness of others shaped a wider narrative, separate to yet closely entangled in women's personal stories.

"…people generally don't get it… they don't understand that your treatment is going to be forever, I think they think, the cancer's come back, okay…it's a bit of a blip, it's like last time, you'll have 6 months of treatment and then you'll be fine again." (pt03)

"I think most people understand secondary breast cancer is incurable…but I think a lot of people, their immediate assumption is you're going to die, and therefore they're very uncomfortable with it and actually, when they realise you're living quite a normal life with it and may do for some time, I think some people are surprised by that…" (pt36)

Women also discussed misconceptions or misconceived narratives of cancer, shared by others and the media, leading to frustrations.

> *"I think a lot of people still sort of labour under the old sort of image from films and stuff of people having chemo and people looking very sickly and, you know, with the head scarf and all that kind of thing… but the reality is you're off and on steroids anyway so you're all plumped up and your skin looks good and you actually look really well, and everybody goes, 'oh you look so well, you wouldn't believe you had cancer!' And it's like, you know, what are you saying by that?" (pt21)*

3.8.1.5 Communication

The role of communication in shaping key moments and making lasting impressions in participants' narrative was clear. Women recalled the specifics of receiving their diagnosis, not only in terms of what was said, but also how it was delivered.

> *"I just didn't know what to say really. I suppose I should have asked loads of questions, but you're sort of knocked back a bit you know… So, he said, 'well (pauses) you know we can't cure this, don't you? You know we can't, you know this is incurable, don't you?' And I, I hadn't realised it was incurable…" (pt18)*

> *"…when I first went to get my treatment plan, the guy said that, his exact words were, 'you don't have an imminently life-threatening disease', at which point, you know, the room kind of calmed down and we were like, 'right, yeah…'" (pt36)*

The use of specific language and terminology also had a poignant influence on women's understanding, sharing and acceptance of their diagnosis.

> *"…you know like when they say on TV, when they say like, so and so's got 'terminal cancer' and I'm thinking, he probably hasn't got terminal cancer, he's probably got like what I've got, you know. It's incurable, but not terminal you know…and that's sort of annoying when people say that… we've all got terminal something haven't we? You know, we're all going to go in the end…" (pt24)*

> *"… (sighs) there's all these metaphors about fighting it and, you know, you've got to fight it and you'll win in the end. I don't like all of those because whatever I do, I'm not going to beat it." (pt12)*

Women's own role in communicating their diagnosis and prognosis was also widely discussed, in terms of challenges faced and choices relating to who they shared this with and in how much detail.

> *"…when somebody says to you, as we'll all say to people, 'how are you?' (Laughs) Do people really want you to tell them how you are, or do they want you to say, 'oh well, it's fine, you know, it's not a problem.' … So I've just tried to keep it as, you know, I'm feeling fine but secondary cancer means there's not a cure you know, so it means constant monitoring, it means, you know, it's always there …and probably…my husband is probably the only one really, I would, really go into it about…" (pt02)*

For mothers, sharing their diagnosis with children, of all ages, was particularly challenging.

"… that's where you get the difficult questions, so the, are you going to die questions, you know, is it ever going to go away? That's a much more difficult answer to give because, you know, with the primary diagnosis we were like, yes, you know, we're going to cut it off and it's going to go away and now we're like, oh it's back…and it's a balance between not wanting them to be worried all the time but not wanting to…lie, you know, it is really difficult." (pt36)

3.8.2 Adjustment

Adjustment was a theme which transcended the data, bringing together significant aspects of life with SBC. Sudden and ongoing physical and psychological adjustments were evident throughout women's experiences, as they described the inherent uncertainty of their cancer and prognosis.

3.8.2.1 Ongoing treatment

The presence and influence of treatment on daily life was central to this theme. Women described variable periods of stability across a variety of treatment pathways, some facing more frequent side-effects and adjustments to their regime than others.

"…well I started off on Capecitabine tablets, which I only managed five days of or something. I had too bad a reaction. I then had Paclitaxel which worked really well and I was on that for six months, but then I had six months like remission, erm… and then I've been on Eribulin since January so six, seven months on Eribulin, which worked for a little bit but then I went on to Abraxane." (pt16)

Women expressed an underlying awareness of the finite efficacy and supply of treatments. Some remained positive at the prospect of ongoing changes, whilst others found this more difficult to come to terms with. Treatment adjustments brought concern about remaining options, but also worries relating to new side-effects, well-being and ability to cope.

" …so the chemo's doing its job, but in the back of your mind it's always (gasps) what if I go next time and it's not? Then you've got to look at another…you're always thinking, what if I go next time and they say, oh well actually, you know, the liver uptake is more so we now have to look at something else, because then in your mind, it's like oh, we're having to look at another one after a year of treatment, then that's taken away another option…" (pt02)

3.8.2.2 Psychological adjustment

More broadly, a diagnosis of SBC precipitated wide ranging emotions and psychological adjustment. Women described experiencing a host of different emotions at the point of diagnosis and over time. These ranged from shock and disbelief, to distress, grief and devastation, and times of anger and frustration.

"It does make me feel… I don't get tearful often because I'm very positive, but I do have moments when I get tearful, and I get quite annoyed when I look at my little boy and I'm like 'grrrrr!' (frustration) you know?" (pt35)

Different emotions appeared to rise and subside over time, in line with fluctuations in their disease and prognosis.

> *"One minute you're getting aggravated in a car park because somebody's just pinched your space, you know, just like everybody else, and then you know, the next minute you're in floods of tears because you've got some new symptom or something's shown up on a scan or some friend's just deteriorated or something." (pt21)*

> *"But we try and stay as positive as we can, you know, and we do, don't we? We get a bit upset if something's given to us that's bad. We'll have a couple of hours of sobbing, you know, and then you put that to the back of your mind and you get on…" (pt29)*

Reaching acceptance also appeared to be an ongoing and shifting process, evolving over time and with perspective.

> *" …when I was told it has gone to secondaries, you know, it is a shock and you do feel that you, that you know, you're walking along a pier ready to jump off or a cliff head ready to jump off and you get the feeling as if, oh, at first I thought, oh you're going to die, we won't bother with you, you know, we'll look after those that we can cure …which obviously is a bit extreme and now I know that isn't the case." (pt01)*

> *"It hangs over you, she says [friend previously treated for primary BC]. She says it's never out of your head, that it might still be lurking. And I describe it as, I don't have that shadow, because I know it's not lurking, I know it's there. I'm not worried about it coming because it's already, it's a part of me now." (pt37)*

Yet acceptance was not a universal experience. Though some women described adjusting to uncertainty, others struggled to adjust to or accept their new outlook.

> *"… obviously nobody can give you a genuine guarantee of anything, which I totally get, and I don't want a genuine, I don't want a definite diagnosis, the other way, so actually having an uncertain diagnosis is a good thing, yeah (laughs)" (pt36)*

> *"This is a death, you know, this is a death sentence now. Now I'm not accepting that, of course but you know, if, from their point of view, it's just a matter of time." (pt14)*

3.8.3 Self-awareness

Self-awareness was another resounding theme, expressed in women's attentiveness to their physical and emotional states and needs, as well as the impact of SBC on the lives of themselves and others.

3.8.3.1 Recognising & responding to side-effects

This was most evident in women's recognition and self-management of side-effects. Indeed, with treatment ongoing, side-effects represented a significant discussion point and were a regular, if not constant, presence in women's lives.

> *"Lots of joint aches and pains, with each of them really. I've had a succession of three hormone treatments and each time it's been joint pain and stiffness and some nausea,*

bad stomach, constipation…and Tamoxifen I've found has made me put on weight…" (pt12)

"I think you have side-effects with everything, and you have it for 2 weeks and then you have a week off and you're just feeling really good again, and then you come back! (Laughs)" (pt29)

Whilst some women were mindful of side-effects, others appeared more acutely aware. This largely related to how burdensome these were and the extent to which they affected their daily life.

" I get some hot flushes but not erm, you know, not all the time, not that they're disturbing my life, you know, it's just a case of oh I'm having a bit of a hot flush, I'll take my cardigan off or something!" (pt01)

"I mean the main one is tiredness really… I always feel awful saying, 'oh I'm tired' but it's like a different kind of tired…I always describe it as like, wringing out a dish cloth so you're like, your energy is the water and you wring it all out until there's none left…" (pt33)

Side-effects were frequently described as being difficult to discern from symptoms of cancer and other health conditions. Unexpected or unrecognised side-effects were also a source of confusion and distress.

"Oh (sighs) all sorts…and this is really where I feel you need some help, really, in terms of advice and support because you never really know whether what you're suffering is a side-effect of the chemo or is caused by the cancer." (pt16)

Differing experiences of side-effects across various treatments were compared, with women's developing awareness of tolerability and toxicity. This also led to the anticipation of side-effects, which did not always match with reality.

"… well I suppose I've been a bit of tenterhooks thinking, you know, when are these side-effects going to kick in and you know my specialist nurse said, you know, you might not get them (laughs) yeah so, I'm quite relieved that nothing too terrible has happened just yet…" (pt22)

3.8.3.2 Coping and support

Women were, however, aware of the self-management and coping strategies which worked best for them, whether self-directed or drawing expertise from elsewhere.

"… having the pain every day, it reminds me of what's going on all the time, you know, whereas if I've got pain, I can control and I'm busy doing other things then I can, I can just get on easier." (pt06)

"Mostly I, yeah I mean I tend to have a little google! (Laughs) and then sort of work out for myself…But, you know, there's always another appointment coming up within three weeks or less so I tend to wait if it's not something I'm really alarmed about." (pt21)

They often self-assessed their need for support, understanding their needs whilst being aware

that these may change over time in line with their disease.

> *"…No, I don't really feel the need to really. I don't feel the need for any sort of support groups or anything because, you know, I've got my friends and my family and that. If I did, I would, you know, I would access them but I don't really feel the need." (pt24)*

3.8.3.3 Reactions of others

Women were also acutely aware of the emotions of loved ones and those around them, discussing the wider reaching psychological impact of their diagnosis.

> *" …my little boy won't ask me any questions because I think he takes his, kind of, emotions from what is actually happening, so whilst I'm well and I'm running about on a football field with him and life's normal and I'm at work, he just, I think that's enough for him, whereas my daughter is now coming up to 12 and she gets it, you know, so she understands it and that is difficult and…so she worries when she knows I'm about to have a, a test or a scan…" (pt36)*

Yet, there was a general consensus that support for others was lacking, with women often taking on this supportive role themselves. Some women also discussed regulating their own emotions and responses to protect those around them.

> *"… you're the one really having to cope with everybody else's emotions and, I mean obviously you have to cope with your own, but then you're having to cope with theirs as well…and probably my way of coping with my husband's emotions, I'm going to say, is probably by being positive." (pt37)*

In relation to this, women were aware of how others perceived them and how 'visible' their cancer was, expressing different emotions towards peoples' reactions and expectations.

> *"I'm in the situation where my hair's growing back quite nicely, quite thickly…so things like that make you feel better, and people say, 'oh you look so well! You look so well!' You know and that's, you know, that positive vibe that you try to portray and gets fed back to you does help your mood, yeah." (pt01)*

> *"…now I'm on this chemo, and have been for two and a half years, and yes, I still have to go to the hospital every three weeks, I still have to have the blood tests I have to do all the waiting around, it makes me feel rubbish for a week, but I've still got my hair and so people think, you know, I'm not on chemo and they think ooh she's in remission or 'ooh, are you cured now?" (pt21)*

3.8.4 Living with incurable cancer

This theme encompasses women's reflections on living their life with SBC. With no end to the story, and for some no discernible beginning, women discussed the reality, both practically and psychologically, of a chronic cancer trajectory.

> *"…it's always there and you know, you know things, a simple thing like planning a holiday, right when am I going to get my chemo tablets? Because you can't get them*

way in advance because they've got to do the blood test, so that affects you… that might sound trivial but it's part of your everyday life…" (pt02)

3.8.4.1 Outlook

Women's underlying perspectives and mentality appeared to significantly influence their outlook and ability to live their lives. Many discussed maintaining a sense of positivity, for themselves and others, trying not to focus on their cancer, living in the present rather than looking to the future and simply 'getting on'.

> *"…I'm very much of the opinion that I've got a limited life expectancy but that doesn't mean I can't sort of enjoy what I've got. So, I don't, I've never let this get me down, because at the end of the day I think that would waste my time that I have left, if that makes sense." (pt37)*

The success of treatment, in part measured by how 'well' women felt and appeared was another key factor.

> *"…now I'm on a different drug so they, they've changed that and that seems to be working okay. So, you know, I feel reasonably healthy. Everybody says I look well so… so when people start saying I'm not looking so well, I'll think oh gosh, the cancer's getting worse! (Laughs)" (pt15)*

3.8.4.2 Seeking health & normality

For some, looking ahead meant making positive changes and optimising their health. Others focused on a return to normality. For those able to continue working, this was discussed in relation to feeling 'normal' and maintaining a sense of purpose.

> *"…people say oh you're mad, you should have just taken the time off but actually that wasn't what I wanted to do, you know, that would have made me feel more ill. So yeah, so for me, staying at work has been part of it, of keeping going and, yeah, keeping sane…" (pt36)*

3.8.4.3 Reminders of SBC

In contrast, visits to the hospital and the realities of living with cancer caused disruption to this normality. Women discussed the practical challenges, the time burden of appointments and treatment, and the difficulties of balancing these with day to day life. Those working described needing significant support and understanding from employers, though experienced this to varying extents.

> *"…when it was all stable and, you know, I was only having to see the oncologist every couple of months or whatever and, you know, maybe a scan every 6 months, it wasn't too, it wasn't too onerous really but more recently it's been, you know, I've been spending far more time at the hospital than I would like…" (pt25)*

The regularity of scans also had great significance, posing both a physical and psychological disruption, acting as a reminder and source of fluctuating anxiety. On the other hand, they could also provide much needed certainty and reassurance, allowing women to look ahead.

> *"It does make you a bit nervous, but on the other side you walk out and you have that, if everything's still alright, you can breathe for the next six months and think we'll plan the next six months now (laughs) so yeah." (pt36)*

For some women, seeking out information and support also compromised their ability to live life as 'normal'.

> *"I obviously joined the community on Macmillan, put something up on there and got some replies, got some other women with metastatic cancer to talk to…not so much now because I feel like I'm just getting on with my life and I'm living with it and I think, I'm not looking to that…I'm not letting, trying to not let it take over and consume me…" (pt35)*

3.8.4.4 Managing uncertainty

Despite differing perspectives and coping strategies, fear of progression and future uncertainty were clear, ongoing concerns, whether in the background or at the forefront of women's minds. Some women wanted to face these longer-term uncertainties, whereas others preferred to focus on the present. For those looking to plan ahead to more difficult times, loved ones were not always receptive to their wishes.

> *" …you just take it day by day, you know, day by day and then hopefully at some point you feel like it's week to week and then hopefully at some point soon after, it's month to month and then maybe even year to year and you just kind of try and build up the momentum as best you can…" (pt24)*

> *"You know, at some point, those treatments will run out and I… well, I think things might be going that way at the moment and it's difficult to find someone to talk to about more serious matters, you know, like, well… death, dying. My husband doesn't want to broach that subject, whereas I would like to… not in a particularly morbid kind of way but just in a sort of practical sense of it." (pt06)*

3.8.4.5 Practicalities & facing life decisions

In living alongside their cancer, women also faced reassessing their priorities and making life decisions much sooner than anticipated; some felt forced to give up work, others felt their focus needed to be elsewhere. Regardless of age, finances, from hospital car parking and holiday insurance, to ill health retirement and pensions, were a key concern.

> *"… I kept asking at the beginning, you know, how do I live? How do I live with this? I don't know how to live because how do you prioritise? … you know, I could have packed in work, I could have packed in everything, and just spent time with my family, and that would have been quite inappropriate, because actually I've had eleven years*

of, you know, relatively good health…and even now, you know, should I continue working because do I need to keep paying into my pension pot?" (pt21)

3.8.4.6 Coping with chronicity

Burden of symptoms and weight of concern varied for women across the trajectory. Whilst some felt able to continue with life, others expressed a sense of physical and/or psychological exhaustion. This was also apparent when women discussed the chronicity of SBC; some saw this as a comfort, whilst others expressed it as more of a weight to carry.

"I always sort of said you know, you sink or swim (pauses) but then now I think, well sometimes you know, you might have to float a little bit, because you can't always keep swimming, because it's absolutely exhausting…" (pt20)

"…I'm dealing with it forever now so I think you've got to talk about those other things… so yeah, it's not like… there's no beginning and end to this in the same way as there was first time."(pt04)

3.8.5 Connection to care

Finally, women's connection to care was a central theme which resonated throughout the data. This encompassed both healthcare professionals and the healthcare setting, to which women expressed varying physical and psychological connections across their trajectory.

3.8.5.1 Experiences of healthcare

Experiences of healthcare appeared to influence the forging and strength of these connections. Positive experiences related to the availability of expert, tailored support, whether within or between appointments, timely referral and initiation of treatment, and holistic considerations. Negative experiences centred around women's concerns of not being taken seriously, lack of support to address their needs and unnecessary delays. Some also discussed their experiences in relation to perceived limitations in NHS resources and remit.

"But you, know, they're understaffed and they've got too many patients. They haven't got the staff to cope, so I understand that…" (pt08)

A medical focus, to the neglect of alternative or complementary therapies, was repeatedly discussed. Whilst their tie to 'conventional' management remained, some women felt that more treatment options would be available to them if their doctors, and the NHS more widely, were able and willing to consider non-pharmacological options.

"I do the mainstream stuff, and some people choose not to do any of that at all and I'm not going down that route, but it is interesting to listen to because they have a very different perspective from the mainstream and I think that's overlooked… and yeah okay, maybe my oncologist kind of rolls her eyes when I say what supplements I'm on and things but to me…it gives me some sort of, kind of control that I feel that I'm doing something by adapting my diet…" (pt09)

3.8.5.2 Roles and remits

The roles of different health professionals in women's past and ongoing care were also defined. For the majority, GPs were most involved around the time of diagnosis, with women subsequently feeling more strongly connected to the hospital setting.

> *"…I mean, I get my Letrozole from the GP practice but very much on a repeat prescription basis…and there is a GP who I did speak to reasonably regularly when I was just diagnosed, but now I would say that they leave everything to the hospital ... although, I mean I know I could go down there if I need to, it's not, it's not an either or thing but in practice, yes, I suppose I feel I know the oncologists better…" (pt04)*

The CNS role appeared to be more central to care and support in primary breast cancer. Yet, where women had been allocated a CNS in SBC, they generally represented a key and highly valued source of support, distinct from that provided by other clinicians.

> *"The nurses do have more… they have more sort of practical, useful suggestions perhaps, than the doctors in the clinic, you know? Who maybe, they've just got focuses elsewhere, perhaps, I don't know, on the medical picture rather than how to get through day to day problems." (pt06)*

In some exceptions, women chose not to access support from their CNS, either because they felt that they did not need the support or they preferred to seek it elsewhere.

> *"But I, I haven't actually needed the, the extra support or input from them… so, if I haven't been in touch with them, it's because I haven't needed to…but I do know that they're there…" (pt28)*

Those who did not have access to a CNS tended to raise this as a significant shortcoming in their care and support; in some cases, this was felt by those assigned to a nurse working across primary and secondary stages, as well as for those lacking any CNS at all. There was also an appreciation of the impact of under staffing and high patient numbers on the ability of specialist nurses to deliver the required support.

> *"I think that you should have more of a, there should be a designated metastatic breast nurse, rather than just a breast care nurse yeah…because I think it is different, because you go from being curable to just treatable and that's the terminology they use and I think, yeah we are treatable but we're not going to get any better and our life is now going to be treatment, treatment, treatment of some sort, scans of some sort. You know there are, you need a different kind of support…" (pt35)*

> *"…it's not their fault, I think they're just overwhelmed to be honest, and probably resources are limited and because I don't demand help, I do things on my own and I do cope…I don't know if it's because they overlook me or there just isn't that support…" (pt09)*

Many women described being actively engaged in their treatment and care. For some, this involved collaborative discussions and decisions shared with their oncologist.

> *"The doctor and I both decided that unless the tumour markers went up, because after three months the tumour markers were fine and they've never gone up since, that we wouldn't bother doing any scans unless I was symptomatic…" (pt24)*

For others, differing priorities or perspectives meant that active involvement led to more conflicting interactions.

> *"…and I talk to my oncologist about all sorts of stuff and she sort of like, it's almost like she goes, 'oh god, here we go again, what have you been seeing on google?' Do you know what I mean? And I think that's not really helping me and a lot of the stuff that I do does help me…" (pt09)*

Some women took a less active role, preferring to trust the expertise of their oncologist.

> *"Oh yes, yes, I'm the sort of person, I would take the, what, what those in charge recommend, I would always accept that…" (pt15)*

In some cases, patient-oncologist interactions, and the extent to which women sought involvement and information during consultations, was influenced by perceived time pressures.

> *"….we as patients sometimes think, oh the oncologist is busy and they're spending so much time telling you what's been discovered, and then talking about the treatment, so anything else you might be thinking you feel, oh I'll leave that 'til next time or, you know, I've already been in here half an hour, you know, my time must be up." (pt02)*

Whilst for some, health professionals remained their primary and preferred source of information and support, others seemed to lack a sense of connection or belonging, feeling as though they fell between or outside health professionals' remits.

> *"They had a breast care nurse for primary but they didn't have one for secondary. So, I was kind of not in her remit anymore… but I wasn't in anybody's remit." (pt01)*

> *"…and one of the problems I think, when you've been a secondary patient for a while, you're likely to have more than one consultant because you have, you develop different problems…so with that, I find, is that you tend to fall between stools. Everyone gets very blinkered." (pt08)*

3.8.5.3 Pathways to support

A similar divide of sorts was observed in relation to pathways to support. For some, additional sources of support were provided via connections to the healthcare setting. Others sought these out independently, whether through choice or out of necessity.

> *"Yeah, it's what I have to do yeah…because I don't get any other support otherwise, everything is what I've sorted out for myself." (pt09)*

A number of women discussed seeking additional support from palliative and hospice services, whether self-referred or guided by health professionals.

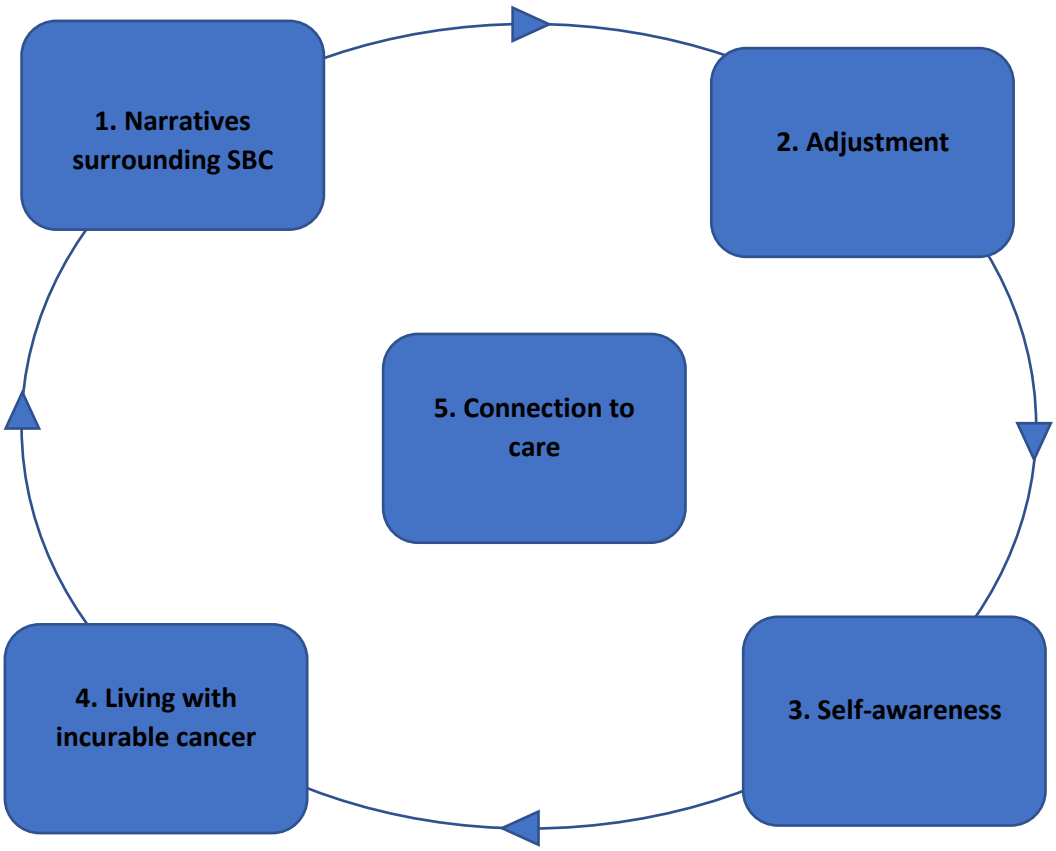
"My clinical nurse specialist put me in touch with the local hospice, so I've had a meeting with them, just to discuss what services they have and how they might be able to help me some point down the line…they've offered you know, they have counselling services, support groups and so on…" (pt23)

3.8.5.4 Ongoing ties to care

Alongside the physical, more 'visible' ties of regular contact for appointments, monitoring and treatment, there was a sense of needing expert reassurance outside of scheduled contact, a more 'invisible' tie to healthcare felt during times of heightened uncertainty or anxiety. Some women expressed a feeling of 'disconnection' from support, particularly out of hours.

"…it's really difficult for the doctor to say, if this happens, then do this, if this happens, then do that, because there's so many different variables so, and then because we can't speak to the breast care nurses you know, straight away, you know we're kind of left hanging thinking you know, well it's Friday, Friday afternoon, but they're probably not going to get the message until Monday or they're not going to ring me back until Monday, you know, and I don't know what to do over the weekend…" (pt25)

Figure 3.2 Thematic map: The perspective of women living with SBC



3.8.6 Thematic overview

Figure 3.2 displays the interconnection of themes. Women's surrounding narratives, their need and capacity for adjustment and their level of self-awareness continually shift and evolve as

they navigate the challenges and uncertainties of living with incurable cancer. Their connection to care is central; the strength of the connection fluctuates over the course of the trajectory, yet their ties to (and dependency on) the healthcare setting always remain.

3.9 Stage 2 results: Health & charity professionals' perspective

These five core themes, identified across women's experiences, were supported and supplemented by three key themes across the professional dataset.

3.9.1 The key timepoints

Across an extended disease trajectory, professionals described key time points where higher-level information and support was needed.

3.9.1.1 Times of greatest need

From an oncologist's perspective, two clearly defined timepoints were a focus for support. These centred around the initial diagnosis and the point at which no further, active treatment options were available.

> *"… at those critical points, the diagnosis of metastatic disease and when we're having the discussion that we have exhausted effective lines of treatment, I think that's somewhere where…I think, I feel very conscious that we have quite, hopefully quite good discussions with patients but even then, even, no matter how good the discussion is with the patients, they're going out of what is essentially an office and into, back outside into a different world, you know…" (pr12)*

Support needs at, and immediately following, the diagnosis stage were widely discussed. Professionals described supporting patients in understanding and coming to terms with their diagnosis, as well as addressing more immediate issues and identifying potential future needs.

> *"I basically bring them back to a nurse led clinic, you know, a couple of weeks afterwards, just once all the dust has settled and basically run through sort of all the, you know, what we need to do and what their needs are, if I need to signpost them anywhere, so I basically, I will reiterate what we have done in the initial diagnosis clinic, so we talk about the diagnosis, treatment intent, treatment options, how we will manage them, you know, through their journey…" (pr06)*

3.9.1.2 Fluctuating needs

Those in nursing and charity support roles also described a host of ongoing, fluctuating times of supportive need right across the trajectory. These encompassed times of heightened psychological distress and uncertainty, as well as physical complexities such as increased symptom burden and disease deterioration.

> *"… we're monitoring them very carefully, but there's always that hanging over them and it's, it's a question of managing those emotions, those negative thoughts but also being, giving them realistic conversations, so if their cancer unfortunately does*

progress, particularly in the triple negative breast cancer patients, it's getting them through the hurdles and their scan, yes, you know, shows the disease has got worse, it's become resistant to that particular drug. Okay, let's see what other drug we can put you on…" (pr11)

3.9.1.3 Targeted support

Professionals recognised key points where patients will need, and be receptive to, particular sorts of information and support.

"…what I will do is, if they are having a lot of ongoing symptoms, that's a nice way to refer through to our community colleagues because symptom control is their sort of bread and butter…" (pr06)

"…so it's very much knowing your patients and judging and assessing when the time is right to be able to explore that and have those open conversations… it's a question of building trust, their trust, rather than rushing in …" (pr11)

Overall, there was a sense of patients having varying disease trajectories yet sharing similar, critical timepoints where support (from either clinical or charitable sources) was most needed.

"…well I think it's helpful for patients to know that there will be these two phases, hopefully, of living with cancer for a longer period, and dying of it for a shorter period, and that we can maybe tailor their information needs to that, that particular stage of, of their disease…" (pr12)

3.9.2 The individual

Both health and charity professionals emphasised the importance of recognising women's needs as a collective, in terms of SBC specific support, whilst also recognising the needs of the individual.

3.9.2.1 Shared needs

Discussing disparities in the support available for early versus later stage breast cancer, professionals highlighted where women's collective needs remained unaddressed.

"… they don't realise that they can come into one of our primary breast cancer clinics and have help with supporting their symptoms… you know, a lot of self-help things, and that's, that's very much flagged up with primary breast cancer patients but with metastatic, I think there's always the assumption, 'oh no they won't be interested' or, 'oh no, they've got bigger fish to fry' with treatments and just being alive… no, actually." (pr11)

Professionals also discussed psychological supportive needs as being of huge, shared significance for this group of patients as a collective.

"So, I, I would have said psychological is really the main one, the, the fear…not knowing the prognosis and living with uncertainty, definitely. They're the ones that patients tell

me often…not knowing what the future holds, really, how that looks or how long…making plans and how long they've got to make plans for really…" (pr05)

In relation to these shared psychological needs, the idea of shared spaces, specifically for women with SBC, was also discussed.

> *"… if they had somewhere that they could actually sit that was separate, they felt that they might be able to break into conversation with other people with secondary breast cancer but, as it was, in the clinic, they didn't want to speak to the person sitting next to them in case they were, you know, somebody that was hoping to be cured of their breast cancer and scare them…" (pr07)*

3.9.2.2 Individual diversity

Yet significant diversity within this group was also evident. A wide array of factors were identified as influencing women's supportive needs and preferences, relating to both the individual and the context in which they experienced SBC. These included sociodemographic factors such as age, family structure, employment status and where they lived.

> *"…we cover topics that perhaps can often be more relevant to younger women. Things like talking to children, fertility, relationships, erm…work and finance, you know, they're relevant to everyone, to a lot of people, I don't like to assume it's just younger women but I think it's fair to say it may be more likely to be relevant to people in that age group." (pr01)*

Biological and physiological factors were also highlighted, with individuals' experiences of disease varying in accordance with the cancer's receptors, sites of metastases, disease burden and response to treatment. As such, SBC was discussed as almost a subgroup of diseases, leading to diverse individual experiences and supportive needs.

> *"…their physical needs can become very complex, particularly when they've got a lot of what we call visceral disease, where it's in their main organs, particularly if it's in the lungs and the brain…bones, you can manage that reasonably well …for instance, patients with bone only disease, they're very much infrequent visitors to the trust because they are living so well, but they're kind of a minority that don't really…get soaked up too much in terms of support so now I've started conducting telephonic clinics to, you know, just maintain contact with them…" (pr11)*

Individual preferences and support seeking tendencies were also emphasised.

> *"…you know, going online and finding things which, you know, it's great because some of the information is invaluable… But I think that, I also think that it really depends on each individual because I think for some people it's really helpful, but for some who are quite anxious, I think that sometimes they can drive themselves mad with all the grim stories that are out there…" (pr06)*

> *"…Some patients are more proactive than others in contacting us and it is a difficult balance because we don't, or personally I don't like to sort of push myself onto somebody who may not want my input because when they're not at hospital, they might be trying to just get on with life as normal as possible…" (pr07)*

3.9.2.3 The patient's perspective

Individual perspectives also factored into patients' care and support, though these were not always in line with professionals'; this was apparent across a number of treatment related discussions.

> *"…we can kind of reduce the dose or support the symptoms and it's about changing treatment if it's really not suiting somebody. It's very difficult because I know people want to keep taking the tablets because it's treating the cancer that's killing them, if you know what I mean, yeah…" (pr05)*

Yet the involvement and consideration of the individual, and their QoL, in treatment decisions was clearly a shared endeavour and key element of patients' care and support.

> *"…it's a pretty continuous process and there isn't, it's not a, it's not defined by easy packets of time, so I tend to encourage them to get, to do what they want to, if they want to go away on holiday or trips, then we will be flexible about when we treat patients, in terms of skipping a treatment or delaying treatments and so, as I say, trying to avoid them, their lives revolving around the treatment…" (pr12)*

3.9.3 The ideal model of support

Professionals across the charitable and clinical settings discussed elements of an ideal model of support, required to meet the complex needs of women living with SBC. These encompassed the timely recognition and delivery of personalised, targeted support.

3.9.3.1 Ideal vs reality

For some, this ideal was very much the reality of the support they provided or shared in the delivery of.

> *"I think the hospital I work in, they are very well served and that's certainly the feedback I've got, and I'm not bragging, I'm just saying…when I meet with other secondary breast cancer nurses, you know, the patients really, or even nurses who are primary but are looking after some secondary breast cancers, they say, you know, there's, these women with secondary breast cancer are just not being supported…and certainly the trust I work in, you know, we definitely have made in-roads into supporting them and it's proof of the pudding really because the calls have dramatically reduced, the admissions have reduced…" (pr11)*

Others identified gaps or barriers to this delivery, highlighting where support for this growing group of patients was less than ideal.

> *"I think the self-management thing and the self-navigation thing is a forced thing rather than…because you know, it's just evolved into the way of, for those people that are able to do that, you know, that's what they spend their time doing because they have to do that because nobody else will do it for them…" (pr02)*

3.9.3.2 Elements of ideal support

Looking at this more closely, the CNS role was highlighted as both central and crucial to the delivery of an 'ideal' and complete model of support. For those working within this role, broad and varied descriptions of the extent of support which they provided to their patients demonstrated the significant shortcoming faced by those without a CNS.

> *"I'll see them from the point of diagnosis and offer them support about sort of helping them to understand what's happening and providing information that is, suits them as an individual if you see what I mean? As much information as they want…and then that also leads on to assessing sort of holistic needs and then signposting to services…" (pr05)*

CNS presence aside, charity professionals described a host of supportive services and sources, to which all patients could be signposted. In their experience, these were ideally delivered as a complementary pathway, with the input and support of clinicians.

> *" …you find it's very hard to convey that in a poster, or in an article or on a website, what helps is when there's an oncologist or a nurse giving some encouragement, some reassurance about what to expect…but we like to think of it as a two way thing. So when we plan our programmes, we always work with the nurse led teams …" (pr01)*

It was recognised, however, that in some cases, charitable services bridged a gap in support.

> *"You know, some hospitals are great at providing information about symptoms already and, you know I think one gap is sometimes those wider needs because they're so varying and hospitals are so busy, it's very hard for them to always look out for all of those things themselves, and as a charity, it's our job to help them do that." (pr01)*

Another key element of well-delivered support appeared to be its multi-disciplinary nature, drawing expertise from within the clinical oncology teams and beyond.

> *"I also liaise with a lot of tertiary teams, work very closely with them so again, we're all singing from the same hymn sheet, so that the patient's needs are fully met and that also includes working with, for instance, citizen's advice who process benefits and things like that on my behalf as well as the community palliative care team, I work closely with them and the GPs or district nurses… it's quite a big group of professionals that are involved with these patients because they are by nature very complex in terms of not only their physical needs but their emotional needs as well…" (pr11)*

The ideal model of support, in terms of the services signposted towards and referral pathways put in place, was also emphasised as needing to be driven by patients' own priorities.

> *"I've started using this phrase with them, that they're living with their cancer, not dying from it, and that I hope, rather than me then defining what it is that's important, that defines as, you know, living, getting on with their life, that leaves them to establish what it is that matters to them, whether it's, you know, looking after grandchildren, going out, so physical, social activities…" (pr12)*

3.9.3.3 Barriers to support provision

Professionals discussed hospice services and palliative care teams as being ideally placed for providing expert, individualised symptom management support across the trajectory. Yet there was strong consensus as to widely held misconceptions amongst patients, causing reluctance to accept this sort of support.

> *" …even, only in the last 7 days, I've had a patient who would really benefit from their services but has recoiled from the thought of a referral… so she's agreeable to go to a GP but not agreeable to the referral to the palliative care team." (pr05)*

> *"I tend to broach that subject with them, that there will generally come a point where we will refer them on to the community team as well, mainly because I suppose most people still think, if you think hospice, everyone thinks, oh my god! They're carting me off to die!" (pr06)*

The most significant barrier to achieving an ideal model of support related to a lack or limited availability of specialist support, namely in the form of assigned CNSs and access to psychological support. Further barriers included time constraints, whether actual or patient-perceived, reluctance to accept support and a lack of awareness of available services.

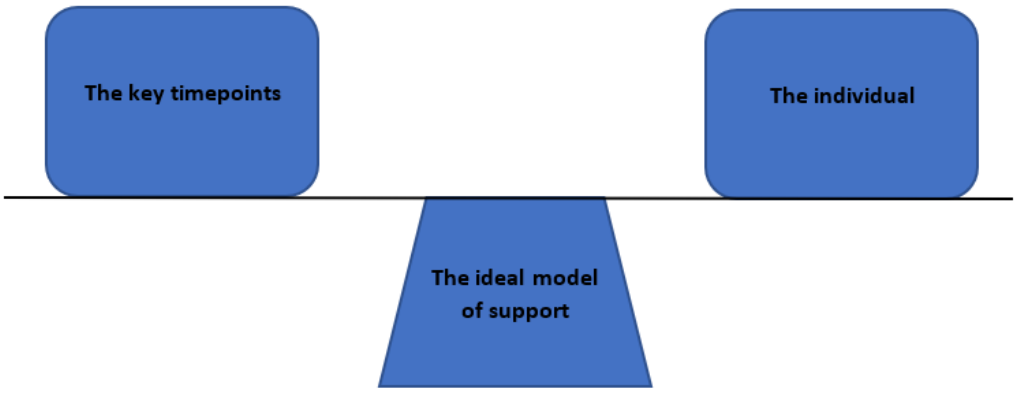
> *" …there's a fairly strong feeling amongst us that, that patients, not only should expect but deserve and indeed they are being failed if they don't have a breast care nurse there when they are told that they've got breast cancer…" (pr12)*

> *" …what is always interesting for me is that sometimes patients don't know about information, where the hospital might assume that they know about it, you know, it might be that they might be able to provide a really good benefits advisor on site and yet the patients don't, just don't know they're there." (pr01)*

3.9.4 Thematic overview

Below, Figure 3.3 brings together the core health professional themes, illustrating how provision of the 'ideal' model of support is intrinsically dependent upon the individuality and timing of supportive needs. Where this equilibrium falters, the 'ideal' is compromised.

Figure 3.3 Thematic map: The perspective of health & charity professionals



3.10 Discussion

3.10.1 Bringing together the patient and professional perspective

These dual perspectives provide both corroborating and contrasting insights into SBC from those managing its far-reaching effects both personally and professionally. Viewed separately, the thematic overviews displayed in Figures 3.2 and 3.3 tell the story from different angles: one from the perspective of those experiencing supportive needs and the other largely focused on support delivery. However, there are numerous close connections between these distinct sets of themes.

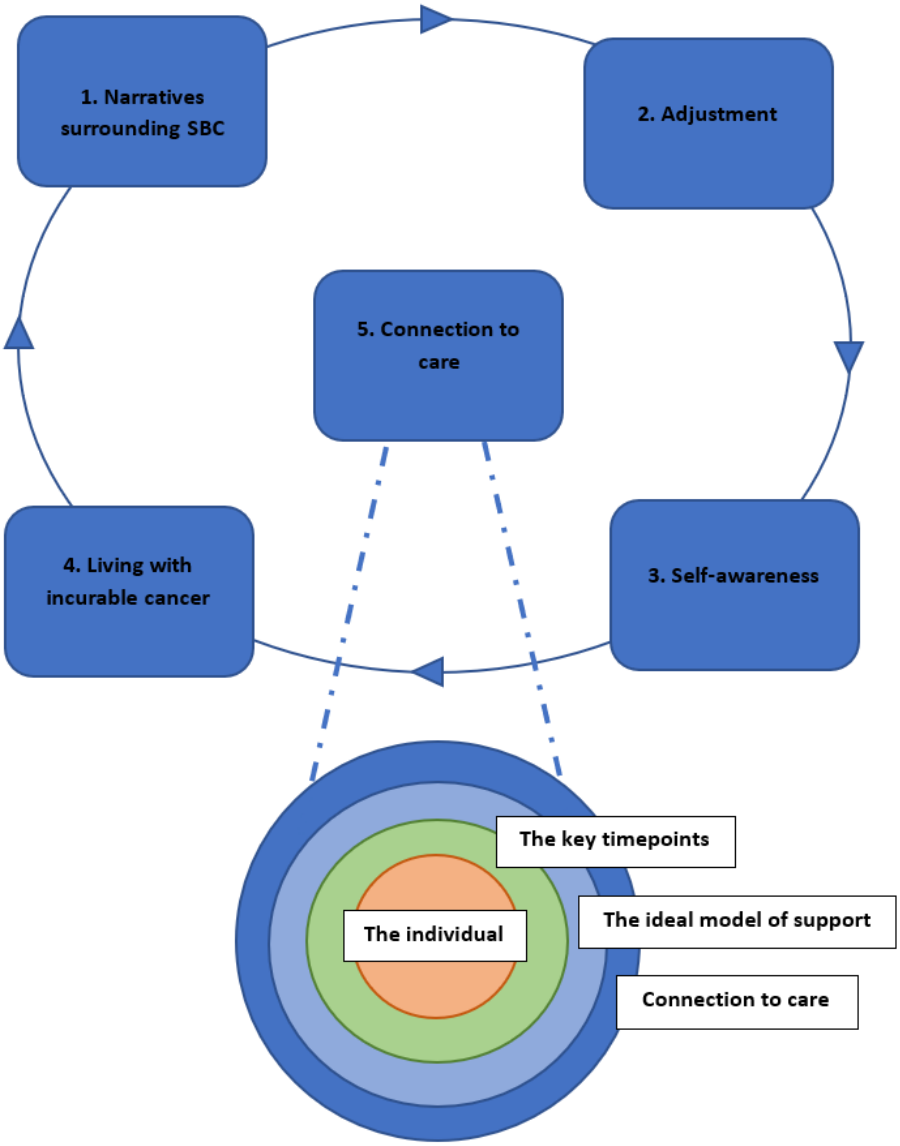
In qualitative research, Braun and Clarke emphasise the importance of including findings which do not necessarily align with what they refer to as 'the predominant story'.[178] In fact, in this study, the predominant story was one of diversity. Despite many threads of commonality, experiences of living with SBC (elicited first and second hand) were not necessarily collective. Opposing findings were reflective not only of the individual, and their personal narrative, but also the stage of their disease trajectory. This was evidenced in differing emotions, mentalities and levels of acceptance, as much as it was in contrasting experiences of symptoms, side-effects and treatment efficacy. Indeed, a psychological trajectory appeared to run alongside the physical disease trajectory, each governing the sort and extent of support required. The ability of professionals to support these women (in other words, to deliver an 'ideal' model of support) was dependent upon their ability to recognise and respond to stage-specific needs experienced by the individual. The needs expressed by women (whether current or anticipated) resonated in the observations of professionals; fluctuating physical symptoms related to treatments and disease burden were often experienced alongside significant psychological struggles. As well as being reflected throughout the findings of this study, varying concepts of different, shifting phases and trajectories in SBC, and chronic disease more generally, are widely reported across the literature.[53, 54, 184]

Uncertainty was a common thread, woven throughout the themes and evident across both physical and psychological domains. Indeed, it appeared to be experienced in different ways, at different stages, across varying trajectories. Women's narratives alluded to preceding uncertainties, taken forwards in their physical and psychological experiences of SBC, and shaping thoughts of the future. This reflects a breadth of research identifying uncertainty as a core experience in SBC, driven by its incurable nature, uncertain course and women's perceived lack of control.[61, 185] Professionals recognised this inherent uncertainty, describing supportive practice which aimed to address and mitigate this as much as possible. Support in a multitude of forms, whether information, expert reassurance or shared experience, had a clear

role in breaking or easing the cycle of uncertainty, with times of heightened needs ('trigger points') felt by women and targeted by professionals. This again supports the conceptualisation of varying and shifting SBC trajectories.

Below, figure 3.4 brings together the patient and professional perspective, highlighting the close thematic connections. Supportive needs (and the extent to which they are addressed) are shaped by the level of support and signposting received in the care setting, whether extensive or minimal, through choice or availability. Women's connection to care is therefore intrinsically linked to professionals' delivery of support, as well as being central to their overall experience of SBC, their 'story'.

Figure 3.4 Thematic map: Integrating the patient & professional perspective



However, these findings also illustrated numerous disconnects between the patients' and professionals' perspective. The first relates to the acceptability of support. Health and charity professionals consistently raised the issue of stigma surrounding hospice and palliative care services, reportedly shunned by patients worrying that such referrals signify a move towards end of life. Whilst these misconceptions have been reflected in the literature,[186] this wasn't necessarily the case for those interviewed. Numerous women discussed accessing these services, some even self-referring, and expressed a good understanding of the support which could be provided right across the trajectory. This could in part be reflective of the small study sample (some self-selected, all with an interest in improving available support) being more receptive to these services.

Yet, it also further highlights the importance of exploring the needs of the individual amidst the collective. This potential mismatch in the expectations of professionals and patients may inhibit timely discussions for women who would be open to, and would benefit from, earlier referral. Looking to the role an online supportive intervention could play, the delivery of education and information as to the potential value of such services could be key, to allow those with an interest in accessing these services the chance to do so at a time which is right for them. Similarly, health professionals discussed working closely and collaboratively with GPs. However, for the most part, women saw GPs' role in their cancer journey as being limited to the diagnosis stage. In fact, research has highlighted the significant level of follow-up care and support which can and should be provided in the primary care setting for longer-term cancer survivors.[187, 188] This disconnect could mean that women are missing out on potentially valuable community-based support.

The most starkly contrasting finding was the limited support reported by women without access to a specialist nurse, when compared to the breadth of support these professionals described providing to their patients. Similarly, though psychological needs were amongst the most widely reported (by patients and professionals), specialist psychological support, such as counselling and clinical psychologists, appeared difficult to access. Given nursing professionals described themselves a key source of psychological support, barriers will be even more profound where women do not have a named CNS contact. This very much reflects the findings of recent reports and research, which have highlighted the limited and inequitable access to expert support amongst women living with SBC across the UK, particularly those without an assigned CNS. With little improvement in the availability and funding of these vital health professionals in recent years, significant gaps in support remain.[26, 27, 77] This has been echoed in wider research, of SBC and of chronic cancer more generally; the support and communication of a key medical professional appears highly valued yet often lacking.[14, 170, 189]

3.10.2 Reflections

This study adds to existing literature by bringing together the patient and professional perspective, providing a more complete and up to date picture of QoL and supportive needs for women living with SBC in today's treatment landscape. It supports the wider qualitative research in this field, with many findings consistent, whilst also providing a much needed UK perspective. Evidence of both strengths and gaps in current support, drawing perspectives from both sides of the patient-clinician relationship and from across the UK, has highlighted how and where a tailored, online supportive intervention might fit. Through looking at this broad data set with a narrow-focus lens and applying in-depth coding, key information pertinent to intervention design was directly identified (as outlined in chapter 6). These went on to inform and shape the proposed intervention, development of which was able to begin in parallel to ongoing qualitative inquiry, balancing the aims and timeframe of the overall project. This two-stage process also allowed for a richer, more in-depth overall analysis, providing both an informative and a more abstract overview of the data.

It is important to acknowledge a number of limitations. Considering reflexivity, my own associations with the clinical setting may have influenced what some participants felt able to share, whether as patients receiving care in that setting, or as health professionals who may have felt that their practices were being judged. Though this may have partly been overcome through online recruitment, drawing participants from across the UK, the inherent self-selectiveness of this approach may have biased the samples towards actively engaged patients and professionals. Such individuals may well have differing experiences to those less likely to seek out research participation. Across both settings, women are more likely to have participated if they were in relatively good health, again potentially biasing the emerging perspectives and reported needs. The flexibility and breadth of the interview schedules, whilst a strength, led to vast and varied data sets which were largely analysed and interpreted independently. Though a second researcher performed double coding and sense checking of a sub-set of the data, differing perspectives and interpretations may have emerged with more collaborative analysis and ongoing consensus, with researchers less embedded in the surrounding literature.

3.10.3 Summary

This study has sought a multi-perspective and up to date overview of the SBC experience. Overall, there is a picture of diverse supportive needs and varying support provision for women across the UK. Ongoing fluctuations in side-effects and psychological struggles are pivotal experiences and targets for support. Support must therefore be tailored to, and available across, key timepoints and trajectories. With continued calls for healthcare services

to expand and improve the support they provide to these women at diagnosis of SBC and beyond, more immediate solutions to address the identified shortcomings and complexities in support are needed. Where connection to care and support provision varies, an online supportive intervention has the potential to bridge gaps and address unmet needs. Though it brings its own issues of equity, the internet is able to reach out to a wide population and provide a more consistent and universal level of support.[190-192] As will be further explored in chapter 6, women generally valued the internet as a widely available and accessible resource, able to supplement or bridge gaps in the support they receive. Related research in the field has also confirmed online routes of support as acceptable amongst women living with SBC and potentially capable of addressing their unmet needs.[167] The next stage of research, outlined in chapter 4, therefore explored *how* the internet and technology could be harnessed to address the diversity of experience and supportive needs identified in this qualitative study.

Chapter 4: A systematic review of online & technology-assisted interventions supporting QoL in advanced cancer

4.1 Chapter overview

Building on the qualitative perspectives outlined in chapter 3, this chapter will seek to determine how the identified supportive needs can be effectively addressed within an online intervention. To do so, it will draw on the existing evidence base, systematically reviewing trials of online and technology-assisted interventions in the field of advanced cancer. A breadth of intervention features and modes of delivery will be synthesised in order to guide the design and development of the LIBERATE intervention. Furthermore, evidence of intervention efficacy relating to QoL and psychosocial well-being will be explored, supporting the design of an intervention able to provide much needed improvement to the QoL of women living with SBC.

4.2 Chapter aims

- To outline the methods and rationale of a systematic review of online and technology-assisted interventions in advanced cancer.
- To narratively synthesise the available evidence, in line with the identified research question.
- To discuss how this evidence will guide the next stage of research.

4.3 Introduction

As highlighted in chapter 1, over the past decade there has been a proliferation in the development of interventions harnessing the internet and other technologies to support patients living with cancer.[88, 101, 193, 194] This has coincided with significant and ongoing advances in the treatment of advanced stage cancers, leading to an extended cancer trajectory increasingly likened to that of other chronic diseases.[11, 189] It stands to reason, therefore, that such technology could be harnessed to provide ongoing, tailored support to the many more people who are living longer with advanced cancer, potentially addressing a host of needs unique to this phase of survivorship.

However, focusing on the SBC context specifically, it would appear that such opportunities are yet to be fully realised. Throughout chapter 3, the extent of women's supportive needs became apparent, from physical symptom management to psychological support and signposting towards information and services. With access to the support of a CNS inconsistent

or lacking completely, more widely accessible, tailored provision is clearly warranted. Furthermore, the recent COVID-19 pandemic has highlighted the significant potential for, and need for continued development in, the remote delivery of cancer support.[195] For clinically vulnerable women living with SBC, the internet could now represent even more of a lifeline. In order to determine how these ongoing and evolving supportive needs can be most effectively addressed within an online intervention, an overview of the current evidence base is needed.

Within the qualitative interview study, both women and professionals expressed disparities in the support available in SBC compared to primary breast cancer. This is also very much reflected in trials of online supportive breast cancer interventions.[196-199] Relatively few interventions specifically tailored to or evaluated in women with SBC were identified during initial literature scoping and research question development. Yet, given widespread consensus of the vastly differing experiences of women in early as opposed to advanced stages of breast cancer, it was apparent that a focus on primary disease would not inform the wider research aims.[54, 58] The decision was therefore made to widen the focus of the review to all advanced and metastatic cancers. In doing so, the review aimed to harness evidence relating to the design, delivery and efficacy of online interventions in the distinct context of later stage disease. Furthermore, this systematic review represented a core component of phase I, aiming to complement qualitative research in providing a foundation of evidence to guide phase II intervention design, development and evaluation.

4.3.1 Previous reviews

Looking to previous systematic reviews in the field, a 2018 review of web-based interventions in cancer symptom management considered all cancer patients as one homogenous group. [200] Very few of the included studies evaluated interventions in the advanced/metastatic cancer context, hence findings and conclusions were early stage centred. Similarly, Corbett et al reviewed the acceptability of, and engagement with, internet-based interventions for patients across the whole cancer survivorship trajectory. [201] They concluded that further work is needed to better tailor interventions to the needs and characteristics of cancer patients at *distinct* phases of survivorship.[201] Two further reviews of online supportive interventions available to all cancer patients were conducted in 2011 and 2014. Not only were all stages of disease and survivorship encompassed, the interventions reviewed were found to be of uncertain efficacy and of varying and short-term benefit throughout heterogeneous study populations. [202, 203]

Given the gaps and shortcomings of this rapidly progressing evidence base, there was justification for an updated review of trial-based evidence with an advanced cancer focus. This

broad overview of evidence sought to guide the LIBERATE research in determining the different features and modes of delivery applied to deliver advanced-stage specific cancer support using the internet and other technology.

4.4 Aims

The aims of this systematic review were to:

1. Describe the design and delivery of online and technology-assisted interventions in the context of advanced cancer.
2. Explore their efficacy in relation to patients' QoL and other psychosocial outcomes.

On this basis, the following research question was defined: *'How can online and technology-assisted interventions be effectively delivered to support QoL in advanced cancer?*

4.5 Methods

Methods were conducted in accordance with Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines and the Cochrane Handbook for Systematic Reviews of Interventions.[204, 205]

4.5.1 Protocol

Prior to undertaking this review, a study protocol was established and registered with the PROSPERO international prospective register of systematic reviews (Reference: CRD42018089153). This is available at https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42018089153

Whilst there were no major deviations from this protocol, early formulated research questions were combined to give a single overall research question which captured all of the review's aims. Similarly, the early working title evolved to encompass intervention delivery, features and efficacy more completely.

4.5.2 Search strategy

A search for randomised and non-randomised controlled trials evaluating online and technology-assisted interventions in patients with advanced cancer was conducted in April 2018. Database specific searches were performed in MEDLINE, Embase, PsycInfo, CINAHL, Web of Science, Cochrane Register of Controlled Trials and ProQuest. Search terms combined both medical subject headings (MeSH) and keywords relating to the research aim. These included terms for advanced cancer (e.g. *advanced* or *stage IV* or *metastatic*), online and technology-

assisted (e.g. *internet* or *electronic* or *mobile*) and types of intervention (e.g. *programme* or *application* or *tool*). No restrictions on language or year of publication were applied.

An example of the full search strategy is detailed in Table 4.1 below.

The Journal of Clinical Oncology and Psycho-oncology, identified as key journals in the field, were searched by hand for any missing, relevant trials. Given the fast-paced, current nature of this research, journals were searched within a recent timeframe (2016-2018). Reference lists of key related systematic reviews were also searched by hand. An updated search was conducted in February 2019.

Table 4.1 Example electronic database search strategy

Electronic database search strategy (OVID Medline)
1. exp Neoplasm Metastasis/ 2. ((metasta* or advanced or secondary or stage 3 or stage three or stage III or stage 4 or stage four or stage IV or late stage) adj4 (cancer or carcinoma or neoplasm or malignan* or tumo?r)).ti,ab,kw. 3. 1 or 2 4. exp Smart Phone/ 5. exp Internet/ 6. (Online or internet or web* or electronic or mobile or smart or computer or virtual or social media).ti, ab,kw. 7. (mobile or smart) adj2 phone.ti, ab,kw 8. 4 or 5 or 6 or 7 9. exp Mobile Applications/ 10. (Intervention* or support* or program* or app* or guid* or tool or resource* or education*).ti,ab,kw. 11. (symptom adj2 (monitor* or report*)).ti,ab,kw. 12. 9 or 10 or 11 13. (random* or non-random*).af 14. 3 and 8 and 12 and 13

4.5.3 Eligibility criteria

The PICOS framework was used to define the eligibility criteria (Table 4.2) against which articles were screened for inclusion.[206] These criteria were piloted on a small number of papers and refined before initiating the process of study selection.

Table 4.2 Eligibility criteria

	Inclusion criteria	Exclusion criteria
Population	Inclusive of adults (≥ 18 years) diagnosed with any advanced or metastatic cancer (stage III or IV).	Studies exclusively targeting patients with early stage cancers or those treated with curative intent.
Intervention	Any form of online or technology-assisted intervention* designed to support patients with cancer.	Telephone interventions (where the main component of the intervention is the delivery of support through verbal discussion). Symptom monitoring interventions lacking feedback, support or guidance for the patient/user.
Comparator	Comparisons between interventions (e.g. online versus face-to-face) or with care as usual.	
Outcome	Effectiveness of the intervention assessed (as a primary or secondary outcome) through measures relating to QoL. This could be through a validated measure of QoL (e.g. EORTC QLQ-C30) OR other psychosocial measures related to QoL e.g. anxiety, distress, functional status etc.	
Study design	Randomised controlled trials (RCTs) and non-randomised controlled trials.	Articles which did not report primary data (e.g. reviews of trials).

**The term 'technology-assisted' refers to interventions using digital and other technologies which may not necessarily be web-based.*

4.5.4 Study selection

Reference management software (EndNote) was used to identify and remove duplicate studies before collating and managing all search results in Microsoft Excel.

Preliminary screening of titles and abstracts was initially performed (stage one), followed by full-text review of potentially eligible articles (stage two). A random sample (20%) of papers were screened a second time by the wider research team (FK, CH, KA). Where clarity was needed in order to determine eligibility, authors were contacted for further details. If, after two weeks, there was no response, articles were excluded on the basis of insufficient information.

During stage 1 screening, a clear consensus as to the definition of the term 'cancer survivor' was lacking. As previously discussed, survivorship terminology is similarly broad throughout

the wider literature, though there is growing acceptance of the NCI's definition of a cancer survivor as being a person living with and beyond a cancer diagnosis, from the point of diagnosis until the end of life.[6, 7] Papers with titles and abstracts referring to participants as 'cancer survivors', with no further details of staging, were therefore reviewed in full to determine eligibility.

4.5.5 Data extraction

Following Cochrane Collaboration guidance for the process of data extraction,[205] a template was developed in Microsoft Excel. After initial piloting with several randomly selected papers, the data extraction form was refined and finalised, gathering a range of data items (summarised below).

- Basic study information, aims & methods.
- Participants: population, site & stage of cancer, inclusion & exclusion criteria, relevant recruitment data and sociodemographic characteristics.
- Intervention: aim, setting, content (components & features), mode & integrity of delivery, uptake & compliance.
- Outcome measures (specifically QoL or psychosocial/QoL-related).
- Results (specific to QoL and related measures).

4.5.6 Risk of bias

Studies were critically appraised using a modified version of the Cochrane Collaboration's tool for assessing risk of bias in randomised controlled trials, which encompasses five domains of bias; selection, performance, detection, attrition and reporting.[207] Each study was assessed for 'high', 'low' or 'unclear' risk of bias for each individual domain.

4.5.7 Data synthesis: a narrative approach

In the context of systematic reviews, a 'narrative synthesis' refers to the use of text or words to summarise and explain findings gathered across a number of different studies. The aim of this method is to describe the 'story' emerging from data otherwise too heterogenous for a meta-analytic approach.[208]

In order to capture, collate and draw inferences from what emerged to be a significant amount of heterogenous data, a narrative synthesis was therefore deemed to be the most appropriate methodological approach. This was conducted in line with the Economic and Social Research Council's guidelines.[208] Data was collated and managed using Microsoft Excel and Microsoft Word. The first stage of analysis involved identifying commonalities and distinctions across interventions. This led to the development of theory and categorisations relating to their

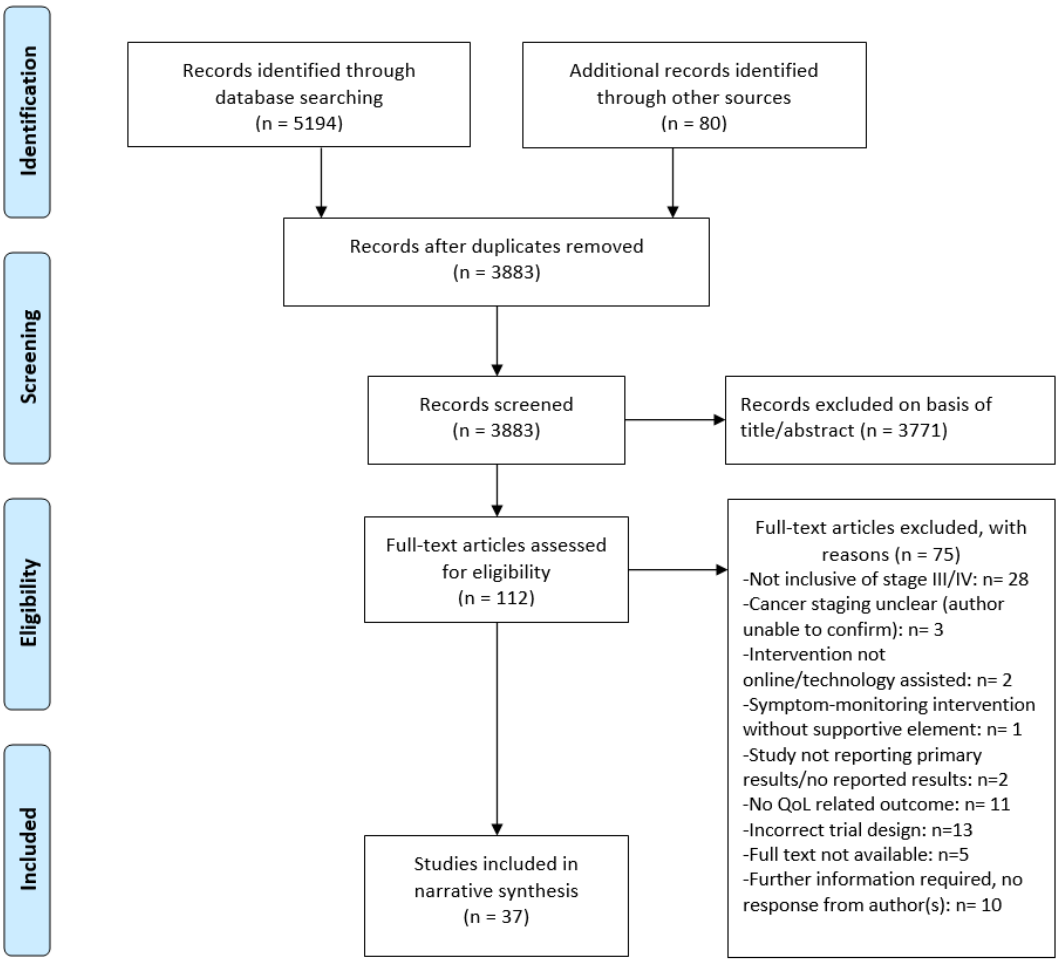
features and delivery. A preliminary synthesis then gathered interventions within their emerging subtypes. From this, patterns and relationships across the data could be explored. These steps will be outlined in detail in the next section.

4.6 Results

4.6.1 Study selection

The search found 5274 articles in total. Following removal of duplicate records, titles and abstracts of 3883 articles were screened, with 112 full text articles subsequently retrieved. In total, 37 studies, evaluating 35 individual interventions, met the inclusion criteria for review. Figure 4.1 outlines the process of selection and screening in full.

Figure 4.1 PRIMSA flow diagram of study identification & selection



4.6.2 Study characteristics

Of the 37 included studies, 30 were randomised controlled trials whilst 7 were pilot or feasibility studies. The vast majority were conducted in the USA (53%) and across Europe (35%). Results were illustrative of a rapidly emerging field, with 42% published between 2017 and 2019. Overall, 13 interventions were designed specifically for patients living with advanced cancer, whilst the remaining 22 were inclusive of early and late stage disease. Most studies included either breast cancer at all stages (n=10) or a mixed population of many disease sites (n=14). Others targeted lung (n=3), ovarian (n=2), prostate (n=1), central nervous system (n=1), haematological (n=1), colorectal (n=1), breast & gynaecological (n=1) and breast & prostate (n=1) cancers. The remaining two studies focused exclusively on SBC. Where assessing efficacy, 25 of the studies applied validated measures of QoL, whilst the remaining (n=12) captured a wide range of psychosocial outcomes.

Table 4.3 provides an overview of each of the interventions and the studies in which they were evaluated. Where abbreviated outcome measures are cited, these are outlined in full in section 4.6.6.

4.6.3 Risk of bias assessment

Pattern of risk varied across studies, though detection bias was extensive (high risk in 78% of studies). This relates to the self-reported nature of the vast majority of QoL and psychosocial outcome measures in the trials evaluated, as well as challenges relating to blinding in interventions of this nature. Most studies safeguarded against selection bias (86% of studies describing random sequence generation, 62% demonstrating allocation concealment). Overall, assessment of risk of bias was limited by the level of detail reported by authors; insufficient information often resulted in 'unclear' judgements. To provide a more complete overview of the evidence base, all articles were included in the review, regardless of their risk of bias. However, this risk (whether high or unclear) and associated study limitations must be considered when drawing inferences from their results. Full risk of bias assessment is displayed in Figure 4.2.

Figure 4.2 Risk of bias assessment applying the Cochrane Collaboration's tool (RCTs)[207]

Study *(first author & year)*	1	2	3	4	5	6	7
Basch et al 2016[105]	✓	✓	X	X	✓	✓	X
Berry et al 2014[109]	✓	?	?	X	?	?	X
Boele et al 2018[221]	✓	✓	X	X		?	?
Borosund et al 2014[209]	✓	✓	X	X	?	?	X
Carpenter et al 2014[222]	✓	?	X	X		?	?
Compen et al 2018[223]	✓	✓	X	X		✓	✓
David et al 2011[237]	?	?	?	X	?	?	X
Denis et al 2017[232]	✓	✓	X	?	?	?	?
Donovan et al 2014[238]	✓	✓	X	X	✓	?	✓
Galiano-Castillo et al 2016[224]	✓	✓	X	X	✓	?	✓
Giesler et al 2017[240]	?	?	X	X	✓	✓	✓
Greer et al 2019[225]	✓	✓	X	?	✓	✓	✓
Gustafson et al 2008[210]	?		?	X	?	?	X
Gustafson et al 2013[211]	✓	?	X	X	?	X	X
Huang et al 2019[212]	✓	✓	X	X	✓	?	✓
Kim et al 2018[213]	✓	✓	X	X	✓	X	✓
Knoerl et al 2018[226]	✓	X	?	?	?	?	?
Nipp et al 2019[233]	✓	?	X	X	✓	✓	
O'Carroll Bantum et al 2014[214]	✓	?	X	X	?	X	✓
Owen et al 2017[215]	✓	?	X	X	✓	?	?
Petzel et al 2018[216]	✓	✓	✓	?	?	?	✓
Post et al 2013[234]	?	?	?	?	✓	?	✓
Ritterband et al 2012[227]	✓	?	X	X	✓	?	X
Rosen et al 2018[228]	✓	?	X	X	?	✓	✓
Ruland et al 2010[235]	✓	✓	X	X	✓	?	✓
Ruland et al 2013[217]	✓	?	X	X	?	?	✓
Ryhanen et al 2013[241]	✓	?	X	X	?	?	?
Stanton et al 2013[242]	✓	✓	X	X	✓	?	?
Steel et al 2016[218]	✓	✓	X	✓	?	?	X
Strasser et al 2016[236]	?	✓	✓	?	✓	?	?
Urech et al 2018[229]	✓	?	X	X	✓	✓	X
Velikova et al 2004[73]	✓	✓	X	X	?	?	?
Vilhauer et al 2010[239]	✓	?	?	X	?	?	?
Wise et al 2018[219]	✓	?	✓	✓	?	?	✓
Yanez et al 2015[230]	?	?	?	?	✓	?	✓
Zernicke et al 2014[231]	✓	✓	X	X	?	✓	?
Zhu et al 2018[220]	✓	✓	X	?	✓	?	✓

Key: Domains of bias	
✓ Low risk ? Unclear risk X High risk	
Selection bias	**1.** *Random sequence generation*
	2. *Allocation concealment*
Performance bias	**3.** *Blinding of participants and personnel*
Detection bias	**4.** *Blinding of outcome assessment*
Attrition bias	**5.** *Incomplete outcome data*
Reporting bias	**6.** *Selective outcome reporting*
Other bias	**7.** *Other bias e.g. baseline imbalance*

Table 4.3 Overview of studies

Article *(first author, year, country).*	**Study** *(design, duration, setting).*	**Participants** *(cancer stage & site, sample size).*	**Mode of delivery**	**Intervention focus* & description**	**Summary of relevant findings**
Interactive Health Communication Applications (IHCAs)					
Børøsund et al. 2014,[209] Norway.	RCT, 12 months, home setting.	Stages I-III, breast. Intervention N=64 Control N=45 IPPC alone N=58 *(Internet based Patient-Provider Communication Service).*	Self-management.	- Focus: S, PS - 'Web Choice' web-based illness management system. - Assessment: symptom self-monitoring. - Self-management support: information & activities tailored to results of self-monitoring. - Information: signposting to other web sources related to e.g. lifestyle, treatment. - Communication: nurse monitored forum & blogs to share experiences. - Electronic diary: for patients to record notes.	Significantly lower symptom distress (p=0.001), anxiety (p=0.03) and depression (p=0.03) in intervention vs usual care group. Significantly lower depression scores for IPPC group (p=0.03) vs usual care (at 6 months).
Gustafson et al. 2008,[210] USA.	RCT, 5 months, home setting.	Stages 0-IV, breast. Intervention N=91 Internet only N=83 Control N=83	Supported self-management.	- Focus: S, PS - 'Comprehensive Health Enhancement Support System' (CHESS). - Information: breast cancer resources, Q&A section, healthcare consumer advice, signposting & links. - Communication: facilitated discussion groups for patients and family, expert responses to patient questions, videos of patient experiences.	Four months post-intervention (T=9 months), CHESS group scored higher than controls for QoL (p=0.018) & social support (p=0.021), but not higher than the internet only group. Social support was also higher for those in CHESS group during intervention period, compared to internet alone (p=0.003, T=2 months) and control (p=0.004, T=4 months).

				- Decision support: physical & psychological symptom monitoring and tailored advice, decision aid & suggested action plans.	
Gustafson et al. 2013,[211] USA.	RCT, 8 months, home setting.	Stage III-IV, non-small cell lung cancer. Intervention N=144 Control (internet) N=141 *(patient-caregiver dyads).*	Supported self-management/ clinically integrated.	- Focus: S, PS - CHESS *'Coping with lung cancer' website.* - Information: lung cancer, bereavement and caregiving, plus tools to support caregiving. - Communication: support from peers, clinicians, experts & channels for social networking. - Decision support: algorithm-driven tailored information provided based on self-reported data. - Clinician involvement: summary of self-reported and caregiver reported patient health status sent to clinician, with patients' questions listed for next visit. - Email alerts to clinicians where reported symptoms ≥7 (on a scale of 0-10).	Patient physical symptom distress (caregiver reported) lower in CHESS vs control (internet) arm (p=0.031 at 4 months & p=0.004 at 6 months). Marginal significance seen at 2 months (p=0.051) and 8 months (p=0.081).
Huang et al. 2019,[212] Taiwan.	RCT, 3 months, home setting.	Stage III-IV, non-small cell lung cancer. Intervention N=27 Control N=28	Supported self-management.	- Focus: S, PS - Web-based health education programme. - Self-monitoring of symptoms & health indicators. - Educational information relating to lung cancer, staging, treatment, care & symptom management. - Social & emotional supportive resources & patient experiences.	Significantly improved global QoL (p<0.05), emotional function (p<0.01) and symptom distress (p<0.01) for intervention vs control group from pre-test to post-test. Three months later, significantly larger group x time interactions for global QoL (p<0.05) and

				- Q&A facility for patients to contact research nurse (24 hour response time).	emotional function (p<0.05) in intervention users vs controls.
Kim et al. 2018,[213] Korea.	RCT, 3 weeks, home setting.	Stage IV, breast. Intervention N=36 Control N=40	Self-management.	- Focus: S, H/L - 'ILOVEBREAST', interactive mobile game. - Multi-player educational game with integrated social networking. - Avatar created based on user information, with quest to carry out activities to minimise chemotherapy side-effects. - Self-monitoring feature using personal avatar. - Education & support for prevention of side-effects and to encourage activities promoting well-being.	Greater QoL in intervention group during chemotherapy compared to control group (p=0.01). Smaller decrease in QoL in intervention vs control group (p=0.01). No significant between group differences for depression or anxiety.
O'Carroll Bantum et al. 2014,[214] USA.	RCT, 6 months, home setting.	Stages 0-IV, mixed sites. Intervention N=176 Control N=176	Supported self-management/ professionally delivered.	- Focus: H/L, PS - 'Surviving and Thriving with Cancer' (STC): website delivering weekly sessions (by trained facilitators) with information & skills development relating to e.g. diet, exercise, relaxation for stress, fatigue etc. - Patients encouraged to develop weekly behaviour change action plans. - Feedback provided by facilitator. - Discussion board & 'post-office' for patients to interact with each other publicly & privately. - 'My tools' where patients can log behaviour, access relaxation exercises & find links to other resources.	Greater improvement in insomnia for intervention group (effect size 0.20, p=0.03). No significant changes for depression or fatigue.

Owen et al. 2017,[215] USA.	RCT, 12 weeks, home setting.	Stages 0-IV, mixed sites. Intervention N=176 Control N=171	Supported self-management/ professionally delivered.	- Focus: PS - 'Health-Space': Social networking intervention targeting distress management. - Personal profiles for patients to describe themselves and their experience of cancer. - Live facilitated chat (weekly), discussion board & email to engage with each other & with facilitators. - Weekly guidance modules: educational information & interactive activities.	Greater reduction in fatigue in intervention versus control group (p=0.04). No significant improvements in psychological functioning, depressive symptoms, anxiety or vigour.
Petzel et al. 2018,[216] USA.	RCT, 60 days, home setting.	Stage III/IV/recurrent, ovarian, peritoneal or fallopian tube. Intervention N=20 Control N=15	Self-management.	- Focus: PS, S - 'Together': Online tool to promote advance care planning, cancer knowledge & address emotional health. - Learning library & recommended reading. - Functions for monitoring distress & goal setting. - Area to record questions for care providers. - Social networking: shared journal & forum.	No significant difference between intervention and control groups for distress/anxiety.
Ruland et al. 2013,[217] Norway.	RCT, 12 months, home setting.	Stages 0-IV, breast & prostate Intervention N=162 Control N=163	Supported self-management.	- Focus: S, PS, H/L - 'WebChoice' (same intervention evaluated in Borosund et al. 2014).[209] - Addition of Q&A area for patients to ask nurses questions.	QoL and self-efficacy scores worsened within control group (p=0.006, p=0.005), but not within intervention group. Between-group differences in symptom distress significant for global distress index (GDI) only (p=0.037).

Steel et al. 2016,[218] USA.	RCT, 6 months, home setting.	Advanced stage, mixed sites. Intervention N=144 Control N=117	Supported self-management/ clinically integrated.	- Focus: PS, S, H/L - Psychoeducational website with library of audio-visual and other resources. - Self-management component enabling symptom recording and self-monitoring. - Patient journal and chat room to engage with others. - Use of IHCA integrated with telephone follow up every 2 weeks & visits with care co-ordinator every 2 months.	Participants presenting with clinical levels of symptoms showed statistically (p=0.05) & clinically significant improvement in QoL at 6 month follow up (intervention n=15, control n=12), with a large effect size (0.99).
Wise et al. 2018,[219] USA.	RCT, 4 months home setting.	Stage III/IV, mixed sites. Intervention N=59 Control N=51	Self-management.	- Focus: PS - '*miLivingStory*': Patient's illness narrative (elicited via telephone) digitalised and incorporated into a multi-component website. - Signposting to information, resources and support. - Social networking to share story and other media.	Improvements in peace (direct positive effect p=0.029) and depressed mood ('trend effect' p=0.097) at 4 months for intervention vs control group.
Zhu et al. 2018,[220] China.	RCT, 12 weeks, home setting.	Stages I-IV, breast Intervention N=57 Control N=57	Supported self-management.	- Focus: S, PS - Breast Cancer e-Support ('BCS') mobile application. - Learning forum: breast cancer education and symptom management strategies. - Discussion & ask the expert forums: support and advice provided by peers & health professionals. - Personal stories forum: selection of patients' experiences shared via video.	Lower QoL and self-efficacy observed with initiation of chemotherapy. However, controlling for baseline scores, intervention group experienced less worsening in QoL (d=0.46, p=0.03) and self-efficacy (d=0.53, p=0.03) at 3 months than care as usual (though not maintained at 6 months).

Virtual programmes of support					
Boele et al. 2018,[221] Netherlands.	RCT, 5 weeks, home setting.	Stages II-IV, neurological. Intervention N=45 Control (glioma) N=44 Non-CNS cancer control N=26	Supported self-management.	- Focus: PS - Online glioma specific guided self-help course for symptoms of depression. - Based on problem-solving therapy. - 5 modules with examples & exercises for patients to work through, plus support from a trained coach to facilitate completion.	No evidence of effectiveness for QoL of glioma patients. No statistically significant differences in depressive symptoms between groups, though borderline significant post-treatment reduction in fatigue was observed in glioma patients (p=0.054).
Carpenter et al. 2014,[222] USA.	RCT, 10 weeks, home setting.	Stages 0-III, breast. Intervention N=71 Control N=61	Professionally delivered.	- Focus: PS - 'Coping with Cancer Workbook': Online stress management taught through didactic instruction. - CBT based coping strategies and guided interactive exercises. - Integrated videos of patient case studies, plus guidance provided by social worker. - Integrated discussion board moderated by oncology health professionals.	No significant improvement for social/functional well-being (FACT-B). Significant for primary outcomes of self-efficacy for coping with cancer (p=0.019) and self-efficacy for coping with negative mood (p=0.007). Cancer related post-traumatic symptoms also lessened with intervention use (p= 0.002*).*
Compen et al. 2018,[223] Netherlands.	RCT, 8 weeks, home setting.	Stages 0-IV, mixed sites. Intervention (eMBCT) N=90 MBCT (face-to-face) N=77 Control N=78	Professionally delivered.	- Focus: PS - Online Mindfulness Based Cognitive Therapy (eMBCT). - Materials for 8-week course provided on website plus weekly interactions with therapist. - Daily practice diaries, with fictional patients' examples for guidance. - Asynchronous feedback and interaction with therapist via email.	Compared to usual care, both MBCT and eMBCT improved scores for mental health related QoL (p< 0.001) but not for physical QoL. Both interventions also reduced distress, fear of recurrence and rumination and improved scores for mindfulness skills and positive mental health (all p<0.025).

Galiano-Castillo et al. 2016,[224] Spain.	RCT, 8 weeks, home setting.	Stages I-III, breast Intervention N=40 Control N=41	Professionally delivered/ supported self-management.	- Focus: H/L - 'e-CUIDATE': Online, individually tailored exercise programme plus information about breast cancer. - Area for patients to write questions, send instant messages & set up video conferences with research staff, who also monitor progress remotely.	Significantly improved scores across all QoL domains (EORTC-QLQ-C30 and BC module) for intervention arm (p<0.01).
Greer et al. 2019,[225] USA.	RCT, 12 weeks home setting.	Stage IV, mixed sites. Intervention N=72 Control N= 73	Self-management.	- Focus: PS - Multi-component mobile application delivering anxiety management skills & exercises over 6 sessions. - Patient-therapist interactions simulated within integrated videos. - Corresponding homework plus review session.	Both intervention and control participants experienced improved QoL, anxiety and mood (d=0.45 – 1.20). No significant between group differences. Subgroup analyses showed intervention users with severe baseline anxiety experienced significantly improved anxiety (p=0.01).
Knoerl et al. 2018,[226] USA.	Pilot RCT, 8 weeks, home setting.	Stages I-IV, mixed sites. Intervention N=30 Control N=30	Self-management.	- Focus: S, PS - 'Proactive Self-management Programme for Effects of Treatment' (PROSPECT). - Self-guided pain management course. - CBT & self-management strategies delivered as modules on password-protected website. - Integrated videos and worksheets. - Self assessment of symptoms to guide content.	No significant differences observed (in mean change scores) for QoL related to peripheral neuropathy - sensory (p=0.41) or motor (p=0.95) subscales (EORTC-QLQ-CIPN20).
Ritterband et al. 2012,[227] USA.	RCT, 6 weeks, home setting.	Stages I-IV, mixed sites.	Self-management.	- Focus: PS, HL - 'Sleep Healthy Using The internet' (SHUTi).	No significant effect on QoL, depression or anxiety with intervention use (though overall

		Intervention N=14 Control N=14		- Web-based CBT with 6 interactive cores encompassing behaviour, education and problem prevention. - Sleep diaries guiding tailored sleep recommendations & feedback. - Automated emails to encourage adherence.	adjusted effect sizes were small-medium, ranging from *d*=0.42 to *d*=0.54). Intervention group did demonstrate improvement in fatigue (*p*=<0.01).
Rosen et al. 2018,[228] USA.	RCT, 12 weeks, home setting.	Stages 0-IV, breast. Intervention N=57 Control N=55	Self-management.	- Focus: PS - 'Headspace' - Audio-visual mindfulness meditation training delivered via mobile application. - 'Take10' 10-day introductory course, with additional training accessible on completion.	Significant improvement in QoL (*p*=<0.01) and mindfulness (*p*=0.04) in intervention vs control group from baseline to follow up.
Urech et al. 2018,[229] Switzerland.	RCT, 8 weeks, home setting.	Localized and metastatic, mixed sites. Intervention N=65 Control N=64	Supported self-management.	- Focus: PS - 'Stress Aktiv Mindern' (STREAM). - Website hosting 8 stress management modules, each incorporating mindfulness exercises, psychoeducation, reflection & strategies, plus additional audio exercises. - Secure chat function with psychologist.	Significantly higher QoL (*p*=0.007) and lower distress (*p*=0.03) in intervention vs control group.
Yanez et al. 2015,[230] USA.	Feasibility RCT, 10 weeks, home setting.	Stage III/IV, prostate. Intervention N=37 Attention control N=37	Professionally delivered.	- Focus: PS - 'Cognitive Behavioural Stress Management' (CBSM). - Online group intervention, delivered via tablet, tailored to advanced prostate cancer (APC). - Each group session (delivered by a facilitator) introduces a new stress reduction technique before focusing on stress management in relation to APC.	No significant effect on QoL, though mean difference between groups exceeded clinical significance (4 points, FACT-G). Symptoms of depression significantly improved for intervention group (*p*=0.03, completers only).

Zernicke et al. 2014,[231] Canada.	Feasibility RCT, 8 weeks, home setting.	Stages I-IV, mixed sites. Intervention N=30 Control N=32	Professionally delivered.	- Focus: PS - eTherapy for Cancer Applying Mindfulness (eCALM). - Online group mindfulness sessions ('Mindfulness Based Cancer Recovery') delivered online by behavioural medicine clinicians via headsets, webcams & manuals. - Sessions covering a range of topics relating to stress & mindfulness. Participants encouraged to apply learning during sessions and in own time.	Significant improvements in intervention group vs control group for mood disturbance (p=0.049), stress (p=0.021), spirituality (p=0.040) and mindfully acting with awareness (p=0.026).
Symptom monitoring tools					
Basch et al. 2016,[105] USA.	RCT, continuous,† home setting, (clinic setting for computer inexperienced subgroup).	Advanced solid tumours, mixed sites. Intervention N= 441 Control N= 325	Clinically integrated.	- Focus: S - 'Symptom Tracking and Reporting' (STAR). - Web-based interface with questions relating to 12 common symptoms for patients to self-report. - Email alerts to nurses triggered where symptoms worsen by ≥2 points or reach ≥3. - Summary report printed for clinical team to review.	More improvement and less worsening in QoL scores seen in STAR arm vs usual care (p=<0.001). No significant difference for computer inexperienced subgroup (p=0.06).
Berry et al. 2014,[109] USA.	RCT, 6-8 weeks, home and clinic setting.	Stages 0-IV, mixed sites. Intervention N= 374 Control N= 378	Supported self-management/ clinically integrated.	- Focus: S - 'Electronic Self-Report Assessment for Cancer' (ESRA-C): online computer program for self-reporting symptoms & tracking QoL. - Alerts to patients when help-seeking advised.	Small statistically significant difference in symptom distress between groups (p=0.02).

				- Self-care strategies & coaching for managing & communicating symptoms. - Graphical summary & option to annotate results.	
Denis et al. 2017,[232] France.	RCT, trial halted,‡ home setting.	Stages III-IV, lung. Intervention N=67 Control N=66	Clinically integrated.	- Focus: S - 'e-Follow up Application' (eFAP). - Web-mediated weekly reporting of 12 items (weight plus 11 symptoms), sent immediately to medical team. - Alerts to clinicians triggered where reported symptoms meet pre-defined criteria. - Graphical summary of scores sent to medical team.	Comparing change in QoL score from baseline to 6 months: stable/improved scores in 80.6% participants in intervention arm vs 58.6% control arm (p=0.04).
Nipp et al. 2018,[233] USA.	Pilot RCT**,** intervention period not defined (average admission 6.45 days), hospital setting.	Advanced cancer, mixed sites. Intervention N=75 Control N=75	Clinically integrated.	- Focus: S - 'Improving Management of Patient Reported Outcomes via Electronic Data' (IMPROVED). - Daily symptom self-monitoring via tablet computer during hospital admission. - Summary reports generated for clinical team review. Alerts to clinicians where symptoms worsen by ≥2 or reach ≥4.	Intervention group reported higher proportion of days with lower psychological distress than control group (p=0.008).
Post et al. 2013,[234] USA.	Pilot RCT, 160 days, home setting.	Stages I-III, breast Intervention N=27 Control N=23	Clinically integrated.	- Focus: S - 'Communicating Health Assisted by Technology' (CHAT). - Symptom monitoring using personal digital assistant (PDA) during chemotherapy.	All participants' QoL scores decreased over course of chemotherapy (lower = worse QoL) but mean pre-post decrease was generally greater for those in intervention group (though study not powered for

				- Videos relating to symptom communication for patients to view ahead of clinical appointment. - Summary graph for clinicians to view.	this outcome). No significant changes for depression/fatigue.
Ruland et al. 2010,[235] Norway.	RCT, intervention period varied,[§] home & hospital settings.	Various stages including advanced, haematological. Intervention N=75 Control N=70	Clinically integrated.	- Focus: S - 'Interactive Tailored Patient's Assessment tool' (Choice ITPA). - Tablet computer application allowing patients to rank symptoms (including distress) according to their priorities & need for support, encouraging communication with clinicians. - Summary report of symptoms (ranked in order of need for support) made available for clinician review.	Significant group differences (2-sided significance set at 1.0) in symptom distress favouring intervention arm for discomfort (p=0.04), sleep/rest (p=0.05), sexuality (p=0.07) and eating/drinking (p=0.09).
Strasser et al. 2016,[236] Switzerland.	Multi-cluster RCT, 6 weeks hospital setting.	Advanced, incurable, mixed sites. Intervention N=145 Control N=119	Clinically integrated.	- Focus: S - 'Electronic Monitoring of Symptoms and syndromes Associated with Cancer' (e-MOSAIC). - Patients complete symptom reporting on palm-based digital device prior to weekly oncologist visit. - PROMs integrated with other clinical data, recorded by study personnel. - Data immediately transferred to local computer, printed & placed in patient's file for clinician review.	No statistically or clinically significant between-group change in global QoL. Symptom distress significantly improved for intervention users from first to last visit (p=0.003).
Velikova et al. 2004,[73] UK.	RCT, 6 months, clinic setting.	Stages 0-IV, mixed sites. Intervention N=144	Clinically integrated.	- Focus: S, PS - Patient self-completion of QoL questionnaires (EORTC-QLQ-C30 & HADS)	QoL significantly improved in intervention (p=0.006) and attention control (p=0.01) groups compared to control. No

		Attention-control N=70 Control N=72		prior to their appointment in clinic using touch-screen computers. - Graphical summary of results printed. - Physicians asked to review results during clinical encounter with patient.	significant difference in QoL between intervention & attention control (p=0.80).
Communication conduits					
David et al. 2011,[237] Germany.	RCT, 8 weeks, home setting.	Stages I-IV, breast. Intervention N=69 Control N=64	Professionally delivered.	- Focus: PS - Individually tailored psychosocial counselling delivered via email by clinical psychologist (24 hour response time). - Welcome email introducing counsellor and suggesting topics for discussion.	No significant difference in QoL or psychological distress between intervention & control groups.
Donovan et al. 2014,[238] USA.	Pilot RCT, 3 weeks, home setting.	Stages I-IV, recurrent ovarian. Intervention N=33 Control N=32	Supported self-management/ professionally delivered.	- Focus: S, PS - 'Written Representational Intervention to Ease Symptoms' (WRITE Symptoms): online message board interactions between patient & nurses to support symptom self-management. - Patients identify 3 target symptoms by completing symptom representation questionnaire (SRQ). - Individualised symptom management information. - Co-creation of care plan & self-management goals. - Self-care guides (provided via email/mail) to consolidate message board learning.	Lower symptom distress (p=0.012) and a trend for lower symptom severity (p=0.058) in intervention vs control arm at 2-weeks post intervention. Repeated measures analysis supported group effect; intervention group reported lower symptom distress than controls (p=0.037).
Vilhauer et al. 2010,[239] USA.	Pilot RCT, 6 months, home setting.	Stage IV, breast. Intervention N=16 Control N=14	Self-management.	- Focus: PS - Peer-peer online support group (unmoderated).	No significant effect of on QoL/psychosocial well-being. Waiting list controls had significant decline in QoL scores

				- Emails sent to all group participants via automated mailing list server. - Participants encouraged to share experiences.	(FACT-B *p*=0.01 and ECOG *p*=0.03) at 1 month.
Information websites					
Giesler et al.[240] 2017, Germany.	RCT, 2 weeks home setting.	Mixed stages, inclusive of stage IV, colorectal. Intervention N=103 Control N= 109	Self-management.	- Focus: S, PS - German language website collating experiences of health & illness. - Patients' experiential information relating to colorectal cancer organised into modules thematically & by individual cases.	No intervention effects on self-efficacy at 2 weeks or 6 weeks post baseline.
Ryhänen et al. 2013,[241] Finland.	RCT, 12 months, home setting.	Stages I-III, breast Intervention N=50 Control N=48	Self-management.	- Focus: S - 'Breast Cancer Patient Pathway' (BCPP). - Flow chart of patients' breast cancer treatment pathway, with integrated links to information.	No statistically significant between group changes in QoL or anxiety.
Stanton et al.[242] 2013, USA.	RCT, 6 months, home setting.	All stages, breast. Intervention N=46 Control N=42	Self-management.	- Focus: PS - 'Project Connect Online': self-designed information website. - Workshop to guide participants in designing personal websites. - Template included: blog, signposting area and 'How you can help' page for visitors to read and post messages.	Improvement in depressive symptoms (*p*=0.009), positive mood (*p*=0.03) and life appreciation (*p*=0.03) at 6 months follow up for intervention group (effect moderated by treatment status).

*Intervention focus: S= symptom management focus, PS= psychosocial focus, H/L= health & lifestyle focus.

† Participants remained on study until discontinuation of cancer treatment, voluntary withdrawal or death.

‡ Interim analysis demonstrated large survival benefit for intervention group leading to trial being stopped early.

§ 50 patients from each group (intervention and control) were followed for a minimum of 100 days; 25 intervention participants and 26 controls were followed up for 1 year.

4.6.4 Categorising interventions

4.6.4.1 Intervention subtypes

As underpinning theory was not always central to the reporting of interventions, this first stage of synthesis instead focused on developing theory relating to differing categories of interventions and the ways in which they were delivered. By collating descriptions of interventions' features and delivery, shared characteristics became apparent. Drawing on literature in the wider field, alongside the articles under review, definitions were assigned to five distinct intervention subtypes (Table 4.4). Some of these definitions mirror those used across the evidence base e.g. 'information websites' and 'symptom monitoring tools'.[243, 244] The term 'Interactive Health Communication Applications' (IHCAs) was outlined by the Science Panel on Interactive Health Communication over two decades ago and has since proliferated across the field of chronic disease management.[245, 246] Other definitions were developed to describe the shared purpose of related interventions, where an appropriate term had not yet been encountered.

The most frequently evaluated interventions were interactive health communication applications (IHCAs) (12/37) and virtual programmes of support (11/37), closely followed by symptom monitoring tools (8/37). A smaller number of information websites (3/37) and communication conduits (3/37) were also evaluated.

4.6.4.2 Intervention focus

In order to describe the overarching focus of the interventions, further categories were assigned (as highlighted in Table 4.3). These were defined by grouping together interventions targeting similar supportive needs, guided by areas of support discussed in the wider literature.[14, 247]

- *'Psychosocial' (PS)*: Targeting psychological behaviours and symptoms or encouraging socio-emotional well-being through shared experience and communication. This was a predominant focus across all subtypes.
- *'Symptom management' (S)*: Focused on the monitoring and management of predominantly physical symptoms and side-effects.
- *'Health & lifestyle' (H/L)*: Encompassing aspects of healthy living more generally, such as diet, exercise and holistic considerations.

Many interventions encompassed more than one focus, most notably the IHCAs.

Table 4.4 Online and technology-assisted intervention subtypes

	Subtype	Definition	No. studies	No. studies evidencing QoL-related efficacy
Increasing complexity →	**Interactive Health Communication Application (IHCA)[245]**	Computer-based (usually web-enabled) packages of information and support, bringing together health information with a range of other features encompassing social support, behaviour change and decision making.	12	11
	Virtual programme of support	Structured programme of support (e.g. modular or a set number of sessions) providing education and/or training, delivered via an online platform or mobile application +/- expert facilitation.	11	9
	Symptom monitoring tool	Web based tool or mobile application allowing patients to self-report occurrence and severity of symptoms, for the purposes of self and/or clinician monitoring, usually generating a written or graphical report of results.	8	7
	Communication conduit	Supportive resource acting as a channel for communication, allowing patients to reach out and receive advice and guidance in the home setting from peers or from professionals such as clinical nurse specialists, counsellors etc.	3	1
	Information website	Web page(s) providing information/content and links on a single platform, in the absence of additional integrated components or tools.	3	1

4.6.4.3 Mode of delivery

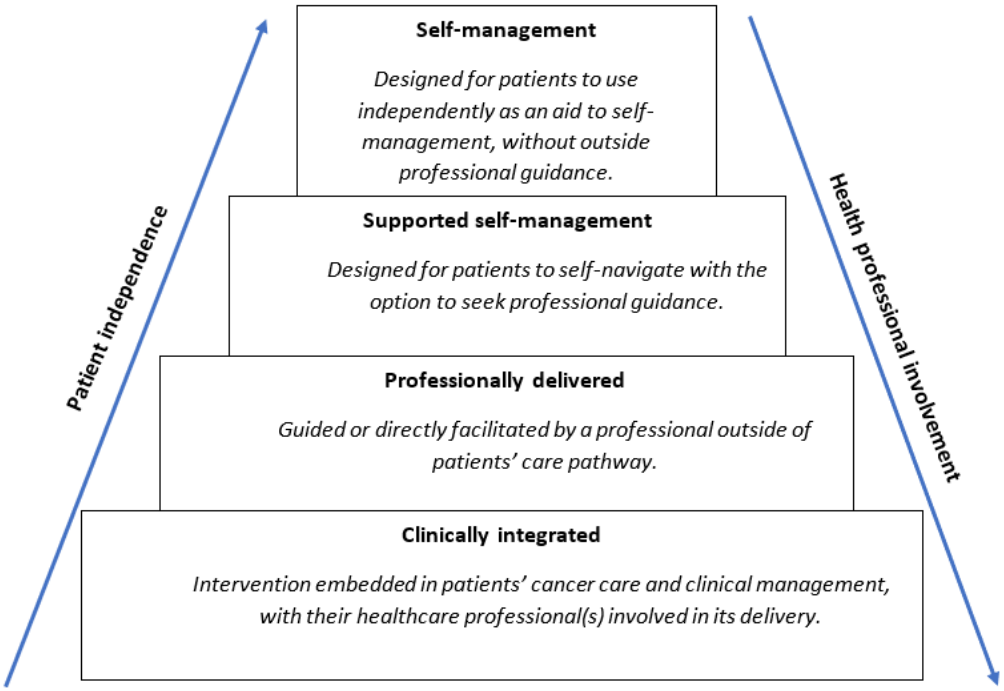
During analysis, it also became apparent that the interventions could be further categorised according to aspects of their delivery; (i) the level of patient versus health professional or other expert involvement and (ii) the extent to which they were integrated within the patients' usual care pathway. From these characteristics, various modes of delivery were identified.

'Self-management' and 'clinically integrated' are terms used to describe what are often contrasting approaches to delivering patient support. However, approaches of the reviewed interventions were much more nuanced. Focusing on the patient and the professional

(healthcare or other expert) as key participators, their varying level of involvement was used as the basis for describing different modes of delivery. 'Supported self-management', a term increasingly encountered in cancer survivorship research,[82] was adopted to describe a 'middle ground' between patients independently self-managing and experts having a key role in facilitation. 'Professionally delivered' acknowledged significant expert input which was distinct from patients' usual care.

These various modes were brought together within the model of intervention delivery (Figure 4.3). Level of patient independence in self-management increases with progression up the pyramid, with those at the top being distinct from the patients' usual care pathway. In contrast, moving down the pyramid, health professionals become increasingly involved in intervention delivery.

Figure 4.3 Model of online & technology-assisted intervention delivery



4.6.5 Intervention features and delivery

4.6.5.1 Interactive health communication applications (IHCAs)

A wide range of IHCAs were evaluated across 12 RCTs, each incorporating diverse components to varying extents. Half of these targeted patients with advanced stage cancer,[211-213, 216, 218, 219] whilst the remaining had diverse cancer patient populations. The multi-faceted nature of these interventions meant that most encompassed more than one focus. Psychosocial and symptom-management support were frequently integrated, with more general health and lifestyle support featuring to a lesser extent.

The majority included an element of educational health information and signposting[209-212, 215-219], some providing self-management guidance as a separate focus.[209, 212, 216-218, 220] One intervention presented topics at varying levels of detail, allowing users to opt for the level of information that matched their needs.[216] The 'Surviving and Thriving with Cancer' intervention delivered a weekly education course, aiming to facilitate both physical and psychological health behaviour change.[214] In some cases, self-management information was accompanied by facilities for varying degrees of physical and psychological symptom and status monitoring.[209-213, 216-218] Uniquely, 'ILOVEBREAST' used a mobile gaming format to promote chemotherapy side-effect self-management, integrating health information with features for social networking and self-assessment.[213]

Decision support was a key component of several IHCAs. These provided users with a range of holistic and disease specific information, supporting them to make decisions about their care needs.[216, 210, 211] 'Planning tools' were also listed as a feature within another of the interventions, though this was not further elaborated.[219]

The majority facilitated user-user communication via forums,[209, 216, 217, 220] a chat room[218] and discussion groups.[210, 211, 215, 219] Additionally, many permitted patients to communicate with and receive support from professionals.[209-212, 216, 217, 220] Further interactive components included audio visual self-management resources[210, 218] and online journals for patients to document experiences.[209, 216-218] The use of patient 'stories' as a means of learning through shared experience was also central to several interventions.[212, 219]

In line with the model of intervention delivery (Figure 4.3), 4 IHCAs could be classed as 'supported self-management', giving users the option to contact experts outside of their own healthcare team.[210, 212, 217, 220] 'Supported self-management' and 'professional delivery' were combined in 2 of the IHCAs, both encouraging self-management with an element of expert guidance as a core feature.[214, 215] Others lacked optional or integrated expert guidance, representing purely self-management tools.[209, 213, 216, 219] The remaining interventions included an element of clinical integration via follow-up with a care co-ordinator[218] and through an in-built symptom monitoring feature which sent reports and alerts to clinicians.[211]

4.6.5.2 Virtual programmes of support

In total, 11 virtual programmes of support were evaluated, few of which (2/11) were specific to advanced cancer.[225, 230] The majority applied cognitive behavioural therapy (CBT) principles to address symptoms such as stress, pain, insomnia and anxiety through guided online courses and exercises.[222, 223, 225-227, 229, 230] Mindfulness and stress-management principles were also incorporated.[222, 229-231] Another programme facilitated self-help through problem solving

therapeutic principles.[221] Contrasting with the predominantly psychological focus, the e-CUIDATE intervention, a rehabilitative healthy lifestyle programme for breast cancer survivors, delivered online information and tailored exercise sessions.[224]

Across the programmes, patients were guided to work through a series of modules,[221, 226, 227, 229] chapters[222] or sessions delivered over a set number of weeks.[223-225, 228, 230, 231] A range of modalities were used to deliver programmes via online platforms and mobile applications, including videos and graphics,[222, 225-229] exercises and worksheets,[221-231] audio content[228-230] and vignettes.[222, 223, 227] Some of the interventions offered an element of personalisation, with content tailored to users' responses and needs.[221, 224, 226, 227] Several also involved virtual group sessions, where patients were collectively guided to develop self-management skills such as stress reduction, relaxation and mindfulness.[230, 231] Numerous programmes included interactive elements, allowing patients to connect with professionals for support or feedback[221-224, 229-231] and with other participants.[222] One intervention applied an alternative approach, integrating videos displaying simulated patient-therapist interactions.[225]

The extent to which patients were supported to self-manage through expert facilitation varied, with programmes incorporating various approaches outlined in the model of intervention delivery (Figure 4.3). Some were professionally delivered (i.e. delivered by a facilitator or provided expert guidance and feedback as a key component).[222-224, 227, 230, 231] Others encouraged more independent self-management, some purely patient-led,[225, 226, 228] several also giving patients the option to access professional support.[221, 229]

4.6.5.3 Symptom monitoring tools

Overall, 8 symptom monitoring tools were identified, supporting patients to manage predominantly physical aspects of health and treatment through a range of self-report functionalities. Half were designed specifically for patients at advanced stages of cancer,[105, 232, 233, 236] whilst the remaining encompassed all stages.

Some used hand-held digital devices,[234, 236] tablet computers[105, 235] and web-applications[109, 232] to enable patients to report symptoms at home, whilst others harnessed similar technology to support shared symptom monitoring during inpatient and outpatient clinical encounters.[73, 109, 233] Some tools combined self-reported symptoms with other clinical data such as weight,[232, 236] height, performance status and medications.[236] Two of the interventions also supplemented objective self-report scores with additional patient input, in the form of free text comments [232] and a journaling feature.[109]

There was significant variability in the depth of symptom reporting permitted, in terms of both the number of symptoms and the specified frequency of reporting. Several involved weekly

completions,[232, 234, 236] whilst others were aligned with clinical encounters.[73, 105, 233, 235] One tool also encouraged patients to report symptoms in line with their needs.[109] Extent of symptom monitoring ranged from between 9-24 specified symptoms or issues[105, 232, 235, 236] (some generating additional questions based on patients' responses or severity grading[235]) to full length health/QoL questionnaires and inventories.[73, 234]

In all cases, summary reports of symptoms were generated for review by a member of the clinical team, some providing a graphical overview,[73, 109, 233, 234] and one ranking the summarised symptoms in order of need for support.[235] Notably, Choice ITPA (Interactive Tailored Patient Assessment) was used across both intervention and control groups, with clinician review of symptom reports being the intervention feature under evaluation.[235]

Extent of integration within the care pathway varied, traversing various modes of delivery (Figure 4.3). Some interventions applied several approaches, ranging from encouraging patients to discuss their symptoms at the next point of contact,[109, 234, 235] making reports available to clinicians for them to review and discuss at appointments[73, 109, 234-236] and using pre-defined thresholds to trigger alerts to clinicians and urgent review outside of scheduled follow-up.[105, 232] Several had the emphasis of supporting[235] or 'coaching' patients to communicate symptoms with their clinician.[109, 234] One tool stands out as being designed specifically for hospitalized patients.[233]

4.6.5.4. Communication conduits

Three interventions specifically used technology to provide channels of communication for patients in the home setting, providing predominantly psychosocial support by connecting them to either experts or peers.[237-239] One was advanced stage focused,[239] whilst the others targeted women with breast cancer of all stages.[237, 238]

One study trialled the provision of individually tailored psychosocial counselling to breast cancer patients, based on cognitive behavioural, rational emotive and solution-focused therapy, via email correspondence with a clinical psychologist.[237] Another intervention had a dual physical and psychosocial focus, aiming to provide tailored symptom management education and support through online message boards. This interactive platform therefore facilitated communication and shared decision making between patients and nurses.[238] Participants completed a questionnaire to identify priority symptoms, around which the intervention was based. Self-care guides were also provided (via email or mail) to consolidate message board-based learning. The final intervention evaluated an online support group which encouraged women living with SBC to share their experiences. The group was unmoderated, the intervention being based on self-facilitation of peer support.[239]

A key feature of these interventions was the rapidity of expert support, with the 2 'expert' communication conduits providing responses to patients within 24 hours. Both were guided by a health professional without being integrated into the patient's usual care pathway.[237, 238] The patient-led social networking intervention, in contrast, was purely self-management and encouraged users to seek support through shared experiences.[239]

4.6.5.5 Information websites

The final 3 studies evaluated the delivery of supportive information via websites of varying formats, all targeting both early and late stages of cancer.[240-242]

One intervention involved patients' self-design of a personal website within a workshop setting, with a template comprising a blog, signposting, message board and 'how you can help' visitor information features.[242] Another used a diagrammatic format to present information relating to breast cancer patients' care pathway, with built-in signposting links.[241] The final website brought together patients' experiences of living with colorectal cancer, organised by themes and by individual case studies.[240]

All 3 websites were delivered separately to patients' care pathway and in the absence of outside support, representing purely self-management tools.

4.6.6 Exploring efficacy: Quality of life and psychosocial outcomes

Significant variation was observed within and across the various intervention subgroups in terms of the definitions and measures of QoL domains and QoL related (psychosocial and symptom specific) constructs applied, as well as their methods of evaluation. It was therefore difficult to draw definitive conclusions regarding efficacy. However, the reporting and application of these measures, and potential indications of efficacy between and within studies, was explored.

Overall, 78% (29/37) of studies demonstrated efficacy, to varying degrees, through measures of QoL and related psychosocial constructs. These were a primary outcome for over two thirds of the studies (25/37, n=4 of which captured them as both primary and secondary outcomes); the remaining 12 captured them as secondary outcomes alone. The studies which did not evidence any efficacy in these areas (n=8) all reported limitations relating to small sample sizes and low statistical power.

Tables 4.5 and 4.6 provide an overview of these outcome measures, their abbreviations and the constructs they capture across all included studies.

A summary of the results is also provided in Table 4.3.

Table 4.5 Overview of QoL outcome measures (as measured by n=number of studies)

	Outcome	Outcome measure
Quality of life (n=22)	Quality of Life (QoL)/ Health Related Quality Life (HRQOL)[73, 105, 212, 213, 217, 218, 221, 223-225, 227, 230, 234-236]	- European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC-QLQ-C30) - EuroQol 5-Dimensions (EQ-5D) - Functional Assessment of Cancer Therapy – General (FACT-G) - Short Form Health survey (SF-12, SF-36) - World Health Organisation Quality of Life abbreviated scale (WHOQOL-BREF) - 15D (15-dimensional instrument for assessing HRQOL)
	Cancer site specific QoL[210, 220-222, 224, 228, 232, 239, 241]	- EORTC-BN20 (Brain tumour module) - EORTC-QLQ-BR23 (Breast cancer module) - Functional Assessment of Cancer Therapy - Breast (FACT-B) - Functional Assessment of Cancer Therapy – Lung (FACT-L) - Quality of Life Instrument - Breast Cancer Patient Version (QOL-BC)
Symptom related QoL (n=19)	Chemotherapy induced peripheral neuropathy (CIPN)[226]	- European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire – CIPN20 (EORTC QLQ-CIPN20)
	Fatigue[214, 215, 218, 221, 227, 229, 231, 234]	- Brief Fatigue Inventory (BFI) - Checklist Individual Strength (CIS) - Fatigue Symptom Inventory (FSI) - Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F) - Functional Assessment of Cancer Therapy-Fatigue (FACT-Fatigue) - Multi-dimensional Fatigue Symptom Inventory - Short Form (MFSI- SF) - Profile of Moods States – Short Form (POMS-SF)
	Insomnia[214, 227]	- Insomnia Severity Index (ISI) Women's Health Initiative Insomnia Rating Scale (WHIIRS)
	Symptom distress[109, 209, 211, 212, 217, 220, 235, 236, 238]	- Edmonton Symptom Assessment Scale (ESAS) - Memorial Symptom Assessment Scale (MSAS-SF) - MD Anderson Symptom Inventory - Modified Edmonton Symptom Assessment Scale (ESAS)† - Symptom Distress Scale (SDS-15, SDS-22) - Symptom Representational Questionnaire (SRQ) - Symptom scoring within intervention[235]
	Symptom severity, consequences & controllability[238]	- Symptom Representational Questionnaire (SRQ)
	Performance status/level of daily activity[212, 239]	- Eastern Co-operative Oncology Group (ECOG) Performance Status Scale

†*Caregivers reported symptom distress on behalf of patient.*[211]

Table 4.6 Overview of psychosocial outcome measures (as measured by n=number of studies)

	Outcome	Outcome measures
Psychological & psychosocial constructs (n=26)	Overall psychological functioning[215]	- Outcomes Questionnaire (OQ-45)
	Depression[209, 213-215, 217, 218, 221, 230, 234, 242, 248, 249] Depressed mood[219] Mood[227]	- Beck Depression Inventory (BDI) - Centre for Epidemiologic Studies Depression Scale (CES-D) - Hospital Anxiety & Depression Scale (HADS-D) - Patient Health Questionnaire (PHQ-8, PHQ-9) - Patient-Reported Outcomes Measurement Information System (PROMIS) – Depression item bank - Profile of Moods States – Short Form (POMS-SF)
	Stress[231]	- Calgary Symptoms of Stress Inventory (CSOSI)
	Anxiety/anxious mood[209, 213, 215, 219, 220, 225, 231, 241]	- Hospital Anxiety and Depression Scale (HADS-A) - Impact of Events Scale – Revised (IES-R) - Profile of Moods States – Short Form (POMS-SF) - Spielberger State Anxiety Inventory (STAI)
	Anger/angry mood[219, 231]	- Profile of Moods States – Short Form (POMS-SF)
	Positive mental health[223]	- Mental Health Continuum – Short Form
	Feelings over past week[242]	- Profile of Moods States – Short Form (POMS-SF)
	Cancer related intrusive thoughts & feelings/post-traumatic symptoms[222, 242] Rumination[223] Fear of cancer recurrence[223]	- Fear of Cancer Recurrence Inventory (FCRI) - Impact of Events Scale – Revised (IES-R) - Posttraumatic Growth Inventory (PTGI) - Rumination and Reflection Questionnaire (RRQ)
	Confusion[231]	- Profile of Moods States (POMS)
	Psychological distress[215, 216, 223, 229, 233, 237] Cancer related distress[230]	- Brief Symptom Inventory (BSI) - Distress Thermometer (DT) - Hospital Anxiety and Depression Scale (HADS) - Impact of Events Scale (IES)/Impact of Events Scale-Revised (IES-R) - Patient Health Questionnaire (PHQ-4)
	Self-efficacy for coping with cancer[209, 217, 220, 222, 240]	- Cancer Behaviour Inventory (CBI)/CBI-B (Brief version) - Stanford Inventory of Cancer Patient Adjustment (SICPA)
	Vigour/positive mood[215, 231, 242]	- Profile of Moods States (POMS, POMS-SF)
	Spirituality[231] Peace/meaning[219] Appreciation of life[242]	- Functional Assessment of Chronic Illness therapy - Spiritual well- being (FACIT-Sp) - Posttraumatic Growth Inventory (PTGI)
	Mindfulness[223, 228, 231]	- Five Facet Mindfulness Questionnaire (FFMQ) Mindful Attention Awareness Scale (MAAS)
	Mental adjustment[237]	- Mental Adjustment to Cancer (MAC) scale
	Perception of positive changes after adversity[231, 242] Relating to others[242]	- Posttraumatic Growth Inventory (PTGI)

	Social & functional well-being[222]	- Functional Assessment of Cancer Therapy – Breast (FACT-B)
	Social support[210, 217, 220]	- Medical Outcomes Study Social Support Survey (MOS-SS) - Multi-dimensional Scale of Perceived Social Support (MSPSS) - Six-item Social Support scale (developed in a previous study).[250]

4.6.6.1 Interactive health communication applications

Most of the IHCAs (11/12) demonstrated measurable improvements, to a varying extent, in QoL and psychosocial constructs. These spanned the range of delivery modes (Figure 4.3) and comprised vastly differing content.

For 5 of the interventions, efficacy was demonstrated through direct measurement of QoL using FACT-G, FACT-B, WHOQOL-BREF and EORTC-QLQ-C30.[210, 212, 213, 218, 220] As well as supporting QoL, one intervention also resulted in less worsening of self-efficacy for users (following initiation of chemotherapy) compared to controls.[220] Another led to improvements in both QoL and symptom distress.[212] Each of these interventions included features for symptom self-management, four of which also integrated some form of expert support.[210]

In the absence of direct QoL measurement, other IHCAs were found to support or improve diverse related constructs such as symptom distress, anxiety, depression and peace. Their content was equally diverse. Two were purely self-management,[209, 219] though both featured user-user communication, and one included expert support through clinical integration.[211]

Users of 'Health Space', an IHCA focusing on user-user engagement with expert input, experienced significant improvement in fatigue (measured as a subscale of the POMS-SF) relative to controls. However, improvements in other psychosocial domains measured (psychological functioning, depressive symptoms, anxiety and vigour) were not significant.[215] Similarly, 'Surviving and Thriving with Cancer' showed marginal efficacy, measuring a range of psychosocial variables (fatigue, insomnia and depression) and finding significant reductions for intervention users in insomnia alone.[214] The 'Together' intervention, taking a self-management approach, also applied a range of psychological measures (HADS-A, DT and IES), though found no significant results.[216]

One study found breast cancer patients using the 'WebChoice' intervention had significant improvements in symptom distress, anxiety and depression when compared to those receiving usual care.[209] However, use of the same intervention, with the addition of expert support, amongst breast and prostate cancer patients demonstrated limited efficacy (though contrasting outcome measures prevent direct comparisons between studies).[217] Use of the

lung cancer (advanced stage) specific version of the 'Comprehensive Health Enhancement Support System' (CHESS) by patient-caregiver dyads resulted in lower physical symptom distress (measured using a modified ESAS) compared to internet use.[211] This was confined to measurements taken at 4 and 6 months after initiating the intervention, however, and was not observed at earlier (2 months) or later (8 months) time points. The study evaluating the breast cancer specific version of CHESS[210] (compared to both controls and use of the internet) demonstrated a similar pattern of efficacy, this time capturing QoL (FACT-B) and social support (using a 6-item scale developed in a previous study).[250] Both versions included varying levels of expert support.

4.6.6.2 Virtual programmes of support

Indications of QoL-related efficacy were also evident for diverse virtual programmes of support (9/11), delivered in a variety of ways. In 3 studies, significant improvements in QoL scores (measured using FACIT-F, FACT-B, EORTC-QLQ-C30 and EORTC-QLQ-BR23) were observed,[224, 228, 229] though programme content and delivery contrasted significantly. Whilst one delivered mindfulness training through self-management[228] (improving scores for both QoL and mindfulness), the others incorporated expert support within a supported self-management programme for coping with stress[229] (supporting QoL and significantly reducing distress) and a professionally guided exercise programme.[224]

Another online mindfulness programme, this time professionally delivered, assessed a host of psychosocial measures. These included total mood disturbance, stress, spirituality, post-traumatic growth (PTG) and mindfulness (captured using POMS, CSOSI, FACIT-Sp and FFMQ respectively). The study found significant improvements, of moderate effect size, for all but PTG in intervention users versus controls.[231]

Less definitive evidence of QoL-related efficacy was observed in 5 studies. For some professionally delivered programmes, trends for improved scores in the applied measures did not reach significance[230] or were confined to a specific subscale (e.g. mental health related QoL).[223] The professionally-delivered online CBT stress management (CBSM) intervention did not lead to a statistically significant improvement in QoL. However, mean difference in FACT-G scores between groups met the threshold for clinical significance (defined as a minimum difference of 4 points for the total scale and 2 points for subscales).[230] Whilst the electronic mindfulness-based cognitive therapy (eMBCT) improved mental health-related QoL, mindfulness skills and positive mental health, and reduced rumination and fear of recurrence, this was also true for the face-to-face equivalent, when compared to usual care.[223] Supported self-management did not lead to improvements in QoL for the 'Coping with Cancer Workbook',

yet users demonstrated significant improvement in self-efficacy and in cancer related post-traumatic symptoms.[222] Whilst participants trialling the self-management 'Sleep Healthy Using The Internet' (SHUTi) did not experience statistically significant improvements in QoL, depression or anxiety, overall adjusted effect sizes for these constructs ranged from small to large. Lack of significance may in part have been related to underpowered analysis of a relatively small sample. Intervention use was, however, associated with significant improvements in fatigue (assessed using the MSFI-SF).[227] For the anxiety self-management mobile application, QoL, anxiety and depression improved for both intervention and control participants, yet there were no significant between group differences. Though further analysis demonstrated efficacy for a distinct subgroup (severely anxious at baseline), cautious interpretation was warranted due to small numbers.[225]

Two programmes, of varying levels of integration in patients' care pathway, were unable to evidence QoL-related efficacy, though both were evaluated within underpowered studies. These applied SF-36 to assess health-related QoL (HRQOL) with use of guided online self-help,[221] and EORTC QLQ-CIPN20 to capture symptom-related QoL following online CBT pain management.[226] Notably, glioma patients using the online guided self-help did experience a post-treatment reduction in fatigue of borderline significance.[221]

4.6.6.3 Symptom monitoring tools

For the symptom monitoring tools, once again efficacy was not confined to a particular style of intervention or mode of delivery and was demonstrated across diverse QoL domains (within 6/8 studies). For those with features to urgently alert clinicians to serious reported symptoms, improvement in QoL scores (FACT-L and EuroQol EQ-5D) were evident.[105, 232] Indications of efficacy were also reported across a diverse range of less intensive symptom monitoring approaches. Completion of touch screen QoL questionnaires in clinic, followed by clinician review, resulted in improved FACT-G scores for the intervention versus control group, though there was no significant difference between intervention users and those in the attention-control group (QoL questionnaire completion without feedback from clinicians).[251] For E-MOSAIC, direct integration of symptom reports completed in clinic did not result in a significant difference in global QoL (EORTC-QLQ-C30) between the intervention and control arms, though symptom distress (ESAS) was significantly less with E-MOSAIC use.[236]

Tools with a focus on coaching patients to communicate their symptoms to their healthcare team resulted in variable outcomes. Patients using the 'Communicating Health Assisted by Technology' (CHAT)[234] intervention experienced worsening HRQOL, measured using SF-36. Conversely, those assigned to the 'Interactive Tailored Patients Assessment tool' (Choice ITPA)

intervention group were significantly less distressed by their symptoms (specifically discomfort, eating and drinking, sleep and rest and sexuality) than control participants (Choice ITPA in absence of clinician review). Notably, the effect of Choice ITPA in comparison to care as usual (i.e. absence of symptom monitoring) was not assessed.[235]

Furthermore, symptom monitoring plus clinician feedback resulted in reductions in symptom distress[109, 236] and psychological distress[233] across other interventions measuring this construct, using the ESAS[233, 236] and the SDS-15.[109]

4.6.6.4 Communication conduits

The professionally guided communication conduits varied in their efficacy. Participants receiving counselling via email experienced no significant improvement in distress or overall QoL, captured using the BSI and EORTC-QLQ-C30, when compared to controls.[237] For patients using the message board based intervention,[238] there was no evidence of impact on consequences or controllability of symptoms between groups. Yet, the intervention group demonstrated significantly lower symptom distress, and a trend (though not significant) for improved symptom severity, compared to the control group. However, this effect, observed using the SRQ, was not maintained 6 weeks post intervention.

For the self-management peer-peer online support group, completion of QoL measures (ECOG and FACT-B) evidenced little difference between study arms, though definitive conclusions regarding efficacy were limited by a small sample size.[239]

4.6.6.5 Information websites

Within the studies evaluating information websites, all of which were purely self-management interventions, 2/3 did not demonstrate significant intervention effects for the QoL related outcome measures applied (Quality of Life Instrument - Breast Cancer Patient Version[241] and the German version of the CBI-B[240]).

However, users creating their own personal website within a workshop setting ('Project Connect Online', which is likely to have involved some expert support), experienced significant effects on broader psychosocial measures of depressive symptoms, positive mood and life appreciation (CES-D, POMS and PTGI).[242]

4.7 Discussion

This systematic review has identified a broad range of online and technology-assisted interventions delivering cancer support, with a focus on those targeting or inclusive of patients living in the advanced stages of disease. On the basis of shared features and functionality, and in consultation with the wider literature, five distinct subtypes emerged: IHCAs, virtual

programmes of support, symptom monitoring tools, communication conduits and information websites. Further categorisation was guided by the extent to which interventions facilitated independent self-management or supported patients to self-manage through varying levels of expert involvement. Numerous approaches were identified and described within the model of online and technology-assisted intervention delivery. These ranged from independent and supported self-management, to those with elements of professional facilitation, and interventions delivered as part of the usual care pathway. Clinical integration was mostly observed in the symptom monitoring tools, with health professional involvement encouraged or directly facilitated, whilst the information websites guided independent self-management. In general, interventions could be placed between these two extremes, encouraging self-management whilst offering varying degrees of expert support.

Psychosocial considerations were an overarching focus of the content and features delivered across interventions. For the virtual programmes of support, psychological behaviours or symptoms were targeted as the main focus of the intervention in almost all cases (10/11), most applying cognitive behavioural therapy (CBT) techniques. Psychosocial needs were also a predominant focus for the multi-faceted IHCAs (11/12), addressed through various forms of psychotherapy, psychoeducation or socio-emotional support. The smaller number of information websites and communication conduits evaluated were also largely shaped by these considerations. The symptom monitoring tools, in contrast, mostly targeted patients' physical health through supported management of symptoms and side-effects. An underlying link to psychosocial well-being was evident, however, with 6/8 of the studies assessing QoL or psychosocial constructs as primary study outcomes.

The past decade has seen a breadth of research emphasising the need for psychosocial considerations as core aspects of patients' cancer care and support.[252, 253] It comes as no surprise, therefore, that a large number of interventions are being developed with a focus on addressing these needs. However, whilst it is difficult to make direct comparisons or draw definitive conclusions, this review has highlighted wide-ranging efficacy across physical, psychosocial, and more general health & lifestyle-related support alike. A tendency for interventions to encompass patients across all stages of cancer makes it difficult to gauge the impact for those specifically in the advanced stages of disease. Yet, these findings support research emphasising the sheer breadth of needs, often unmet, encountered across the cancer trajectory.[14, 254] Whilst psychosocial care and support is fundamental, it is one aspect of what has been described as a 'spectrum' of patient needs.[255] More complete support must also encompass the physical, functional and spiritual needs which collectively determine QoL.[256]

Furthermore, perhaps what is most evident from the significant variation in efficacy between studies, interventions, patient populations and modes of delivery, is the fact that a standardised 'one size fits all' template does not exist when it comes to cancer support. In contrast, IHCAs offer the possibility of meeting a host of supportive needs via a multitude of ways. This may explain why they were the most widely evaluated of the interventions. Whilst their main focus was largely psychosocial, they brought together a range of other support and offer the scope to tailor to specific patient groups. Self-management and self-care were encouraged through a variety of integrated features such as educational exercises, discussion forums and decision-making tools, delivered with varying levels of expert input and guidance. Most conferred some level of psychosocial or QoL-related benefit for users, albeit to varying extents and across heterogenous populations.

The substantial complexity and variation within and across the intervention subtypes meant that it was not possible to attribute efficacy to specific features or components. However, looking more closely, a potential relationship between QoL-related efficacy and features for expert or health professional support, of varying intensity, appeared evident. Though not always the case, this was observed in interventions offering supported self-management, professionally guided support or clinical integration of support as part of patients' usual care. Features for physical symptom monitoring and self-management were also frequently seen in interventions demonstrating widespread efficacy, whether as the main focus or as one of multiple supportive components. Indeed, these features often incorporated some form of expert support or feedback, making the two elements inextricably linked in many cases. However, the potential value of both is clear. Support in the form of peer to peer communication, social networking or shared experiences was also a feature of multiple interventions demonstrating QoL-related efficacy. Whilst there is increasing emphasis on empowering patients with chronic diseases to self-manage and to have a central role in their care,[13] these findings remind us of the value of collaboration and shared input, engaging the patient, professionals and peers. Indeed, this lessens the burden of support at both an individual and a service level.[257] Crucially, the model of online and technology-assisted intervention delivery should not be seen as a hierarchy, rather as a group of potential approaches, any number of which may be harnessed to support diverse patient needs.

This has been evidenced through widespread efficacy spanning the interventions described, 78% of studies demonstrating some measurable improvement in QoL and/or psychosocial well-being. Whilst this evidence guides us in supporting the needs of advanced cancer patients more generally, future intervention development and evaluation must target and involve these patients more specifically. Corbett et al emphasised the potential value of patient involvement

in intervention design, to ensure challenges specific to their stage of the cancer trajectory are addressed.[258] Collectively, this greatly supports the LIBERATE research goals. Beyond the development phase (for the LIBERATE intervention and others), greater representation of advanced cancer patients within larger scale intervention trials will strengthen the evidence base guiding their support.

4.8 Reflections

The evolving chronicity of cancer has significant implications on cancer services, in terms of both growing demand and changing patient needs. Online and technology-assisted resources offer the possibility for more cost-effective, tailored and accessible monitoring and support, reducing the burden of follow-up on healthcare services and patients alike.[87, 255] Indeed, the need for such remote technologies has been further heightened by the current COVID-19 pandemic and its impact on the delivery of care for vulnerable patients.[195]

Whilst research in this field is largely inclusive of patients with advanced cancer, they are far from being the focus of such innovations. A breadth of research has recognised that the needs of these patients extend far beyond the psychosocial domain, with significant physical, functional and spiritual issues encountered over an ongoing and uncertain disease trajectory.[13, 14] Overall, this review highlighted multi-modal, holistic and collaborative approaches as having the potential to address these varied needs remotely. As clinical advancements in cancer treatment continue to progress, so too must the evidence base guiding us in how best to address the complex supportive needs of the many patients who will, as a direct result, live longer in the advanced stages of disease. Furthermore, there is a need for more standardised methods of evaluation and reporting to allow for more definitive conclusions regarding the most effective means of supporting this steadily growing group of patients. The conclusions drawn from this review therefore served to further justify and guide the development and evaluation of the LIBERATE intervention in a multitude of ways. Their application to the next steps of research will be outlined in subsequent chapters.

Given the significant heterogeneity of study populations, it is hard to distinguish what works well for the advanced cancer patients amongst them. Whilst this review aimed to explore the features and efficacy of online interventions for patients living with advanced stage cancers, just 13 of the 35 interventions specifically targeted these patients. Of those with mixed populations, representation of advanced cancer patients was variable. This highlights a methodological conflict for researchers in terms of the value of focusing on a particular patient group versus the ability to achieve greater sample sizes when drawing from a more diverse patient population.

Further heterogeneity, this time related to studies' design and methods of outcome measurement, meant that it was not possible to determine the most effective intervention features through meta-analysis. It was also difficult to ascertain how many of the studies were sufficiently powered to detect changes in the outcomes of interest, since this wasn't always reported for QoL and psychosocial measures. As risk of bias varied significantly across studies, with judgement limited by inadequate reporting in some cases, findings must also be interpreted cautiously. In terms of the methods of the review itself, due to limited time and resources, only 20% of papers were screened by a second reviewer. Furthermore, as indicated by the high proportion of recent publications (at the time the searches were conducted), this field of research is extremely fast moving and it is likely that some articles may have been published outside of the search timeframe.

Whilst recognised as a crucial consideration, theoretical underpinnings of included interventions were not a focus of this review. During initial scoping, it was found that studies did not always report this aspect of development in sufficient detail, posing potential challenges to data extraction, synthesis and interpretation. The decision was instead made to explore a range of relevant theory (and to develop an underlying programme theory) in much greater depth, as will be outlined in the next chapter, providing a solid theoretical foundation upon which to design the LIBERATE intervention. This also meant that the systematic review had the space and remit to focus on the intervention components, modes of delivery and QoL/psychosocial efficacy in detail.

4.9 Summary

There is much to learn from the breadth of online and technology-assisted interventions providing support in advanced cancer. This narrative synthesis of evidence has identified diverse intervention features and modes of delivery, allowing for exploration of potential indications of efficacy through wide-ranging measures of QoL and psychosocial domains.

However, there is also a need for these innovations to more exclusively tailor their design and target their evaluation to the growing number of patients living longer with advanced cancer. Guided by these findings, phase II of the LIBERATE research will look to expand upon the current psychosocial focus of remote cancer support, harnessing the experiences of women living with SBC in order to more holistically address their health and well-being.

Chapter 5: Intervention theory

5.1 Chapter overview

Identification and application of the theory central to a complex intervention's mechanisms of action is a key element of the MRC Framework's 'development' stage.[116, 117] Indeed, the success of an intervention is very much dependent upon adequate understanding of *who* and *what* it will be targeting, *how* it will do so and *where* this will happen. A vast array of established theory can support researchers in laying these foundations ahead of intervention development and evaluation.[116, 259] Setting out the over-arching self-management focus of the proposed intervention, this chapter will explore a range of interacting and interrelated concepts before outlining the theories most relevant to the goals of this research. Guided by these conceptual underpinnings, programme theory will be applied in line with principles of realist evaluation. The underlying causal mechanisms, driven by theoretical hypotheses and shaped by contextual factors, will be outlined in order to determine how the proposed complex intervention will ultimately lead to improved QoL for women living with SBC.

5.2 Chapter aims

- To explore the concepts and theory relevant to the goals of this research.
- To outline the theoretical underpinnings of the proposed intervention, applying programme theory and constructing a logic model to explain the likely mechanisms of action and change.
- To identify measurable constructs for subsequent evaluation based on this collective theoretical overview.

5.3 Introduction

The LIBERATE intervention sets out to provide 'symptom monitoring, self-management and signposting support', yet the underlying theory and conceptualisations of such goals or 'targets' must be explored in order to determine *how* this can be effectively achieved by the proposed intervention. These goals encompass several forms of self-management: the monitoring and management of symptoms, alongside information and support seeking guided by signposting. As touched upon in previous chapters, the term 'self-management' has been increasingly applied throughout health research in recent decades, particularly in relation to the increasing prevalence of chronic disease. This must be carefully defined and clearly distinguished from closely related terminology and concepts. Furthermore, the theory as to how self-management can be effectively instigated in order to produce the desired outcome(s) must be clearly outlined.

5.4 Self-management

Self-management is a concept widely applied across a breadth of health conditions, encompassing diverse activities which seek to engage patients in their own care. This is especially the case in chronic disease, where such participation becomes integral to living with and managing disease over a longer-term trajectory.[260] As growing numbers of people continue to live longer with and beyond a cancer diagnosis, its chronicity is increasingly affirmed and the role of self-management in cancer survivorship is well established across a vast array of research.[85, 261-263] Such efforts serve not only to support patients in living with the diverse range of symptoms, side-effects and late effects of cancer and treatment, but also to support overburdened healthcare services in meeting the complex and longer term needs of this expanding population.[261]

For many decades, self-management has been successfully harnessed across a breadth of chronic conditions such as asthma, arthritis and diabetes. Whilst the role of self-management in the treatment and support of those living with cancer is clear, its realisation and integration in routine care is yet to be fully harnessed. Key to unlocking the potential of self-management across an increasingly chronic cancer trajectory is the understanding and application of underlying concepts and theory.[74, 264]

5.4.1 Concept analysis

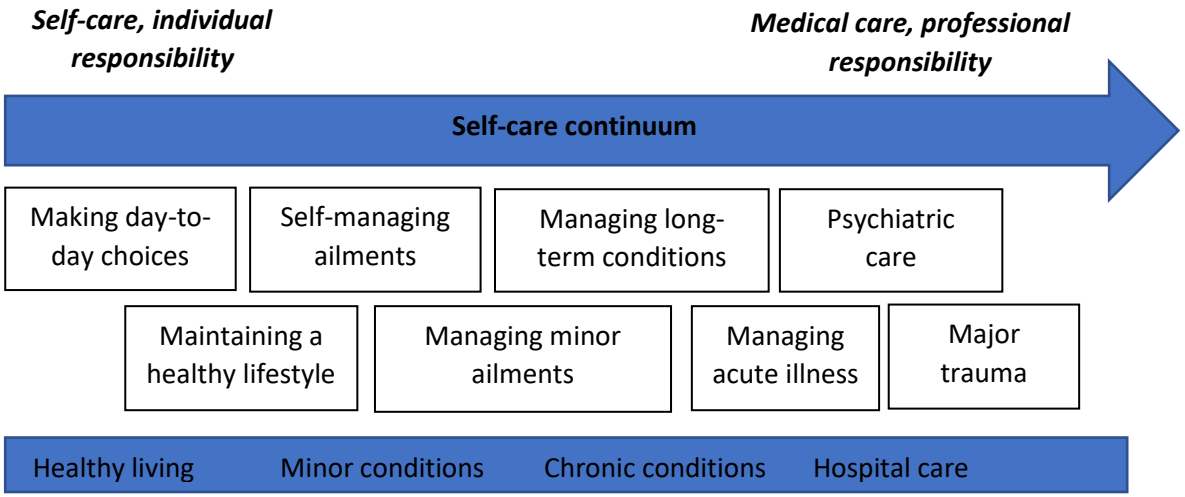
Based on the foundational work of Corbin and Strauss, Lorig and Holman defined self-management in relation to three core groups of 'tasks'.[260, 265] The first relates to the medical management of a condition, with the individual involved, for example, in taking prescribed medications and adhering to lifestyle advice. The second encompasses the various day-to-day behaviours or roles which an individual must embrace or adapt to as part of living with their condition, such as limiting physical exertion or accepting support. The third relates to the management of the range of emotions which may be experienced as part of the ongoing psychological response to living with a health condition.[260] Indeed, in relation to the latter, Patterson suggests that an individual's perspective of their health state fluctuates between 'illness' and 'wellness' in chronic disease. Successful self-management, embracing all three of the core 'tasks', supports individuals in maintaining the perspective of good health or of being 'well'.[266] Barlow and colleagues bring these various tasks together, collectively defining self-management as a person's capability to manage the treatment, symptoms and side effects associated with their health condition, as well as the farther reaching consequences, including other physical sequelae, social impacts and lifestyle factors.[267]

In the cancer context, self-management poses a challenge to the out-dated notion that the management of cancer, on the part of the patient and the oncologist, abruptly ends when treatment finishes. Instead, self-management is embraced within the survivorship model of care, traversing all stages from diagnosis through to end of life.[268] As discussed in chapter 1, in the case of SBC and other advanced cancers, 'surviving' means to live *with* (and, usually, to continue ongoing treatment for) their disease, meaning that the need for self-management is equally ongoing.

5.4.2 Self-care vs self-management

Lorig and Holman propose that, even in the absence of illness (chronic or otherwise), self-management is an integral aspect of normal daily living.[260] To maintain health, individuals engage in self-management behaviours across their lifetime.[269] In this way, it is easy to see how the terms 'self-management' and 'self-care' have become so closely entangled.

Figure 5.1 The Self-care Spectrum (adapted from the Self-Care Forum)[269]



Whilst attempts have been made to distinguish the two concepts on the basis of health versus illness (self-care denoting the act of maintaining health as part of every-day living, whilst self-management seeks to maintain health in the presence of illness)[270] there is also a strong argument to consider both as part of a spectrum. The Self-care Forum propose that activities relating to self-care and self-management fall within the continuum outlined above. They define self-care as the actions which an individual takes, independently and collaboratively, for the protection, maintenance and improvement of their health and well-being.[271] Self-management of a health condition therefore sits within this definition. Across this continuum, the responsibility shifts from the individual (where self-care is performed to maintain health and manage more minor conditions) towards the health professional (who supports the management of chronic conditions and takes over the care of more acute and serious ill health, until the point at which self-care can resume as part of recovery).[269]

5.4.3 Self-management behaviours

It stands to a reason that a range of behaviours are needed (or must be activated) for an individual to successfully perform self-management. The definitions outlined clearly require an individual to be both motivated and engaged in the management of their health. Lorig and Holman furthered their definition by specifying the need for what they describe as core 'self-management skills'. These include the ability to problem solve and make decisions relating to one's care, to take appropriate action and utilize resources, and to forge relationships with health professionals.[260] In relation to the latter, through encouraging a shift in the balance of the doctor-patient relationship and the onus of responsibility, self-management interventions support the development of a partnership rather than a paternalistic model of care. This moves chronic disease management beyond the clinical context and into the processes and behaviours performed as part of everyday living.[272]

A host of self-management interventions are guided by the Theory of Planned Behaviour (TPB), which describes how an individual's intentions are linked to their subsequent behaviours.[273] Originating as the Theory of Reasoned Action (TRA), this theory proposes that a person's intention to perform a behaviour is directly influenced by both their attitude towards doing so and by subjective norms surrounding the behaviour.[274] Central to this concept, however, is the caveat that the individual must be able to exert self-control over the behaviour in question.[275, 276] The TPB evolved from the TRA with the additional consideration of 'perceived behavioural control' (PBC), recognising where an individual's perception of their ability to control a behaviour may vary and, as a result , influence their intention to perform it. Both TRA and TPB share a central focus on behavioural intention, looking to the constructs which influence this and, as such, comprise a crucial step in the causal mechanism leading to behaviour. Critics, however, question the capacity for a theoretical leap to be made between intention and action. These theories also make the assumption that, intention aside, individuals have the available opportunities and resources needed to perform the behaviour.[276, 277]

Across phase I qualitative findings (chapter 3), it became evident that, whilst the intention to self-manage was largely present (through choice or perceived necessity), the opportunity and/or resources were not always available. Self-management behaviours were therefore outside of some women's control, regardless of their intention to perform them. In other words, behavioural intention is not the necessary focus of change for the proposed intervention; it must instead support women to feel able to enact these behaviours and to have the opportunity to build confidence in doing so. To explore how this could be supported, a more contextually-grounded theory was sought.

5.5 Middle Range Theory of Self-care of Chronic Illness

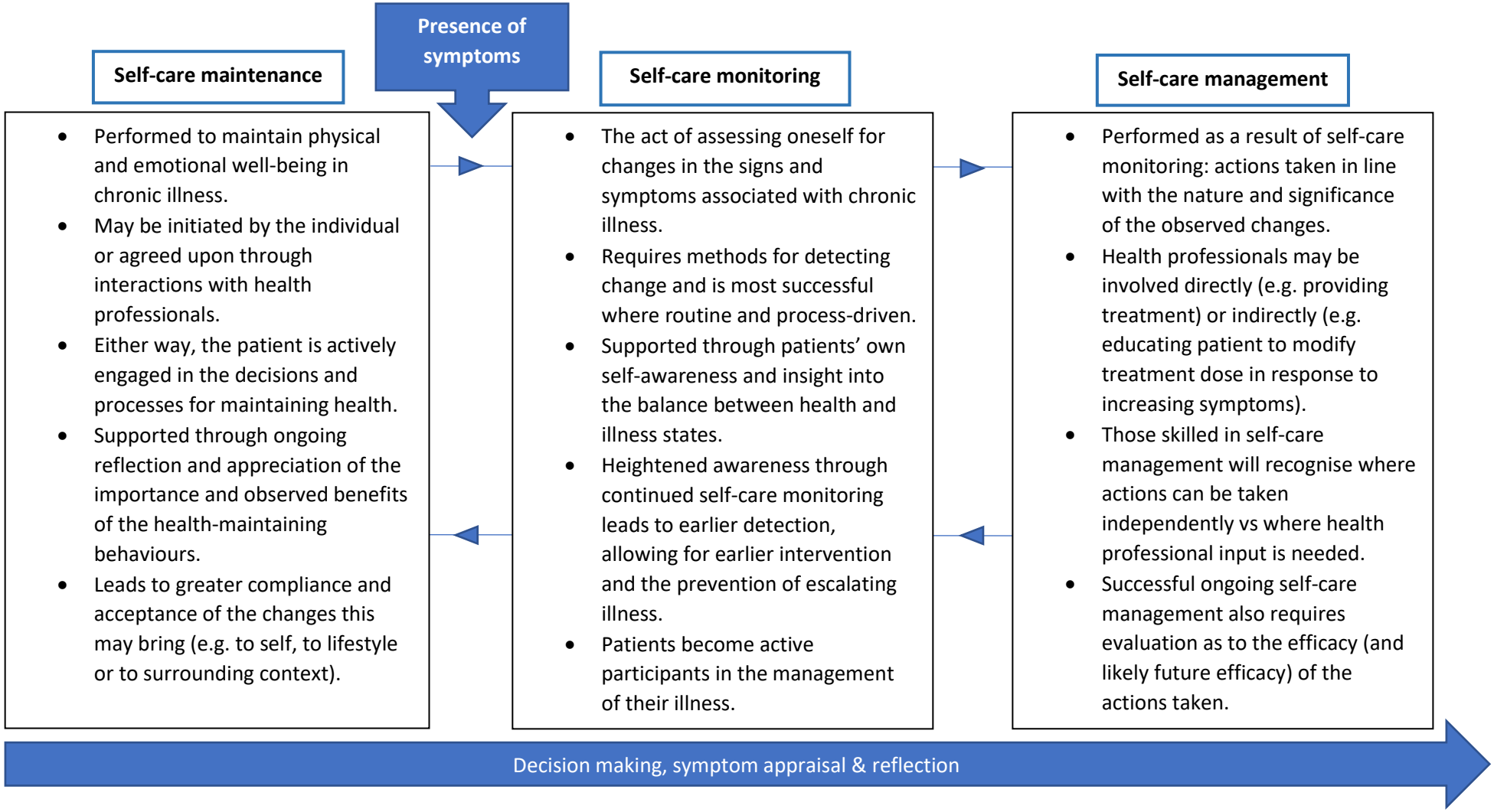
As highlighted, self-care is embedded in the activities we perform as part of daily living in order to maintain health; in this way, self-care is performed in states of both health and illness.[278] However, when living with illness over a chronic trajectory, self-care may take on new meaning and significance, demanding a distinct and sustained set of behaviours in order to adequately control the illness, minimise the burden of symptoms and side-effects and, in the case of life-limiting disease such as SBC, prolong survival.[279, 280]

Riegel, Jaarsma and Stromberg outlined a Middle Range Theory of Self-Care of Chronic Illness.[279, 280] Middle range theories can be described as theoretical frameworks which are applied to empirical research. They are concerned with empirical data and the understanding of phenomena at the level of such data.[281, 282] In this way, middle range theory seeks to understand a particular reality; it is therefore highly compatible with realist evaluation.

Riegel et al situate the concept of self-care within a broader theoretical framework shaped by considerations of how individuals live and adapt to illness over a chronic trajectory. They specify that chronic illness, where managed within the structure of the healthcare system, demands a distinct set of behaviours which must be performed for its effective management. Within this system, self-care becomes a mutual endeavour between a patient and their healthcare professional. Through this partnership, the patient is motivated to undertake self-care activities as part of their daily living.[279] Self-care in the context of chronic illness is carefully distinguished from self-care in a broader sense. Orem's 'grand theory' (a higher-level conceptual theory as opposed to one concerned with empiricism and social reality)[281] defines self-care as the activities which are initiated and performed by an individual, of their own volition, as part of day-to-day living and for the maintenance of health and well-being.[283] For example, maintaining dental hygiene and eating healthily. Clearly, this is distinct from self-care conducted in the face of illness. According to Riegel et al, this is the process of maintaining health through behaviours centred around illness management and health promotion.[284] Yet, even in a state of illness, the need for more general self-care remains. In this way, self-care is a fluctuating process, the goals of which change over time and are unique to the individual.

For Riegel et al, self-care in chronic illness comprises three core elements: self-care maintenance, self-care monitoring and self-care management.[279] Each of these are outlined in Figure 5.2 below.

Figure 5.2 The Middle Range Theory of Self-Care of Chronic Illness: Self-care behaviours[279, 280]



5.5.1 Underlying processes & proficiency

Riegel et al specify the interrelatedness of these core behaviours (as indicated by the multi-directional arrows in Figure 5.2), all of which must be performed to achieve effective self-care. However, the theory also recognises that varying levels of proficiency in self-care may mean that behaviours are mastered and applied to differing extents. Indeed, self-care maintenance is usually the foundational behaviour, upon which skills in self-care monitoring and self-care management are developed.[279] Furthermore, several key, underlying processes are identified.[279, 280]

5.5.1.1 Decision making

The first, and perhaps most crucial, is the process of decision making, which is described as occurring in a 'naturalistic' manner.[279] This refers to the dynamic and rapidly changing situations and contexts in which patients must often make decisions relating to self-care, when facing uncertainty and the potential for serious consequences. With acute onset symptoms, for example, a patient may not have the time or the capability to weigh up the pros and cons and apply rationality to the decision making process. Decisions are instead made in response to the situation at hand, guided by the available information.[279]

5.5.1.2 Reflection

Indeed, knowledge in self-care is crucial to both decision making and to another closely linked, underlying process: reflection.[285] Riegel et al theorise that patients who reflect on the knowledge they have gathered, considering what this means and how it can be applied to the situation at hand, are those most capable of performing 'sufficient' self-care. Less successful self-care is evident where patients lack both knowledge and reflective practice; they may perform behaviours (e.g. taking a medication or assessing for a clinical change) without understanding the underlying significance or being able to adapt their response in line with changing situations.[279]

5.5.1.3 Symptom appraisal

Central to the processes of both decision making and reflection in the context of chronic illness is the concept of symptom appraisal. A breadth of research has explored how patients appraise the symptoms they experience and the impact this can have on health outcomes.[286] By definition, a symptom is a subjective change to a person's physical or psychological state.[280] In a later iteration of their theory, Riegel et al sought to incorporate their own considerations of symptom theories and the process of symptom appraisal (the detection and interpretation of change followed by appropriate, responsive action)[286] in order to strengthen the concept of

self-care monitoring, the key link between the three self-care behaviours.[280] They proposed that the presence and recognition of symptoms, attributed to the chronic illness, was crucial in instigating self-care monitoring and, in response, self-care management.[286]

5.5.2 Factors influencing self-care

It is important to acknowledge that symptoms may not always be accurately appraised or appropriately acted upon, whether due to misinterpretation, misheld beliefs or insufficient knowledge, compromising the efficacy of self-care.[279, 280] In the context of cancer diagnosis, a range of sociodemographic factors, such as older age and lower health literacy, have been linked to poor appraisal of symptoms, negatively impacting upon health outcomes.[286]

Furthermore, Riegel et al identified a broader range of factors which may facilitate or pose challenges to the process of self-care, demonstrating its significant complexity and the demands placed on both the patient and the healthcare professional. These include those personal to the individual (e.g. motivation, experiences and skills in self-care, confidence, and their level of functional and cognitive capabilities) as well those related to context (e.g. the support of others and access to healthcare). Returning to the findings of chapter 3, the LIBERATE intervention aimed to support women to develop the skills and confidence to self-manage their illness and (frequently unmet) supportive needs, where this is currently lacking due to limited relevant opportunities or resources to do so. This research therefore focused on several of the identified factors in particular (confidence, experience and skills), drawing on further established theory to support the development of an intervention capable of supporting sufficient and effective self-care.

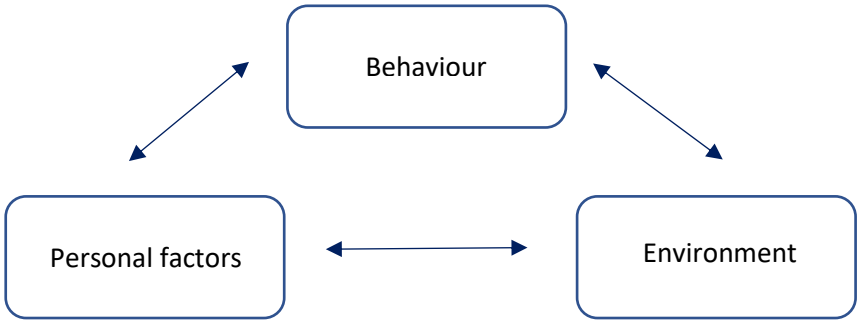
These three factors, crucial and interlinked facilitators of effective self-care, are encompassed within another key theoretical construct: self-efficacy.

5.6 Self-efficacy & the Social Cognitive Theory

Self-efficacy describes an individual's belief as to whether they are capable of achieving a particular goal.[287] This concept was first proposed by Bandura, as a crucial tenet of his Social Cognitive Theory.[288] Within this theory, individuals' learning and behaviours are directly influenced by a range of external influences. These influences relate to the environment (i.e. the situation and context in which the behaviour is performed) and the individual themselves (i.e. personal factors such as personality traits, individual instinct and level of motivation as drivers of behaviour). The theorised interaction between the person, their behaviour and the environment is displayed in Figure 5.3. This is referred to as '*reciprocal determinism*', with

personal factors, contextual factors and behaviour all interacting to influence one another.[276, 288]

Figure 5.3 Bandura's Social Cognitive Theory: Reciprocal determinism[288]



Self-Efficacy Theory is embedded within this wider Social Cognitive Theory, focusing on the construct of self-efficacy as a fundamental personal factor at play in the reciprocal relationship outlined above.[288] As part of this further theory, 'perceived self-efficacy' (an individual's perception of their ability to perform a behaviour required to produce a desired outcome) is carefully distinguished from an 'outcome expectation' (the assessment of whether or not a particular behaviour will lead to an outcome). Both of these constructs are core determinants of behaviour, though the former has been found to have greater importance in the enactment of more complex or progressively difficult behaviours.[275, 287]

Bandura theorised that an individual's perception of their self-efficacy is positively re-enforced through four key influences (Table 5.1 below).[288]

Table 5.1 Re-enforcing self-efficacy: four key influences[275, 288]

Experiences of past accomplishments	In successfully **performing** a behaviour, individuals develop experience in '**mastery**' of the necessary skills, **re-enforcing** their confidence that they will be able to do so again in the future. This is said to be the **strongest influence** of self-efficacy.
Experiences of others	Through **vicarious experience**, a person is able to envisage or '**socially model**' how they can perform the same behaviour(s) to **achieve the same outcome(s)** as others.
Verbal persuasion	**Positive verbal feedback** can act as a strong form of **encouragement**, instilling in a person the **belief** that they can succeed in performing a particular behaviour.
Psychological/physiological states	The **emotions/physiological sensations** a person is experiencing can influence their self-efficacy **belief**. For example, being in a state of anxiety or depression can lead to an individual **judging themselves as less capable** of achieving their goal than if they were in a more positive psychological state.

5.6.1 Self-efficacy and health behaviour

Through these various components, self-efficacy theory has been extensively applied to explain health behaviour at both an individual and community level.[275] In the context of illness, self-efficacy relates to a person's confidence in being able to manage the issues and necessary tasks imposed by their ill health.[263, 288] Higher levels of self-efficacy are associated with increased efforts and ongoing motivation to overcome challenges, as well as greater overall well-being.[289, 290] Indeed, such challenges may be related to the behaviours outlined within the Middle Range Theory of Self-Care of Chronic illness, with self-efficacy cited as one of the many factors influencing an individual's ability to effectively perform self-care.[280] Evaluating an intervention targeting self-efficacy amongst breast cancer patients, Lev and colleagues' findings supported this theory, evidencing improved self-efficacy for self-care behaviours.[290] This is further explained when looking to the range of causal pathways which Bandura describes as being implicated in the link between perceived self-efficacy (or self-efficacy 'beliefs') and health behaviour.[291] The first relates to goal-setting; an individual with higher self-efficacy will set themselves more ambitious goals and will be more motivated and driven to achieve them. The second relates to outcome expectations, identified earlier as another key determinant of behaviour. With higher self-efficacy comes the expectation of more positive outcomes. Conversely, those with lower self-efficacy are more likely to have lower expectations, instead anticipating poorer outcomes. The third causal pathway relates to the interpretation of challenges and obstacles. An individual with high self-efficacy will again demonstrate greater motivation and effort, feeling confident in their ability (and self-management skills) to overcome such obstacles. However, where self-efficacy is lacking, these are likely to be perceived as insurmountable barriers to their achievement of the desired outcome (i.e. effective self-management).[291] In sum, the greater a person's belief in their self-efficacy to achieve a particular outcome, the stronger the likelihood that they will be able to do so.[275]

5.6.2 Cancer-specific self-efficacy

Across psycho-oncology research, self-efficacy has been more specifically referred to as 'cancer relevant', 'cancer related' or 'coping' self-efficacy.[292-295] Whilst variously defined, in this context, self-efficacy relates to the significant (and, for some, ongoing) adaptation and coping behaviours which are demanded of cancer survivors. In 1983, Taylor proposed that a person's confidence in their ability to control their surroundings when faced with a 'threatening event' (such as a cancer diagnosis) directly influences their appraisal of and adaptation to stress.[296] Therefore, the greater a person's confidence in their ability to exert control in their experience of cancer, the more positively they appraise the inherent stressors and the better able they are

to cope.[296, 297] Indeed, in the decades since, a vast array of studies have evidenced a breadth of positive outcomes related to higher self-efficacy in cancer, from reduced physical and psychological symptoms, less distress and improved self-care, to greater adaptation to stress, better mood and higher QoL.[295, 298-302] In addition, situational specificity is highlighted as a crucial aspect of self-efficacy; confidence to perform one particular behaviour is not a determinant of confidence to perform other related behaviours.[287, 303] A person may demonstrate high self-efficacy in accessing supportive information, for example, but not in monitoring their symptoms.[292, 304] As such, in looking to develop an intervention to address diverse supportive needs, it was recognised that self-efficacy would need to be supported across a wide range of self-care behaviours.

5.7 Quality of life

The concept and measurement of QoL has been explored within earlier chapters and represents the over-arching focus of this research. Furthermore, it forms a key bridge between the various underpinning theories described. As highlighted, greater QoL is one of a host of positive outcomes demonstrated in cancer survivors with higher self-efficacy.[290, 295, 299] Exploring this relationship, Kreitler et al evidenced the potential for self-efficacy to act as a mediator of the range of stressors which compromise QoL in cancer.[305] Furthermore, in the oncology setting and beyond, it has been long established that greater self-efficacy leads to increased and successful performance of self-care behaviours.[306] A breadth of research in the context of heart failure (the foundation upon which the Middle Range Theory of Self-care of Chronic Illness was developed) has also firmly evidenced the link between effective self-care and greater QoL.[307-309]

The relationship between QoL and the presence of symptoms, however, is less clear cut. Whilst, as might be intuitively expected, a smaller burden of symptoms have been shown to result in greater QoL, so too has a higher or more severe symptom burden.[307] This may relate to the fact that symptom burden is itself a key driving force of self-care; increased severity of symptoms has been shown to result in greater engagement with self-care behaviours, whether independently or due to more frequent interactions with healthcare professionals as a result of a need for support in symptom management.[307, 310-312] Indeed, a recent study applied statistical methods to determine the relationship between all of these various concepts and provided definitive evidence of the mediating role of self-care. Greater self-efficacy in symptom management led to improvements in QoL in the presence of increased self-care behaviours.[313] This confirmed the importance and interconnectedness of these various

theoretical concepts and considerations, justifying their collective application to guide the development of the LIBERATE intervention.

5.8 Developing a programme theory

Whilst it is the subject of a complex array of differing terminologies and applications, at its very essence, programme theory describes how an intervention leads to outcomes. Whether these outcomes are intended or observed, a programme theory seeks to outline their underlying causal mechanisms.[314, 315] It is therefore a vital aspect of any realist evaluation and, as outlined by Funnell and Rogers, fundamentally comprises two key components: theory of change and theory of action.[315, 316] A theory of change describes the underpinning processes or influencing factors which bring about change, whilst a theory of action outlines how a programme or intervention works to instigate this change (in other words, how the theory of change is 'activated').[315]

Bringing these concepts together, a logic model is a visual representation of a programme theory and its component parts. At their most simplistic, these models outline the inputs (intervention components), the processes involved, and the outputs which follow (mechanisms of change and action), as well as an indication of impact (measurable or observable outcomes).[317] This visual portrayal makes the goals of the intervention clear, as well as supporting evaluation planning and the identification of potential measurable variables.[315, 317] However, there is debate as to how capable such models are of accounting for the inherent complexity of many interventions, as well as criticisms as to the omission of crucial contextual considerations and other factors which may interact to contribute to any observed change. A simple logic model may overestimate the role of the intervention (and underestimate the role of context) in the causal pathway.[314]

Pawson and Tilley's approach to realistic evaluation (which guided phase II of this research) can be thought of as a programme theory of sorts, shaped by considerations of the interplay between 'context-mechanism-outcome.'[143] For realist evaluators, intervention context is central to the theory of change, since this will determine whether or not the causal mechanisms are activated.[315, 316] For the LIBERATE intervention, the theory of change is informed by earlier outlined theories relating to self-care in chronic illness and self-efficacy, guided by overarching principles of realist evaluation. Developing a programme theory of the proposed LIBERATE intervention was the final stage of its theoretical development, outlining how exactly it would work to achieve its aims. Indeed, incorporation of theory of change has been recommended as a complementary 'tool' to support and strengthen the MRC framework for the development and evaluation of complex interventions.[318]

The theoretical underpinnings discussed earlier in this chapter were brought together to explain how the intervention's context and underlying mechanisms would interact to result in the targeted outcomes of self-efficacy and QoL, accounting for the crucial role of self-care behaviours as a mediating factor. This programme theory is first outlined within a simple logic model (Figure 5.4), before being mapped out within a realist matrix (Table 5.2), drawing out crucial further contextual considerations.

Figure 5.4 Proposed logic model for the LIBERATE intervention

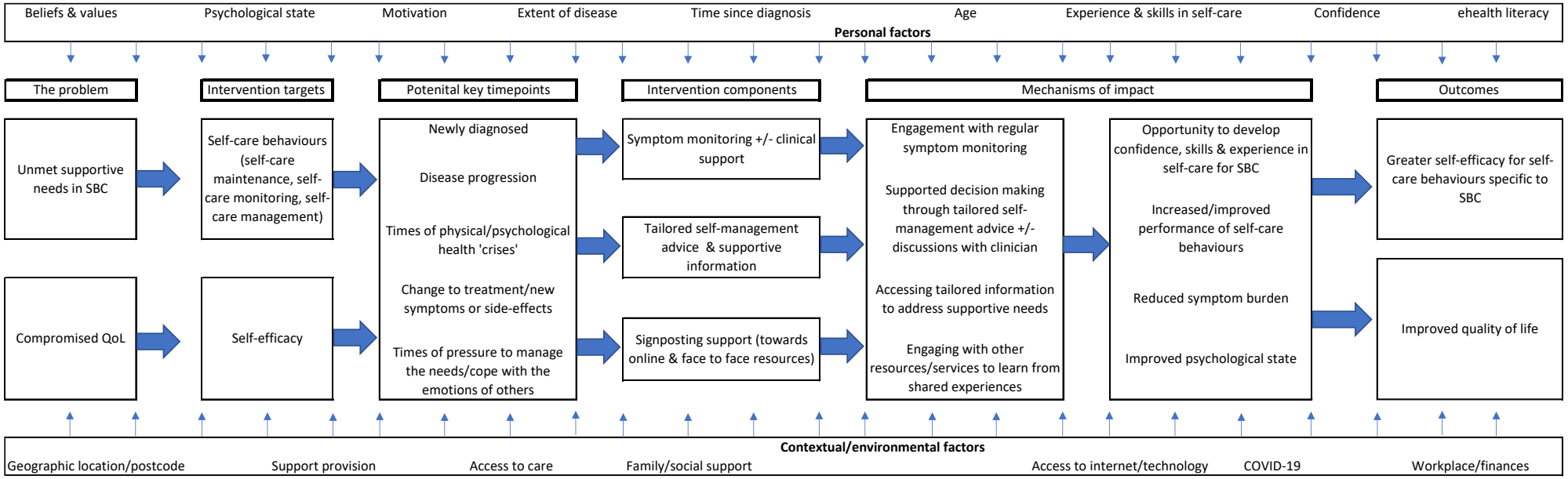


Table 5.2 Realist matrix of the proposed mechanisms of action & change

Context	Mechanism	Outcome
Newly diagnosed: Uncertain of information and supportive needs. Lack of knowledge and experience in the self-management of SBC. Low self-efficacy.	The intervention will provide a range of opportunities and resources to develop or re-enforce skills in self-care maintenance, self-care monitoring and self-care management. • Provision of tailored information and signposting to guide users in performing self-care behaviours to address specific/evolving supportive needs. • Integrated tool for self-monitoring, supporting the appraisal of symptoms. Tailored, responsive onscreen self-management advice supporting decision making as to appropriate self-management actions and encouragement to adhere to continued symptom monitoring. • Opportunity to reflect on and review symptoms through on screen results (feedback) +/- interactions with health professionals (verbal persuasion). • Reminders to regularly complete symptom monitoring, supporting the development of performance accomplishment. • Potential for case studies (developed on the basis of qualitative findings) to support social modelling and learning through the experiences of others.	Increased self-efficacy as a result of: • Experience of effective self-management of symptoms and supportive needs. • Reduced uncertainty, leading to greater confidence in ability (and resources) to manage current and future supportive needs. • Reduced distress, leading to improved psychological state. Greater quality of life as a result of: • Increased self-efficacy. • Improved symptom management. • Fewer unmet supportive needs. • Improved psychological state.
Living with SBC in medium to longer term: Change to circumstances (*e.g. change of treatment, disease progression*) or evolving supportive needs (*e.g. advance care planning, need for psychological support due to increasing anxiety/uncertainty*). High self-efficacy, though increased distress and uncertainty. OR Low self-efficacy due to previously limited opportunities/resources to address supportive needs.		

5.9 Reflections

This chapter has drawn on a breadth of established theory, as well as the strengths of programme theory and principles of realist evaluation, outlining how these informed the early conceptual planning and design of the LIBERATE intervention. This stage of the research established an understanding of the intervention which extended beyond the component parts and into the surrounding context. On the other hand, it focused on just two of a plethora of potential theoretical underpinnings. Whilst efforts have been made to justify their selection over other less relevant theory (such as the TRA and TPB), the pragmatics of the research timeline required an element of deductive selection in exploring those most likely to apply to this context. Given subsequent intervention development and evaluation was to be conducted within the feasibility setting, it was acknowledged that there would be the opportunity, however, to test out the proposed theory and use this grounding to guide recommendations for further iterative development and evaluation.

5.10 Summary

Collectively, the outlined theories supported the identification of self-efficacy as the key theoretical construct to be targeted by the LIBERATE intervention, as a factor which is both integral to and mediated by self-care behaviours. This therefore represented the core measurable outcome. Given LIBERATE's overarching goal to better understand and seek to support QoL, as well as the identified links between QoL, self-care and self-efficacy, this broad construct was also highlighted as a crucial measure. As will be explored in the next chapter, this breadth of theory was taken forwards in the developmental phase, complementing and strengthening the evidence base and lived experiences so far explored.

Chapter 6: Intervention design & development

6.1 Chapter overview

This chapter brings together the various strands of research which have so far contributed to the process of intervention design. The evidence base for online and technology-assisted health interventions is often found to be lacking in detail when it comes to descriptions of their underlying theory, proposed mechanisms of action and the steps leading to their design and development.[202, 203, 319] This hinders the understanding and application of findings, which may prevent interventions from being implemented outside of the study setting.

6.2 Chapter aims

Across three sections, this chapter will therefore aim to:

- Clearly outline how phase I research was interpreted and applied to shape the design of the LIBERATE intervention.
- Provide a detailed overview of the steps taken across key stages of intervention design and development, guided by a range of approaches and evidence.
- Describe the processes followed to reach a finalised intervention design through expert consensus.
- Present the LIBERATE intervention and discuss the development of its various components.

Section one: Bringing the evidence together

6.3 Intervention design: results of stage 1 qualitative analysis

As discussed extensively in chapter 3, the rich data set gathered through qualitative interviews with the key 'stakeholders' (i.e. women living with SBC and professionals involved in their care and support) fed into multiple aspects of this research. As well as generating more in-depth understanding of women's QoL and the context in which support will be delivered (stage 2 analysis, chapter 3), the data also directly informed the content and delivery of the proposed online supportive intervention. This latter research goal required more specific, granular information, which can be lost when moving beyond the codes to identify patterns and themes and gain a more conceptual overview. The relevant data was therefore extracted following in-depth coding.

Key information relating to information and supportive needs, identified as important and/or unmet, was collated. Alongside this, women's attitudes (first and second hand) towards and experiences of online support and face-to-face alternatives were gathered, allowing for early assessment of whether the proposed online delivery was a viable research pursuit. The results of stage 1 qualitative analysis are summarised below.

6.3.1 Supportive needs

Across the data, a breadth of identified supportive needs centred around five key areas:

- Information relating to SBC and treatments.
- Management of ongoing symptoms and side-effects.
- Psychological and emotional support.
- Holistic well-being.
- Support for family, loved ones & wider circle.

Each of the core areas of supportive need appeared to be met to varying extents for different women. Their prominence is also reflected across the identified themes discussed in chapter 3. Figure 6.1 collates these supportive needs (identified by both women and health/charity professionals) to give a full picture of potential gaps to be bridged in the design and delivery of the proposed intervention.

6.3.2 Factors influencing information and support needs

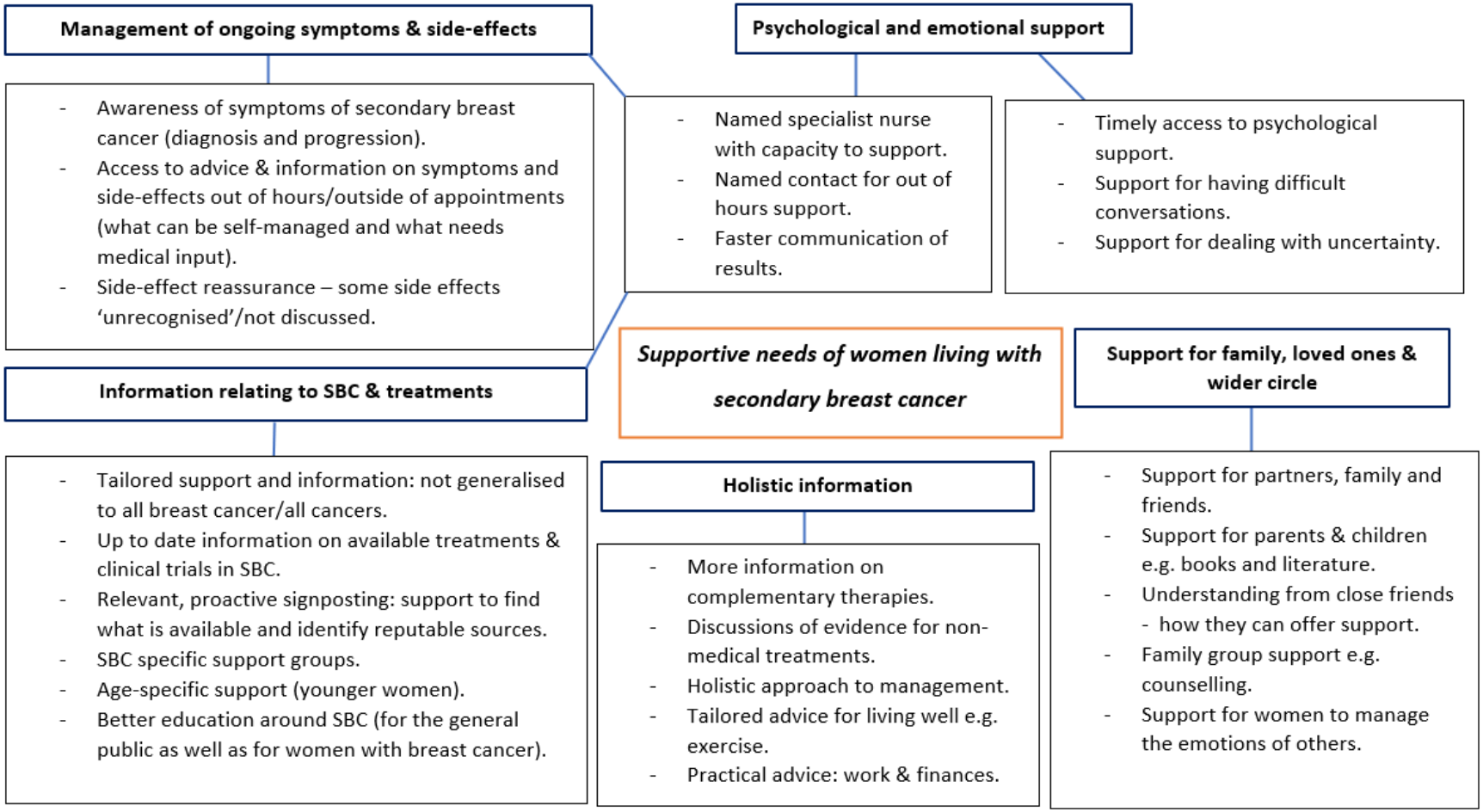
Crucially, a range of factors influencing the type and extent of information and support women needed were identified. These included their age, stage of disease progression and individual readiness for information and support. These findings provide vital insight into where intervention tailoring should focus.

6.3.2.1 Age

Age was highlighted as significant determinant of supportive needs, preferences and priorities, with certain issues identified as more relevant to younger age groups. Since age can be a determinant of family and working situations, this also influenced supportive needs in terms of accessibility and available time. Diagnosis at a younger age led to feelings of isolation for some women and support for this age group was felt to be limited. Age also appeared to influence acceptance of and reaction to diagnosis, in turn influencing the level of support women needed.

> *"…that's a big thing about having cancer at quite a young age… I'd say I'm getting better at this now but when I was first diagnosed, that was, that's a really, really hard thing. I really felt very isolated." (pt09)*

Figure 6.1 Supportive needs of women living with SBC



6.3.2.2 Stage of trajectory

Varying stages along the advanced cancer trajectory were evident, determining the sort of information and support that was felt to be appropriate to the individual and their current experience of SBC. Women also recognised where their information and support needs may shift and evolve further down the line, with treatment changes and disease progression. In this respect, there was a sense that their journey differed drastically from those with primary breast cancer and some were therefore reluctant to share feelings, experiences and concerns amongst those with earlier stage disease for fear of upsetting them. Some women also found it distressing to encounter information and experiences relating to more progressed stages of SBC; information specific to an individual's current 'status' and site of disease was very much valued.

> *"… it is different, because you go from being curable to just treatable and that's the terminology they use and I think, yeah we are treatable but we're not going to get any better and our life is now going to be treatment, treatment, treatment of some sort, scans of some sort. You know, there are, you need a different kind of support..." (pt35)*

> *"…everything is sort of geared up to people who really are going to survive it and you feel like there's almost, sort of, they don't really want to address those who won't or you know, you're a sub section. A very small subsection." (pt37)*

6.3.2.3 'Readiness' for information & support

There was evident diversity in the stages at which women felt 'ready' for certain sorts, amounts and depths of information and women acknowledged the difficulty for health professionals and other services to anticipate and gauge this. Some women described not feeling ready or in need of information or support, whilst recognising sources they could access at some point in the future. Others felt that they didn't yet know what they were looking for. For some, not feeling ready for support was a welcome indicator of normality.

> *"…you know, we're not at that point yet, right now, erm, we're happy enough and to be honest, part of the fact that we don't need that support is good. The fact that we don't, you know…" (pt36)*

6.3.3 Key attitudes, values & support seeking tendencies

Women's support seeking needs and tendencies were also shaped by a range of attitudes, values and preferences.

6.3.3.1 Expert input

Expert input, in various forms, was particularly highly valued across areas of supportive need. This appeared to be viewed as a marker of trustworthiness and quality of support, even for those actively seeking out supportive resources independently. Great value was placed on having a 'named contact' who could be contacted outside of appointments for advice and

timely support, particularly in relation to symptom and side-effect management. As previously discussed, this need appears to be met to varying extents. Women with a named CNS particularly valued this source of expertise.

> *"…but to have one person that you could email or pick up the phone, who would respond straight away, well within 24 hours, without making you feel that you're being a pain, would be great." (pt08)*

Women also described seeking expertise from a range of professionals, across community, hospital and alternative & complementary healthcare settings. There appeared to be a general willingness to seek expertise elsewhere, but a tendency to see consultant/hospital-derived support and information as reassuring and reliable. A need for expert moderation was also emphasised in support group settings.

6.3.3.2 Self-directed

Though there was a definite sense of expert health professional input being valued and sought after, women spanned a spectrum of 'pro-activeness', seeking out information to either complement or bridge a gap in information and support provided to them. For some, this was felt to be more of a necessity than a conscious choice.

> *"…So I tend to, to sort it out myself, really. You get to be your own project manager, I think. I don't think there's any choice, whether you want to or not." (pt08)*

Certain tendencies, such as recording notes, asking questions and following up on decisions in consultations were described in the sense of patients establishing an element of control and involvement. Others, however, preferred to be directed by their health professional, taking a less active role in their care.

> *"… I tend to just go with things and accept what doctors say, that they know a lot more than me, you know so…" (pt18)*

6.3.3.3 Shared experiences

Generally, there was an appetite for shared experience, with great value placed on meeting or connecting with women in a similar situation, driving positivity, hope, a sense of release and feeling better prepared. Women described feeling more comfortable opening up to others who shared their experiences, and were keen to discuss tips for coping with treatment and side-effects. Some also expressed being comforted by supporting others. For women with a de novo diagnosis, there was a sense of feeling 'unique' and distinct from those who had an initial primary diagnosis, with shared experience of their own journey to diagnosis being vitally important yet more difficult to find.

> *"I mean, nobody knows better than someone else who's got the same thing really." (pt22)*

However, shared experience was not universally valued. Some felt that this could lead them to dwell on negative experiences which they may or may not encounter and detracted from efforts to achieve day to day normality. Attitudes towards shared experience gained in group settings were particularly polarised, some finding these useful and supportive contexts, whilst others were clear that they did not address their needs.

> *"…it's not for me. I would much rather live a normal life as best I can and I know that's slightly burying my head in the sand but that's what keeps me well, is doing what I like to do and spending time with people I want to spend time with, not people who are in the same club as me, I don't want to be in…" (pt25)*

6.3.3.4 Evidence basis

Women frequently acknowledged a need to be guided by evidence and expertise. Discussions surrounding evidence bases were largely centred on alternative and complementary therapies. Whilst opinions as to their efficacy and use were divergent, or uncertain, there was a shared interest for these options to be discussed. 'Evidence-base' was recognised and cited as a marker of trustworthiness and was generally felt to be more likely where women were signposted to a source, as opposed to 'googling'. Women also expressed interest in being kept up to date and made aware of clinical trials and new treatments which may be relevant to them.

> *"…sometimes you get these headlines, you know, your daily mail headlines, turmeric or broccoli or whatever is the, you know, the be all and end all and the cure, and sometimes the sensationalist headlines, when you look into them… you don't get the full story is what I'm getting at, so sometimes I think some good advice as opposed to knee jerk or scaremongering type of trends would be good, yeah." (pt01)*

6.3.3.5 Optimising health

There was a strong, shared interest in 'living well' with cancer and striving to achieve a healthy lifestyle. There was therefore an expressed need for information and support in this area, ranging from tailored dietary and exercise advice to more holistic considerations of supplements and complementary or alternative therapies. This also factored into the management of symptoms and side-effects, with widespread efforts to optimise health alongside treatment and its fluctuating impact on daily living and well-being.

> *"…it gives me some sort of kind of control that I feel that I'm doing something by adapting my diet, and you know it's not completely kind of keto, vegan extreme but I do, I do, and I've had birthday cake this week and I do eat chocolate, you know, I'm not, I'm not kind of that severe on it but I think it's really important…" (pt09)*

6.3.4 Routes to support

Gaining an accurate overview of existing support pathways in SBC was another important aim at this stage of analysis. To guide the ongoing research, it was important to understand what is

currently available, what works well, what is missing or lacking, and what could be improved. This information was determined by exploring women's and professionals' experiences of the pathways and barriers to support in SBC.

6.3.4.1 Face-to-face support

Some women placed great value on talking through experiences in a group context. Others found it difficult to ask for support in this context or felt pressured to be a source of support themselves. Some women preferred to seek support from their own friends and family, or less formally when meeting other patients in the healthcare setting.

Positive experiences included establishing support networks and friendships, allowing women to share expertise and put their own experiences in perspective. Negative experiences included support groups attempting to appeal to a broad and varied audience, limiting their value and relevance. Women described finding it difficult to remain positive or feeling drained in poorly facilitated groups dominated by negative experiences and women with differing outlooks and mentalities.

> *"…the time that you probably feel most relaxed, if I was going to open up it would probably be to these people, is when you're in a room of people going through the same thing because they can support you, they know what you're going through, they can advise you and quite often, you know, people can give each other hope…" (pt20)*

6.3.4.2 Online support

The internet was described as a widely-used, valued and accessible source of support, allowing women to supplement information received in healthcare settings, particularly where time is lacking and where they encounter queries and issues outside of appointments. The unlimited availability of web-based sources, and the potential for constant engagement, was described as both a benefit and a burden. The internet appears to be a particularly valued source of information on symptoms, side-effects and treatments, experiences of others, and for gauging when to self-manage versus when to seek out help from healthcare professionals. The usefulness and relevance of information was often said to be minimised by generic as opposed to tailored content. Value is potentially time-dependent, with some non-internet users describing use earlier on in diagnosis. A degree of age-dependency was evident for some women, but not all, with internet use spanning all age groups.

> *"…yeah, and I think what I often, if I have side-effects, I'll always go to the Macmillan site, look under my drugs and I'll just read, or the Breast Cancer Care, and I'll go, 'oh yeah, so it's expected', just to go like, 'do I need to ring up?' So that's, and because it's Macmillan, I know it's evidence based." (pt09)*

Positive experiences included opportunities to share and learn from experiences of side-effects and treatments, tips for coping and self-management, and feeling a sense of hope and positivity from connecting with, or encountering experiences of, women living well and in the longer term. Whilst some particularly valued engagement with forums and interactive sources, others preferred to use these more passively as a means of eliciting information. Women also valued evidence-based information and being signposted to other relevant sources of support. Negative experiences mainly involved encountering negative or distressing information, experiences and statistics. This was particularly upsetting where women felt unprepared for, or previously unaware of, such information.

> *"…I always feel with online you're opening a very large can of worms, really, I think it can be a lot more frightening than…it depends who, where you go for it, I suppose, but there's so much out there. It can be quite confusing." (pt17)*

6.3.4.3 Navigating online support

Further information was elicited as to what has been referred to as patients' 'navigational needs.' These are defined as the needs of those requiring support to locate health information online,[92, 320] and were self-identified amongst women of varying levels of apparent engagement and experience in navigating both their health needs and the internet. In discussing the vast amount of information available on the internet, women described feeling overwhelmed and uncertain where to look and what to trust. They expressed a need for support to identify online information sources which were relevant (SBC specific and UK specific), evidence-based and reliable. Some internet-based information was felt to be out of date, conflicting, lacking in evidence or irrelevant to those with SBC. Health professionals and the role of expert signposting were identified as being key to addressing these barriers.

> *"Yeah well, you know we all, with all these new drugs, of course I Google you know, I know you shouldn't but I've done a bit of that…" (pt22)*

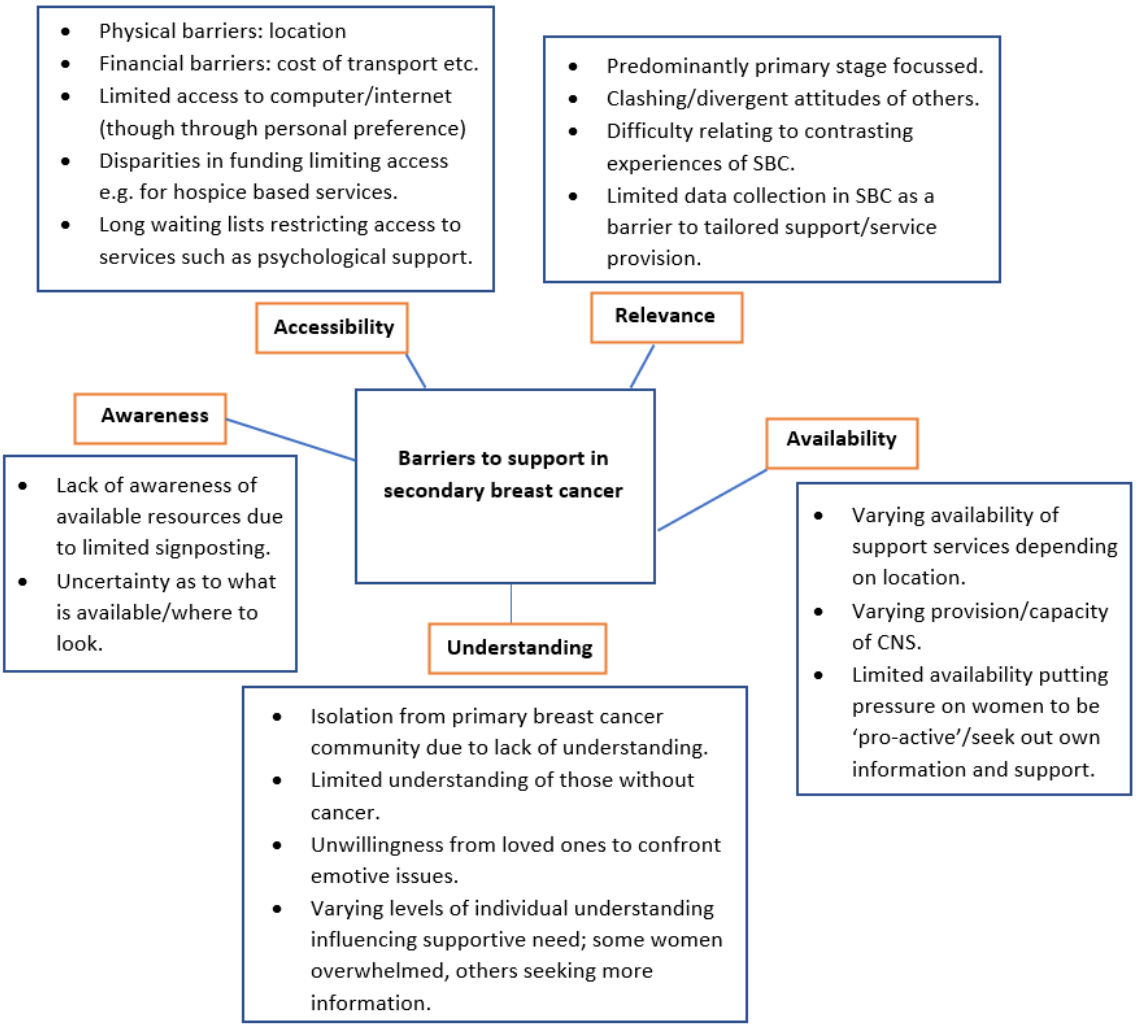
Some women expressed a preference for health professional input in delivering and signposting towards trustworthy information and support, as opposed to 'self-searching' the internet. Indeed, even for those women who appeared actively engaged in their healthcare and demonstrated self-directed behaviours such as online information seeking, health professionals' overseeing expertise was clearly highly valued and seen to be the 'ideal'.

> *"I go to like websites like that, like I said like Breast Cancer Now, Macmillan, rather than just googling… I never just put it in google, I'll go to those websites that I know are talking sense basically, yeah. And then if it's something that it says, you know, it's likely to be worrying, then I will bring it up at an appointment yeah, if it persists, and get further information that way…" (pt33)*

6.3.5 Barriers

A range of barriers to the access and provision of support in SBC were also identified, as summarised in Figure 6.2. Collectively, these barriers guided elements of design and content, embedded in contextual considerations, with the intention of mitigating their impact on support provision.

Figure 6.2 Barriers to the access and provision of support in SBC



6.4 Intervention design: theory & the evidence base

Collectively, the systematic review findings and development of intervention theory have provided a strong theoretical and evidence-basis upon which to design and structure an intervention which is shaped by the pivotal findings of the qualitative interview study.

6.4.1 Applying phase I evidence & theory

The systematic review of evidence (chapter 4) highlighted Interactive Health Communication Applications (IHCAs) as an intervention design widely applied across cancer support. The

evolution of these applications, which by definition combine the provision of health information with interactive components for tailored support, has been documented over several decades. IHCAs have progressed from non-web based sources of support to the mainstay of online supportive interventions.[321] Their inherent flexibility and adaptability lends them to the diversity of support needs and trajectories encountered across cancer survivorship, particularly for the level of tailoring and personalisation evidently required in SBC. Whist more traditional websites (comprising information in the absence of integrated features and tailoring) permit more passive acquisition of information, the advent of IHCAs and other interactive online tools allows users to access information and support in a way which is targeted and multi-modal, meeting their individual needs as both a cancer patient and an internet user.[322]

The need for multi-faceted support in this patient group in particular was evident in the complexity of the logic model outlined within the proposed programme theory (chapter 5). Drawing on such theory, the multiple interacting components characteristic of IHCAs facilitate a range of mechanisms underlying self-efficacy and self-care. Their targeted nature is inclusive of users across a spectrum of ehealth literacy, as well being capable of addressing a range of barriers and navigational needs. This model of intervention is therefore considered to be well-suited to deliver the complex and tailored support which women living with SBC so clearly need.

6.4.2 Drawing on the wider evidence base

Synthesising the evidence for interventions supporting self-management across the context of cancer survivorship, Davies and Batehup described many different potential modes of delivery.[323] This crucial overview was conducted as part of the National Cancer Survivorship Initiative's efforts to shine a spotlight on self-management, as one of five key shifts envisioned to improve the well-being of those living with and beyond cancer. Whilst acknowledging an increasing move towards internet-based platforms and delivery (notably, 11 years prior to the current research), there was a predominance of group, peer and face-to-face supportive interventions, with demonstrable efficacy amongst varied groups. Technology was incorporated mainly in the form of telephone consultations. For breast cancer survivors in particular, authors observed that modes of delivery facilitating group-based interactions and the active involvement of health professionals were preferable.[323] Whilst these studies focused on women living with and beyond early stage cancer (stages I-II), parallels can be drawn with the more recent synthesis conducted as part of this research (chapter 4). This demonstrates more than a decade of significant progress in internet and technology-assisted delivery, with a proliferation of online interventions to support self-management across the cancer trajectory,

whilst also permitting varying degrees of, and widening access to, expert and peer support. Indeed, the systematic review highlighted that, even in the remote, web-based and technology-assisted context, interventions demonstrating QoL-related efficacy often incorporated features facilitating a more collaborative, supported approach to self-management. This was also reflected in the preferences and tendencies of the women interviewed as part of this research, with health professional input and a named clinical contact widely valued avenues of support.

Interestingly, of the 41 self-management cancer survivorship interventions included in a recent systematic review (encompassing all potential modes of delivery), just 6 were delivered via the internet.[262] Across the significant breadth and diversity of self-management interventions reviewed, there evidently remains an overwhelming predominance of in-person, directly facilitated support. This suggests that the perceived importance of expert involvement in the delivery of cancer-related self-management interventions is maintained (though studies demonstrate widely varying efficacy),[262] despite significant advancements in remote technology which could otherwise facilitate more independent, patient-led support. However, the implementation of interventions which rely heavily on expert involvement are costly and resource-dependent; they are unlikely to be able to address the escalating need for support at the scale required as ever more people live longer with cancer. Furthermore, professionals with the necessary expertise (e.g. psychologists, behavioural counsellors etc.) may be in short supply and clinicians may lack the necessary time and skills.[319]

However, expert (and, for that matter, peer or 'expert patient') input in the delivery of self-care and self-management can now be very much harnessed within IHCAs and digital interventions more widely. These offer the potential to reach out to a wider audience and to provide more targeted and tailored support, in a way which is both remote yet collaborative.[319]

6.4.3 Applying theory & evidence: guidance for developing health interventions

Alongside the MRC Framework,[116, 117] a breath of guidance, evidence syntheses and recommendations have been established to support the stages of health intervention design and development more specifically. These include:

- Typologies and operational definitions.
- Taxonomies of approaches to developing interventions & delivering self-management.
- Frameworks guiding intervention development and core features.

As explored in detail in chapter 5, theories surrounding self-management, self-care and self-efficacy underly the goals of this intervention. Translating this theory (and the proposed

mechanisms of action outlined within the logic model) into the LIBERATE intervention required careful consideration of operational definitions, as well as established approaches to, and features of, intervention design and development.

6.4.3.1 Defining a self-management intervention

A recent systematic review of self-management interventions for cancer survivorship demonstrated the sheer breadth of conceptualisations of the term 'self-management intervention', with significant diversity in intervention design, content and components, alongside varying application of theoretical frameworks.[262] In attempting to provide a more standardised definition as to what constitutes a self-management intervention, Jonkman et al conducted a review of the evidence and proposed the following:[324]

> A self-management intervention aims to provide patients with the skills to be actively engaged in, and take responsibility for, managing their chronic condition. This is achieved through the acquisition of knowledge/provision of information AND ≥ 2 of:[324]
>
> - Encouraging independent monitoring of symptoms/side-effects/health status.
> - Guiding the management of medications.
> - Supporting the development of problem-solving and decision-making skills.
> - Facilitating health behaviour change (e.g. increasing physical activity or changing diet).

Authors were keen to highlight the inherent need for self-management support to be delivered in a way which is multi-faceted, with interventions therefore comprising multiple components.[324] Again, this supports the decision to follow the IHCA template for the design of the LIBERATE intervention.

Lorig also highlights the importance of elements encouraging patients to develop the confidence and self-efficacy for managing their chronic condition (e.g. goal setting, provision of feedback, social support and learning from others).[325] This definition very much reflects that of the USA's Institute of Medicine (IOM), which emphasises the need for patients to develop skills in the medical, role and emotional aspects of illness management, guided by monitoring, feedback and supported problem-solving, in order to confidently manage and live well with a chronic condition.[81] Pearce and colleagues adopt the IOM definition of self-management, yet add further emphasis on the context in which interventions are placed, stressing the importance of the surrounding health system and the collaboration of health professionals to support patients and share in the responsibility of self-management.[326]

Taking the highlighted definitions a step further, Davies and Batehup applied additional terminology to categorise self-management interventions for cancer survivors as *'adjustment-focused'* or *'problem-focused'*.[323] These terms distinguish between interventions with the overall aim of facilitating a transition or adjustment to the survivorship phase (adjustment-focused) versus those more specifically aiming to support behaviours and skills for coping with issues such as physical side-effects or psychological distress (problem-focused). Across phase I of this research, a need for both an adjustment-focused and problem-focused approach has been consistently highlighted. Indeed, for women with SBC, transition to 'survivorship' is a more nuanced shift, given they are living alongside, as opposed to beyond, their cancer and treatment. As such, support for ongoing problems, as well as for the transition to life with incurable cancer, is paramount. Both of these models were therefore drawn upon during the development of the LIBERATE intervention.

6.4.3.2 Approaches to intervention development

The current research seeks to learn from this evidence base for self-management interventions, recognising the strengths of numerous as opposed to a singular approach to development. A recent review brought many of these together within a taxonomy, outlining 8 categories of approaches and actions.[327] Whilst the MRC Framework underpins the LIBERATE project as a whole, itself pertaining to what is described as a 'theory and evidence-based approach', the research aims are most strongly aligned with what has been defined as a 'target-population centred' approach. This approach looks to harness the perspective of those for whom the intervention is being designed.[158] It has often been applied to self-management and behaviour change delivered via eHealth platforms, aiming to encourage independent use of an intervention which is tailored to its users. In defining this approach, O'Cathain and colleagues characterise its iterative nature and use of mixed methods to support an in-depth understanding of feasibility, acceptability and the context in which the intervention will be embedded.[327] Qualitative methods, such as those which represented a focal point of phase I, placing women's needs and perspectives central to subsequent design and development, are therefore pivotal.

Closely linked to this target-population focus, Yardley et al developed what they defined as a 'person-based approach' to the development of digital interventions.[328] Ultimately, this aims to harness in-depth understanding of the experiences, needs and perspective of those who will be using the intervention, placing them central to the ('person-centred') processes of design, development, evaluation and implementation. Through methods such as qualitative evidence syntheses, interviews and focus groups, user-based usability testing and case studies, this approach seeks to contextualise well-established evidence and theory-based approaches,

supporting their application to the individuals targeted by a particular intervention. Key to this approach is the development of what Yardley and colleagues describe as 'guiding principles.' These encompass the intervention's overarching objectives (and the features intended to deliver these objectives), shaped by and evaluated in the context of its target population. Grounded in health psychology and behaviour change, this approach is highly applicable to online and 'offline' interventions alike. Yet its developers argue that, given the independence and autonomy which comes hand in hand with digital intervention use, in-depth understanding of factors likely to affect relevance and engagement for users is even more crucial.[328]

Reporting on their development of a digital intervention for cancer survivors, 'Renewed', Bradbury et al provide a key, guiding example of an approach combining theory, evidence and target population-centred or 'person-based' considerations.[319] An initial scoping review of intervention evidence helped to shape the Renewed guiding principles and supported subsequent underpinning theoretical considerations. The guiding principles outlined the needs and behaviours of cancer survivors, as well as any potential challenges they may encounter when using the intervention. Subsequent analysis of behavioural determinants and development of a logic model incorporated underpinning theory and supported a proposed mechanism of action. Crucially, qualitative research (including interviews and focus groups with cancer survivors and other key stakeholders) ensured that this evidence and theory was applied within a person-based approach, delivering a person-centred finalised intervention.[319]

Following this example of a multi-faceted, multi-source approach allows for the integration of all strands of phase I research in the development of the final LIBERATE intervention. In placing the experiences and perspective of women living with SBC as the centre of its design, it is hoped that the resulting intervention will not only address their needs but also ensure that they are able and willing to effectively engage with it.

6.4.3.3 Intervention features

Of further crucial importance was the consideration of the key features which will be used to shape and deliver intervention content. Reviewing the evidence for self-care, self-management and self-monitoring interventions (within a broader evidence synthesis of 'patient focused' interventions), Coulter and Ellins highlighted ongoing uncertainty as to the causal relationships between intervention features and measures of efficacy.[329] This uncertainty mirrors conclusions drawn in the systematic review (chapter 4) and is widely reflected across the evidence base for self-management interventions targeting cancer and other chronic conditions, online and otherwise.[83, 85, 102, 330, 331] Yet the reporting of online interventions

remains limited, hampering efforts to understand the efficacy of their constituent components. Acknowledging this, Morrison et al sought to gather together and define a range of different features, applied across a diverse array of eHealth interventions, within a conceptual framework.[332] In doing so, they also explored relationships between specific features and health-related efficacy. Amongst 11 identified features of health interventions delivered via the internet, 4 were hypothesised to be key mediators of health outcomes (Table 6.1). The authors hypothesised that the remaining 7 features had a potential moderating influence on these effects. These encompassed considerations of how information is structured and updated, its credibility, how useable and visually appealing the intervention is, whether activities provide an element of entertainment and how long the user is exposed to the intervention.[332] These, alongside the design features explored within the systematic review (chapter 4), helped to guide thinking around the planned design and delivery of the LIBERATE intervention (as highlighted in the final column of Table 6.1 below).

Table 6.1 Designing effective ehealth interventions: core features to consider[332]

Design feature	Definition of feature	Potential application of feature within LIBERATE intervention
Self-management component(s)	Applies user information to encourage self-management actions and behaviours e.g. reflection, symptom/status monitoring etc.	Individual symptom monitoring reports generating tailored self-management advice.
Social support and/or social context	Facilitates social support and/or awareness of social context, usually in the form of interaction, whether direct (human interaction e.g. peer to peer communication) or indirect ('human-like' interaction, e.g. use of case studies, vignettes etc.)	Case studies to harness the value of shared experience without the resource intensity of interactive features such as forums, live chat etc.
Tailored or targeted content	Specific content delivered in line with the needs of a wider group or of individual users.	Content targeted to SBC with further tailoring to 'subgroups' e.g. different treatment pathways, sites of metastases, informational needs etc.
Contact with intervention	Supports contact with the intervention or those delivering the intervention and can be distinguished as 'user-initiated' (e.g. 'ask the expert' facility) or 'expert-initiated' (e.g. emails/texts to users to encourage use).	Reminder emails/texts to encourage intervention use and support adherence. Facilities for clinical integration of symptom-monitoring features, allowing reported symptoms to be reviewed and followed up by clinicians.

(i) Self-management components

To support the development of such features, another taxonomy was consulted. The PRISMS taxonomy was established to provide a framework for those developing and reviewing self-management interventions, recognising a need for such guidance in order to better characterise and understand their diversity and complexity.[326] This taxonomy was therefore applied during the design and development of the LIBERATE intervention, embedding it in recognised self-management approaches and allowing for more standardised reporting in later stages. As Pearce et al acknowledge, whilst a comprehensive (93-item) taxonomy of behaviour change techniques has been extensively developed and well established,[333] the PRISMS (14-item) taxonomy looks to guide the delivery of self-management support more broadly, where the identification of a technique to elicit a specific behaviour change may not be as clear-cut.[326] Indeed, as with the LIBERATE intervention, self-management support may be targeting more overarching aspects of chronic disease management, such as improving self-efficacy across numerous actions and behaviours. The 14 identified components of self-management support (any number of which may be present in self-management interventions) centre around the following:[326]

- Provision of information relating to the condition, its management and where to access additional supportive resources (including social support and lifestyle advice).
- Support to monitor and manage the condition, and adhere to this management, with clinical review and access to expert support, action plans and/or equipment.
- Strategies and training in (+/- opportunities to rehearse) health communication, psychological well-being, practical self-management and everyday activities.

(ii) Social support

In reference to this key feature, Morrison and colleagues discuss digitally delivered social support and its various categorisations (whether asynchronous, such a discussion boards, synchronous, such as chat rooms, or simulated interactions, made possible through automated conversation i.e. 'chatbots' or, increasingly, avatars).[332] 'Social context' refers to features allowing the user to contextualise their experiences with those of others. Their review demonstrated varying efficacy across these varying forms, yet, generally, authors hypothesised that the provision of information about other real-life users will support intervention efficacy.[332, 334] This notion is supported across the wider literature, with the term 'peer to peer health care' coined to describe collaborative learning and support amongst people living with the same health conditions, a phenomenon made ever more possible thanks to the internet.[335]

The systemic review (chapter 4) highlighted social/peer-peer support related features as being prevalent across interventions demonstrating wide-ranging efficacy. However, as discussed in

section 6.3, qualitative interviews evidenced varying attitudes towards more direct forms of social support, with some women expressing apprehension or discomfort, most often in relation to encountering negative or unwanted information, or the challenges of opening up in the presence of women with earlier stage breast cancer. These barriers could be present in online and face-to-face settings alike. The value of shared experiences more widely, however, in terms of learning from the experiences of others (where relevant to and in keeping with the experiences of the individual), was widely acknowledged. The use of case studies and vignettes to provide a social context to information and support is an interesting and practical alternative to more direct, interactive forms of peer-peer support.[332] Such features offer the potential for shared experience to be harnessed in a more controlled environment, with individuals able to access particular cases or stories in line with their 'readiness' and current needs. Furthermore, features facilitating direct social contact may not always be feasible in terms of the skills, time and technological infrastructure needed to build, maintain and moderate online support groups and forums.

(iii) Tailoring

Perhaps most significant to this research is the need for an intervention to be targeted very specifically towards SBC, rather than generalising to all stages of breast cancer. This was widely cited in research preceding (and indeed, shaping) the LIBERATE project and by the women interviewed as part of this research itself. The power of the internet to deliver tailored support is well recognised. A meta-analysis of web-based behaviour change interventions found that those incorporating tailoring resulted in significantly better health outcomes than those without.[336] Yet the LIBERATE systematic review findings (specific to the advanced cancer context) suggest that online and technology-assisted interventions to date have a broad and all-encompassing remit when it comes to different stages of cancer and cancer survivorship.

In contrast, the qualitative interview study (chapter 3) demonstrated a clear need for any supportive intervention to be targeted at both a collective and individual level, relevant to differing trajectories, values and needs. These findings also provided contextual insights in terms of women's healthcare setting, surrounding support services and, more specifically, how these factors influence their supportive needs. The need for an intervention to be embedded across varying contexts (and hence to possess an inherent degree of flexibility and tailoring) was thus another crucial consideration ahead of intervention development.

(iv) Contact

The value of a variety of forms of contact between users and the intervention is also acknowledged within Morrison et al's framework, supported by a range of evidence. Whilst contact initiated by users (e.g. 'ask the expert' chat features) were not clearly associated with

more effective interventions, contact initiated by experts themselves, particularly where this involved behaviour change guidance, appeared to support efficacy.[332] Such 'contact' encompasses health professional involvement in, or facilitation of, intervention delivery, which, as highlighted throughout phase I, varies widely across online supportive interventions and self-management interventions more broadly. Whilst studies support the value, and demonstrate patients' prioritisation, of health professional input, evidence for its efficacy as a component of self-management interventions is less clear.[83, 85] The systematic review (chapter 4) highlighted a potential relationship between intervention efficacy (relating to QoL and psychosocial well-being specifically) and expert involvement, yet further research and more conclusive evidence is needed. Indeed, as Boland et al concluded in their own systematic review of (online and 'offline') self-management interventions, studies directly comparing interventions with and without expert facilitation are needed to bridge this gap.[85]

Evidence in the digital context, however, is growing. A systematic review of internet delivered mental health interventions compared those featuring an element of expert guidance to those which were user-guided. Whilst limited to a relatively small number of studies (14 RCTs) and specific to the context of depression and social phobia, meta-analysis demonstrated significantly better outcomes for those with guidance versus those without.[337] Another such study is the ongoing RCT evaluating the 'Renewed' digital intervention for cancer survivors, with and without supplementary expert support. Participants accessing the online intervention independently will be compared to intervention users also offered support via telephone or email, as well as to a control group receiving usual care.[90] The LIBERATE project itself sought to add to this growing body of research exploring the role of (health) professionals in supporting patients to effectively engage with online interventions. As such, one of the over-arching research aims was to evaluate the feasibility of the finalised intervention (specifically, its anticipated element of symptom monitoring) as both an independently delivered and a clinically integrated source of support, recognising the increasing move towards more chronic, home-based management of SBC over the longer-term.

As part of 'expert initiated contact', Morrison et al also highlighted the efficacy of features encouraging intervention engagement (e.g. emails or text messages). Further research has also evidenced the benefits of such features in supporting efficacy and adherence to 'unguided' (i.e. without expert facilitation or support) interventions in particular.[338, 339] This supported plans for the finalised LIBERATE intervention, in its independent monitoring and clinically integrated versions, to harness these features (reminder emails/text messages) with the aim of assessing their feasibility and efficacy in supporting intervention engagement.

Section two: Finalising the intervention design

6.5 Design proposal & expert consensus

Early on in the project, following initial scoping of the literature and on the basis of the wider research group's expertise, it was envisaged that the intervention would involve features for symptom monitoring, self-management and signposting support. This would largely be supported by an established online symptom monitoring system and complex intervention (eRAPID), discussed in detail later in this chapter (section 6.6.2). The wide range of evidence gathered throughout phase I allowed this early concept to be expanded and further developed in line with the experiences and considerations of women living with SBC.

An initial intervention design was proposed on the basis of identified issues and solutions. Issues were identified from across the primary qualitative data, directly guided by the experiences of women living with SBC and professionals involved in their care and support. Solutions were developed in consideration of definitions, features and components of self-care and self-management support from across the breath of guidance and evidence discussed, as well as women's preferences, values and attitudes towards support-seeking. This intervention proposal was central to the process of expert consensus. Formal or expert consensus is a broad term describing the process of gathering and collectively reviewing the knowledge and thinking of a group of people (identified as 'experts' in a particular area). This is done so in a structured and systematic way in order to reach an evidence-based conclusion as to the overall consensus.[340] This methodology was chosen as the next key step in moving from evidence gathering to intervention design and development.

6.5.1 A modified approach to expert consensus

Expert consensus may traditionally be seen as a multi-stage, time-consuming and exhaustive process, precluding its use from time-limited studies or the involvement of time-pressured participants. The Delphi method, for example, is a well-established consensus approach which involves multiple rounds of surveys. These gather participants' responses to a range of statements, which they re-review across rounds and in line with the responses of others. Statistical methods are applied to determine consensus.[341, 342] The 'Nominal Group Technique', another commonly applied method, follows a structured protocol detailing rigorous steps, designed to foster the generation and sharing of ideas through expert group facilitation.[343, 344]

To meet the needs of the LIBERATE research, a modified approach was adapted. This encompassed aspects of both of the aforementioned methods, tailored to the project's timescale, the researcher's experience and the collaborators' availability. This followed what is

described as a 'deliberative process', facilitating the shared face-to-face discussion and interpretation of evidence amongst a group of experts (in this case, women living with SBC, health professionals and researchers in the field), all of whom participate in debating the pros and cons of various options before reaching a collective decision.[345]

6.5.2 Gathering the expert group

The expert group comprised a range of key stakeholders. Women who had taken part in the interview study, and who had expressed a keen interest in remaining involved in the research, were invited to participate as 'patient collaborators.' In total, 4 patient collaborators took part, alongside the LIBERATE project's Patient Advisor (CM), two researchers (FK, KA), a Consultant Medical Oncologist (GV), two Clinical Nurse Specialists (one working within LTHT and one within Breast Cancer Now) and a facilitator (KK).

Participants were asked to consider whether the proposed intervention (Table 6.2), with its 5 core components, correlated with the evidence presented in the summary report of the qualitative findings, and with their own experiences and expertise. These documents were circulated several weeks ahead of the meeting. The meeting was held in person, with a teleconference facility for collaborators to attend virtually should they prefer.

Following an initial presentation, providing an overview of findings and objectives, the group were invited to discuss each of the proposed issues, solutions and components in turn. A rich and varied discussion followed, providing further thoughts and insights in relation to each of the 5 intervention components. At the end of the session, these were summarised and collectively prioritised through group discussion. Participants emphasised considerations relating to ease of navigation, to give users the autonomy to choose what information they access and when. They also advocated for the inclusion of specific content to guide users in how to appraise online health information. In addition, consensus was reached on the importance of content and support for 'others', with agreement that this should extend beyond family and loved ones, targeting employers, teachers and GPs. The group were also keen that women should be empowered to monitor and manage symptoms right across the disease trajectory, from recognising early signs of disease progression to dealing with late effects of cancer and treatment.

Table 6.2 LIBERATE intervention proposal

Identified issue	Proposed solution	Proposed intervention component
1. Generic information or early-stage focused information and support.	Intervention designed specifically for women with secondary breast cancer, with information and advice tailored to this stage of disease.	**Holistic health information component**: Educational, self-management and supportive information for secondary breast cancer, gathered from evidence-based sources, highlighted at distinct phases along the disease trajectory. Potential topics to include: general information, managing symptoms and side-effects, treatments (including information on complementary and alternative therapies) lifestyle, work & finances, psychosocial and sexual health and well-being.
2. Lack of awareness of the 'symptoms to look out for'.	General educational information section detailing the 'what, why and how' of secondary breast cancer.	
3. Time-dependency of information and support needs.	Information presented according to distinct phases of a 'typical' disease trajectory and at different levels of detail e.g. 'overview/summary' vs 'further information'.	
4. Need for reassurance and tailored advice surrounding management of symptoms and side-effects.	Facility for patients to self-report symptoms and side-effects and receive tailored self-management advice.	**Symptom monitoring component (+/- clinical review):** utilising ePROMs to tailor evidence-based advice and information to the individual patient, encompassing age-specific needs.
5. Limited information and support for younger age groups.	Self-management information and ePROMs covering issues pertinent to younger age groups (and signposting to relevant sources & services).	
6. Interest & value in learning from experiences of others, though potential for unwanted, negative encounters and differing needs of women at differing stages of 'advanced'.	Use of case studies/narratives to allow for diverse experiences to be explored in a controlled environment, where the patient has the autonomy to choose which cases they read.	**Virtual 'waiting room' component**: case studies/narratives categorised by a range of factors (e.g. age, treatment, site of metastases) detailing experiences, tips and advice, as may be encountered in discussions shared in clinic waiting rooms.
7. Limited support for family and loved ones of women living with secondary breast cancer. Burden of managing the emotions of others falling upon patients.	Supporting patients through supporting their loved ones, providing a dedicated section for them to learn about secondary breast cancer and seek out support.	**Support for family & loved ones component**: information and signposting to tailored support, including support for patients to have difficult conversations with loved ones.
8. Wariness regarding the reliability of sources encountered on internet.	Use of signposting to direct patients to trusted, evidence-based resources and to services health professionals may not have had the opportunity to direct them towards.	**Signposting component:** collection of resources, websites and services (e.g. support groups, forums, sources of employment advice, benefits advisors, psychological support services) categorised and gathered in one space.
9. Disparities in access to Clinical Nurse Specialists.		

Crucially, there was unanimous agreement that the 5 core components addressed the identified supportive needs (Table 6.2). After the meeting, a summary of discussions, outcomes and actions was shared with the group via email and they were invited to provide any additional thoughts and feedback.

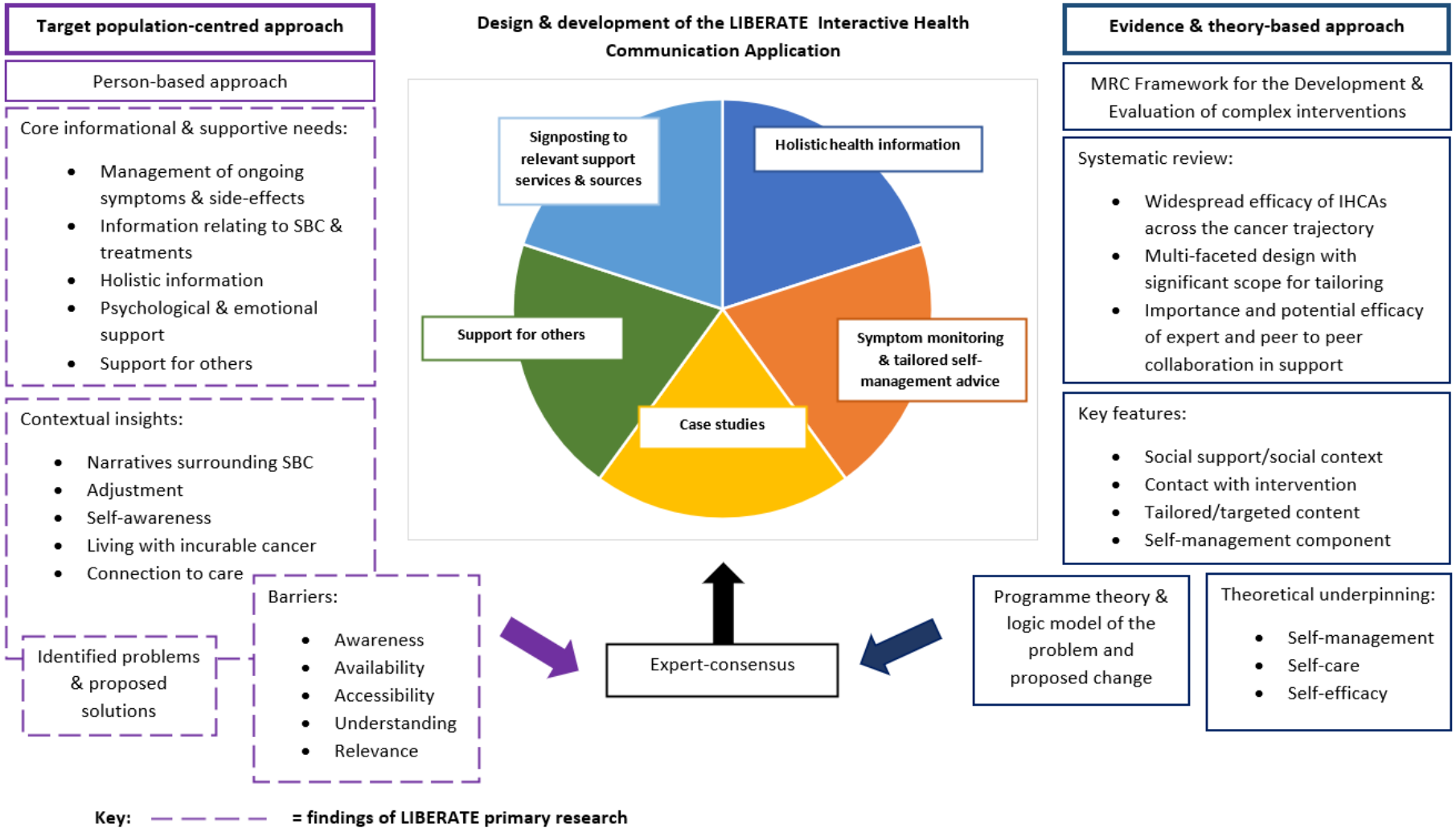
As the final step in the design process, all phase I evidence and the expert consensus group outcomes were consolidated into 4 key guiding principles, in line with the person-based approach,[328] to be taken forwards in intervention development. Figure 6.3 collates the evidence and guidance which shaped the final LIBERATE intervention.

Guiding principles

The LIBERATE intervention will look to:

- Bring together relevant, evidence-based, up to date information and resources in one trustworthy and easy-to-navigate resource, addressing the identified core needs and supporting self-efficacy.
- Address these collective, SBC-specific needs, whilst also providing a level of individualisation and tailoring, promoting participant activation and engagement.
- Provide information and sources of support relevant to women across different stages of their disease trajectory, with clear signposting to ensure that they have the autonomy to access different sorts and amounts of information if and when they choose to.
- Support women to perform self-care behaviours with facilities for integrating and/or encouraging health professional involvement.

Figure 6.3 The LIBERATE IHCA: Target population-centred, evidence and theory-based approach bridged through expert consensus



Section three: Stages of intervention development

6.6 Intervention development

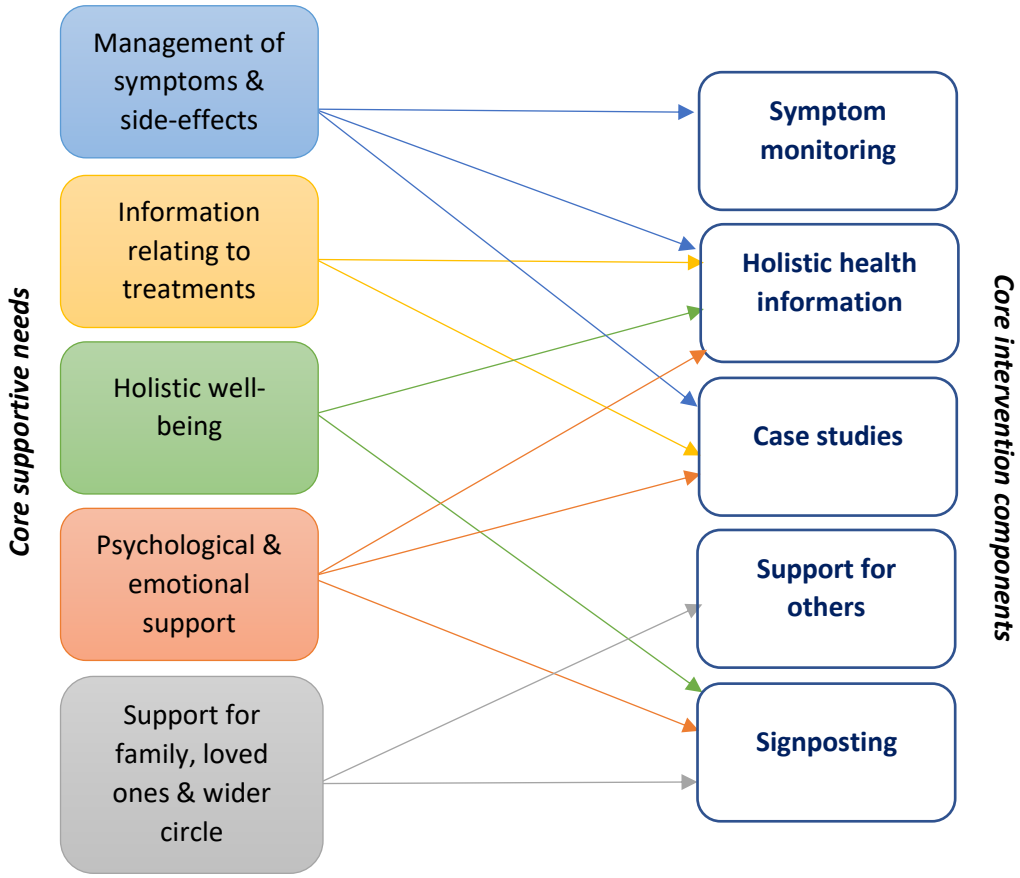
The intervention's 5 core components were developed across 3 key stages:

1. Content collation & development
2. Symptom questionnaire design and development
3. Website design and development

6.6.1 Content collation & development

Content encompassing the 5 core areas of supportive need was developed across the intervention's 5 key components, as mapped in Figure 6.4 below.

Figure 6.4 Mapping core areas of supportive need to the LIBERATE intervention components



Following identification of the key areas of content, shaped by women's supportive needs, information was summarised and adapted from online sources identified as reputable, relevant and evidence-based by health and charity professionals. These included the websites Breast Cancer Now, Macmillan and Cancer Research UK.[346-348] Information from across these

sources was collated in one place, expanding upon and re-wording information to provide as much tailoring and specificity to SBC as possible. A CNS at Breast Cancer Now reviewed all content for relevance and accuracy.

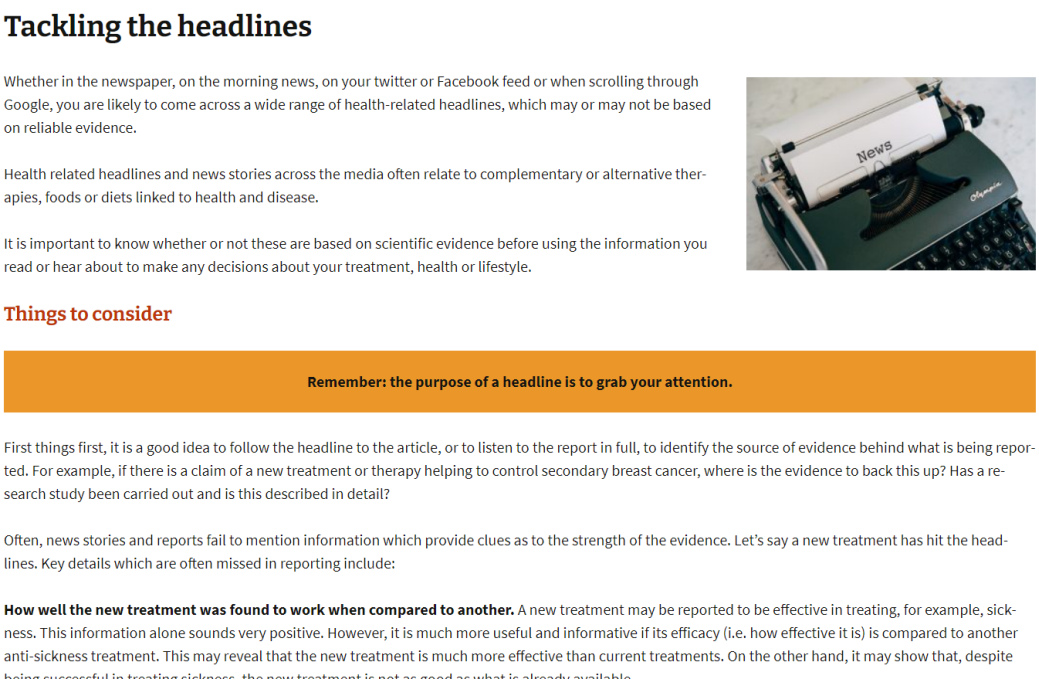
Furthermore, where information was gathered from online sources which had not been cited by health and charity professionals, the quality of the content was first assessed. As online sources of health information have amassed over the past several decades, so too have concerns surrounding their quality standards and the potential for 'mis-information'.[349, 350] Websites were therefore appraised in line with so called 'JAMA benchmarks' for the quality of online medical information, cited in the Journal of the American Medical Association and evaluated within a study assessing the quality of breast cancer websites.[351] These benchmarks encompassed 'Authorship' (details relating to the site's author and contributors), 'Attribution' (all content referenced with sources cited and listed in full), 'Disclosure' (information relating to site funding, sponsorship and ownership clearly displayed) and 'Currency' (clear indication of the date published and any subsequent updates).[352] These quality indicators also guided development of the LIBERATE intervention itself. Following the specified standards, information relating to the website's aims and authorship were clearly displayed on the main page, alongside the research project's funding and affiliations. Each web page also cited and referenced all sources of information and the date on which the page was last updated.

Given the expressed concerns relating to the trustworthiness and evidence basis of online sources, combined with expert consensus as to the importance of empowering women to access and appraise high-quality health information, guidance was also added to the intervention itself. This aimed to support women in performing their own self-appraisal when encountering online information. An extract is displayed in figure 6.5.

6.6.1.1. Holistic health information

With the desire for a holistic outlook and evidence-based information on living well widely discussed amongst the women interviewed, 'healthy living' and 'complementary therapies' represented significant elements of the 'Holistic health information' component of the intervention. A range of evidence was gathered and summarised from across reputable sources, citing all references and signposting to a breadth of further, trusted sources of information. This approach was also taken in gathering a wide range of information on individual treatments and on SBC more generally, encompassing signs, symptoms and the range of imaging and tests women may encounter along the way.

Figure 6.5 Example web page from the 'How to read the evidence' section of LIBERATE's *Holistic health information* component.



Tackling the headlines

Whether in the newspaper, on the morning news, on your twitter or Facebook feed or when scrolling through Google, you are likely to come across a wide range of health-related headlines, which may or may not be based on reliable evidence.

Health related headlines and news stories across the media often relate to complementary or alternative therapies, foods or diets linked to health and disease.

It is important to know whether or not these are based on scientific evidence before using the information you read or hear about to make any decisions about your treatment, health or lifestyle.

Things to consider

Remember: the purpose of a headline is to grab your attention.

First things first, it is a good idea to follow the headline to the article, or to listen to the report in full, to identify the source of evidence behind what is being reported. For example, if there is a claim of a new treatment or therapy helping to control secondary breast cancer, where is the evidence to back this up? Has a research study been carried out and is this described in detail?

Often, news stories and reports fail to mention information which provide clues as to the strength of the evidence. Let's say a new treatment has hit the headlines. Key details which are often missed in reporting include:

How well the new treatment was found to work when compared to another. A new treatment may be reported to be effective in treating, for example, sickness. This information alone sounds very positive. However, it is much more useful and informative if its efficacy (i.e. how effective it is) is compared to another anti-sickness treatment. This may reveal that the new treatment is much more effective than current treatments. On the other hand, it may show that, despite being successful in treating sickness, the new treatment is not as good as what is already available

A dedicated section on psychological support brought together evidence, resources, tips and advice, signposting to additional online and face-to-face services, whilst a further section focussed on a range of holistic issues relevant to younger women. Information relating to sexual health and well-being was also collated within a separate section, ensuring it was clearly accessible to women of all ages. A breadth of information and guidance relating to advance care planning, death and dying was gathered within another section, clearly signposted to allow user autonomy in accessing this information, with a range of links for further expert advice and support.

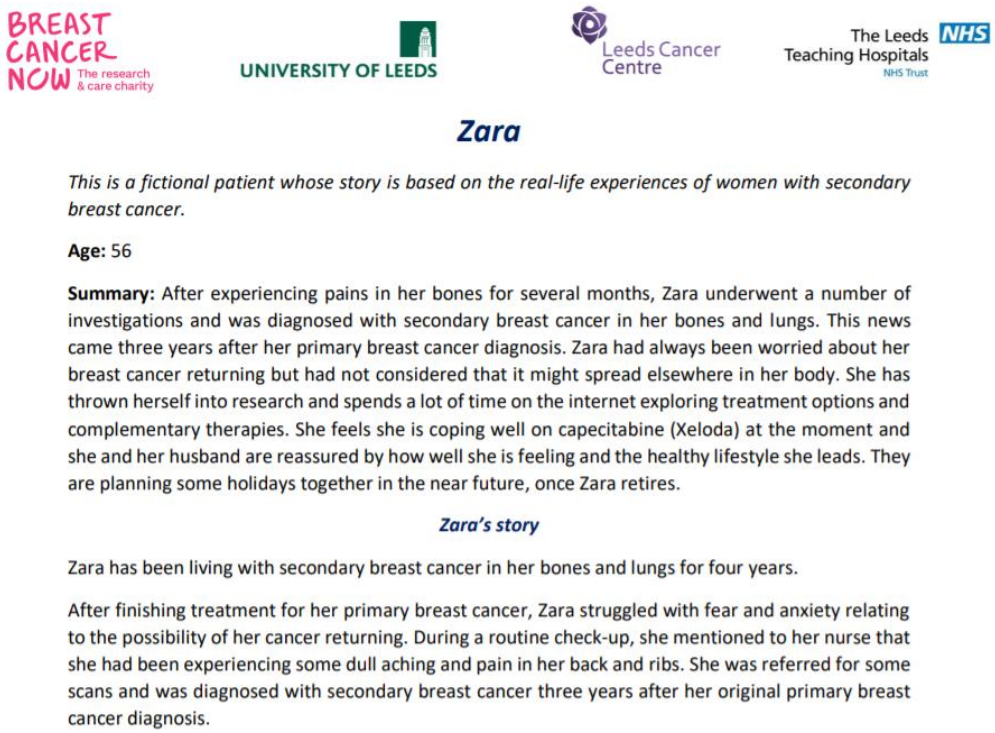
6.6.1.2 Symptom management advice

Symptom management information was largely based on the established, clinically approved advice which was extensively developed as part of the eRAPID programme of research.[353] Further breast-cancer specific (and, where possible, SBC specific) detail was also added in line with other evidence-based sources (e.g. Breast Cancer Now and Macmillan websites). Advice relating to symptoms which were outside the scope of eRAPID's focus (e.g. side-effects of hormone and targeted therapies) was collated and summarised from these approved sources, providing as much tailoring and relevance to SBC as possible, with the oversight of clinical experts within the wider research group.

6.6.1.3 Case studies

Based on the breadth of experiences shared within the qualitative interview study, 5 case studies were developed, incorporating different themes, treatments, ages, sites of metastases and supportive needs. Interactive links were embedded to provide direct access to relevant information and sources of support relating to the themes covered in each case study. An extract is displayed in figure 6.6 below.

Figure 6.6 An extract from the collection of case studies, available for users to download.



BREAST CANCER NOW The research & care charity

UNIVERSITY OF LEEDS

Leeds Cancer Centre

The Leeds Teaching Hospitals NHS Trust

Zara

This is a fictional patient whose story is based on the real-life experiences of women with secondary breast cancer.

Age: 56

Summary: After experiencing pains in her bones for several months, Zara underwent a number of investigations and was diagnosed with secondary breast cancer in her bones and lungs. This news came three years after her primary breast cancer diagnosis. Zara had always been worried about her breast cancer returning but had not considered that it might spread elsewhere in her body. She has thrown herself into research and spends a lot of time on the internet exploring treatment options and complementary therapies. She feels she is coping well on capecitabine (Xeloda) at the moment and she and her husband are reassured by how well she is feeling and the healthy lifestyle she leads. They are planning some holidays together in the near future, once Zara retires.

Zara's story

Zara has been living with secondary breast cancer in her bones and lungs for four years.

After finishing treatment for her primary breast cancer, Zara struggled with fear and anxiety relating to the possibility of her cancer returning. During a routine check-up, she mentioned to her nurse that she had been experiencing some dull aching and pain in her back and ribs. She was referred for some scans and was diagnosed with secondary breast cancer three years after her original primary breast cancer diagnosis.

Without the resources for interactive features such as a forum or a discussion group, these case studies sought to harness the value of shared experience and peer-peer learning for cancer survivors (emphasised within this research and beyond) by an alternative means, as advocated within Morrison and colleagues' framework of potential features for effective eHealth interventions.[332]

6.6.1.4 Signposting

Opportunities for more direct forms of shared experience (both online and face-to-face) were also highlighted within the signposting section. This section was developed by gathering the wide range of sources and services for SBC-specific information and support highlighted in interviews with both women and professionals. An in-depth online search was also conducted to ensure a comprehensive catalogue. All signposted resources were assessed against principles of website quality, highlighted above, prior to their inclusion.

6.6.1.5 Support for others

A breadth of information and guidance was collated and summarised (largely from Macmillan, Breast Cancer Now and Hospice UK)[346, 347, 354] with a range of target audiences in mind, encompassing loved ones, people and professionals in women's close and wider circles, who may be affected by their diagnosis. This aimed to provide a space in which this range of individuals may be able to seek support for themselves and find out how best to provide support to those living with SBC. Topics included:

- Secondary breast cancer: the facts
- How to support someone with SBC
- When a loved one is diagnosed with SBC: sources of support for you
- Support for professionals: employers, GPs and teachers
- Support for partners
- Support for children & teenagers
- Support for carers
- Talking about death & dying
- Grieving and bereavement
- Bereavement support for children & young people
- Practical support: dealing with the death of a loved one

6.6.2 Symptom monitoring questionnaire development

The symptom monitoring component was planned and built around an established, clinically integrated electronic questionnaire system, described in detail below, which has been developed and extensively evaluated within the wider research group. Given the strength of evidence for the remote, digital monitoring of patients' symptoms (PROs) during systemic treatment for advanced cancer,[73, 105, 107] this was planned as a core element of the supportive intervention from the earliest stages of the research. Phase I research further confirmed the value and need for this form of support in advanced cancer, specifically for women with SBC.

6.6.2.1 An established platform for ePROMs

The 'Electronic Patient reported Outcomes from Cancer Survivors (EPOCS)' prospective study trialled the use of a secure, online questionnaire builder (QTool) to collect online PROs and integrate these with cancer registry data.[355, 356] Between 2011-2013, as part of the eRAPID (Electronic patient self-Reporting of Adverse events: Patient Information and aDvice) programme of research, the Patient Centred Outcomes Research (PCOR) group further developed QTool, in collaboration with a private software company (X-Lab). In its latest version, this software allows for the creation and delivery of customisable PRO-based

questionnaires (i.e. electronic patient reported outcome measures, ePROMs) which, when combined with pre-defined clinical algorithms, enable patients to report symptoms remotely and to receive automatic, tailored self-management advice for the presence of mild/moderate symptoms. In the event of severe symptoms, these algorithms can also generate alerts to clinicians, thereby potentially triggering urgent medical review. Subsequent integration with the electronic patient record (EPR) in Leeds (Patient Pathway Manager, PPM) paved the way for real-time assessment of and response to ePROMs by clinicians.[110]

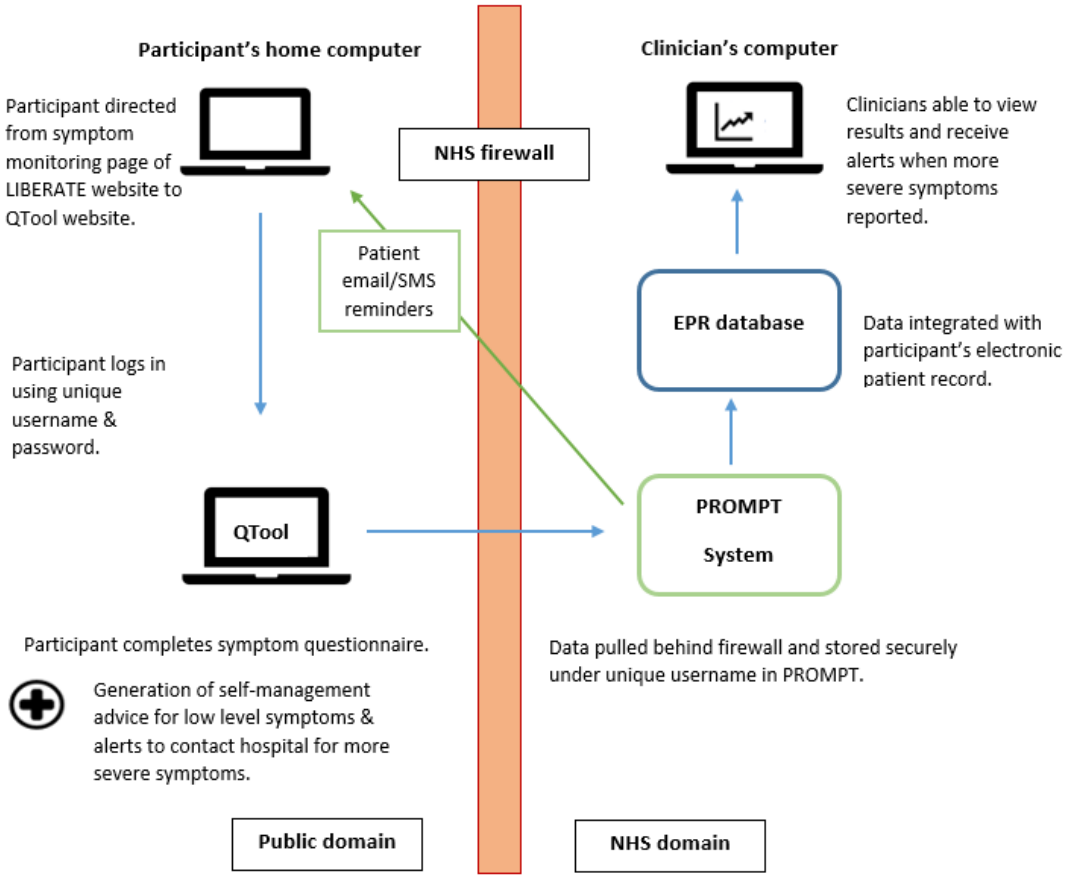
PROMPT is a further piece of software, developed within the PCOR group and integral to the eRAPID intervention, which facilitates the creation of reusable PROMs 'pathways', allowing multiple PROMs related tasks or questionnaire completions to be scheduled over any pre-defined time period. Patients can be registered onto these pathways and the system tracks compliance, manages reminders, triggers notifications and displays patient results real-time, whilst also supporting integration with the EPR. PROMPT is managed and maintained by the group's IT Manager in Health Informatics (RC). Various iterations of this system have been evaluated across a number of trials, for patients undergoing a range of cancer treatments, conducted by the wider research group.[108, 357-359] The LIBERATE research project sought to build on the successes and ongoing evaluation of this system, specifically its development within the eRAPID programme of research.[110, 161, 360]

At the time of the LIBERATE intervention development, eRAPID was under evaluation within a large-scale RCT (n=508), assessing its efficacy in supporting patients undergoing systemic treatment for predominantly early-stage cancer. The study population did, however, include women with SBC (n=13).[108] The eRAPID intervention harnessed the group's facility for secure online symptom monitoring, combining this with an innovative, 5-level tailored clinical algorithm which generated automated symptom-dependent, severity-graded advice to guide patients in self-managing or in seeking medical review. The development of data linkage infrastructure, a crucial innovation and major outcome of eRAPID research, permitted real-time integration of users' symptom monitoring reports with their EPR, supporting clinicians to review and make use of these results in their consultations. Automated emails also alerted clinicians when users reported any severe symptoms. In addition, a website (the platform from which users accessed QTool) provided a range of self-management and self-care advice.[361] Recently reported results of this trial reflected improvements in patients' physical well-being and self-efficacy with eRAPID use, as well as demonstrating no added burden to cancer service delivery.[108]

During this stage of the LIBERATE intervention development, various components of the eRAPID intervention (Figure 6.7) were harnessed and tailored in line with the LIBERATE research aims,

to meet the needs of women living with SBC. Application of the 'QTool/PROMPT/EPR' system to this setting is detailed below.

Figure 6.7 The established QTool/PROMPT/EPR system



6.6.2.2 How the system works: the user perspective

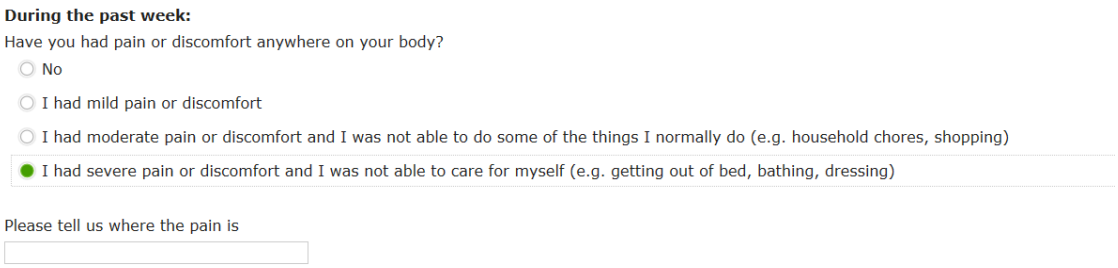
1. Users are directed to complete symptom monitoring questionnaires (using the QTool website) from the home page of the main LIBERATE website and throughout its symptom-monitoring section (see figure 6.8 below).

Figure 6.8 Example of symptom monitoring questionnaire navigation

2. Each user is provided with a unique username and password to access the QTool website. Here, they view the questionnaire to which they have been allocated (with questionnaire items tailored in accordance with their treatment pathway).

3. Users are taken through a series of symptoms, side-effects and psychosocial concerns and, for those they are experiencing (or have recently experienced), they are asked to rate the severity, as demonstrated in Figure 6.9.

Figure 6.9 Example of questionnaire item and rating



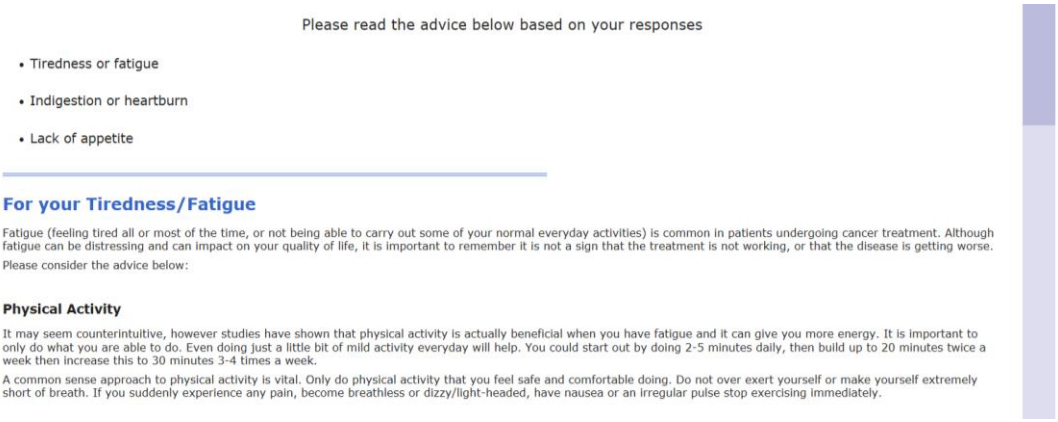
In the case of severe symptoms, an on-screen alert message (below) advises them to contact their hospital for further guidance.

You have indicated a severe problem in this area. This may be a longstanding issue for you, which you are managing or receiving support with.

However, if it is new, changing or causing you concern, we advise you to contact your hospital for further guidance.

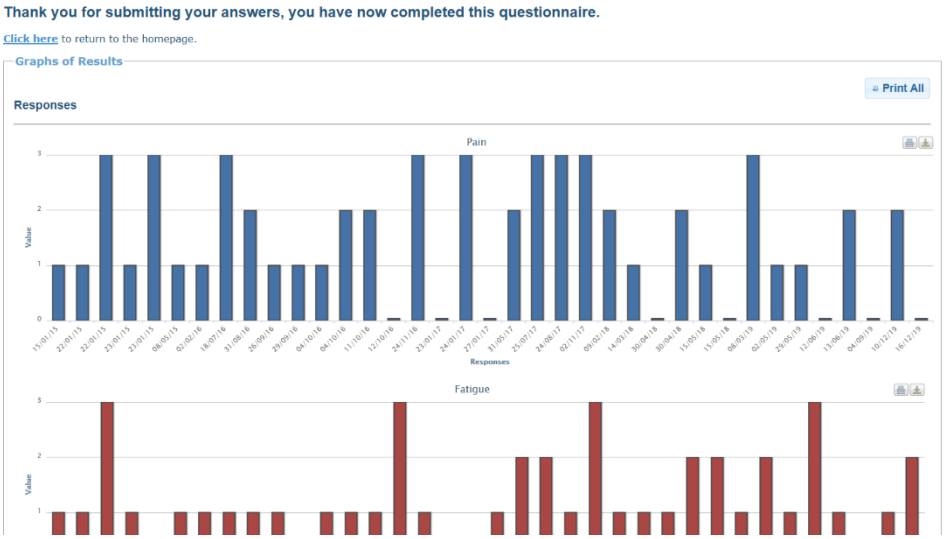
4. Where users report symptoms or issues graded as low or moderate severity, they are provided with automated tailored self-management advice at the end of the questionnaire (an example is provided in Figure 6.10). Short summaries are provided on screen, with links to further in-depth information in the symptom monitoring section of the LIBERATE website.

Figure 6.10 Example of self-management advice summary



5. Users are also able to review and monitor their symptoms graphically (as displayed in figure 6.11), tracking their occurrence and severity over time.

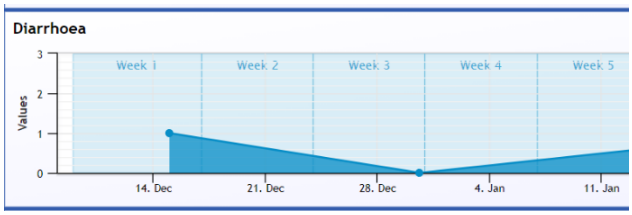
Figure 6.11 Example of users' display of results



6. The clinically integrated system allows clinicians to review the results via patients' EPR. Here, results are displayed graphically and tabulated, using a traffic-light coding system for easy interpretation (Figure 6.12 below). Email alerts are also generated to clinicians (with the facility to select who receives these alerts) to prompt urgent review of severe symptoms outside of scheduled follow up.

Figure 6.12 Example of clinicians' display of results

Sore mouth	0	1	0	1
Rash	0	1	0	0
Diarrhoea	0	1	0	1
Pain	1	1	2	1
Fatigue	1	2	2	2
Physical ability	0	1	1	1
Indigestion	1	1	2	1
Menopausal arthralgia	1	1	1	1
General muscle	1	1	1	1
Headache	1	1	3	2
Liver symptoms	0	0	0	1
Vomiting	0	0	0	0



6.6.2.3 Development of the questionnaire items

Guided by the extensive development of the eRAPID intervention, which targeted patients commencing chemotherapy treatment for a range of different cancers, the aim was to develop questionnaires which would be relevant to women living with SBC. A strong emphasis was placed on tailoring to their diverse and evolving treatment pathways, allowing users to report cancer-related symptoms, treatment side-effects and psychosocial concerns. 'Patient reported adverse events' (PRAE) refer to any side-effects or adverse reactions reported by the patient which can be directly attributed to a treatment.[360] Across this stage of development, mirroring the eRAPID approach, the term 'symptoms' is used to collectively refer to any (physical and/or psychosocial) reported issue, whether related to treatment or to the cancer itself.

Questionnaire items previously developed for women with SBC undergoing chemotherapy (within the eRAPID trial) formed the initial starting point. Question wording, responses and severity grading of the eRAPID questionnaires were guided by the National Cancer Institute's (NCI) Common Terminology Criteria for Adverse Events (CTCAE version 5.0).[362] Whilst the CTCAE provides a standardized description of adverse events which may be encountered by patients undergoing cancer treatment (considered a 'gold standard' for the clinical reporting of AE), the extensively developed Patient Reported Outcome (PRO) version of the CTCAE provides wording in line with the experiences and comprehension of patients.[363] Notably, validation data for the PRO-CTCAE guidance was not available during the development of eRAPID questionnaires. However, guided by earlier pivotal research in the area,[364] clinically derived CTCAE items were translated into patient reported adverse events (PRAEs),tailored to the patient experience, as demonstrated in Table 6.3 below. Crucially, the adapted PRAEs maintained the clinically established CTCAE severity grading which is crucial to the application of the eRAPID clinical algorithm. The acceptability and clinical validity of the items developed through this pragmatic approach was confirmed through in-depth cognitive interviewing with patients undergoing treatment for a range of cancers.[360]

Table 6.3 Example of clinically reported symptom (CTCAE) translated for use as a patient reported symptom (PRAE).

	Question item/symptom	Response: Mild	Response: moderate	Response: Severe
CTCAE	Arthralgia	Mild pain.	Moderate pain; limiting instrumental ADL.	Severe pain; limiting self-care ADL.
Patient reported translation	Have you experienced any aching, pains or stiffness in your joints?	I had a little pain or discomfort in my joint(s).	I had quite a bit of pain or discomfort in my joint(s) and I was not able to do some of the things I normally do (e.g. household chores, shopping).	I had severe pain or discomfort and I was not able to care for myself (e.g. getting out of bed, bathing, dressing).

The eRAPID (chemotherapy focussed) questionnaires were expanded upon and tailored to SBC by gathering information from a number of other sources, with particular emphasis on incorporating symptoms and side-effects encountered during treatment with hormone and/or targeted therapies. These sources included:

- Symptoms and side-effects reported across phase I qualitative interviews.
- Side-effects gathered from drug profiles of treatments commonly prescribed in SBC.
- Scoping of the wider literature, conducted as part of background development for the research.

Relevant symptoms were incorporated from the eRAPID intervention's extensive 'item bank'. PRAE-style items and responses for additional SBC specific symptoms were developed in line with the outlined, established processes[110, 360]and in discussion with clinical experts within the wider research group (Consultant Medical Oncologist, GV and Research Nurse, AG). For the LIBERATE questionnaires, whilst the PRO-CTCAE guidance was consulted, new items were largely developed in line with structure and wording of validated eRAPID items. This allowed for consistency and ensured that the CTCAE grading (crucial to the scoring algorithm) could be applied. All items were collated, reviewed and revised, before a finalised list of symptoms was sorted into two distinct questionnaires (Questionnaire A and Questionnaire B), to which participants would be allocated on the basis of their current treatment:

- Treatment group A: Monoclonal Antibodies (MABs) +/- chemotherapy
- Treatment group B: Hormonotherapy +/- targeted therapy

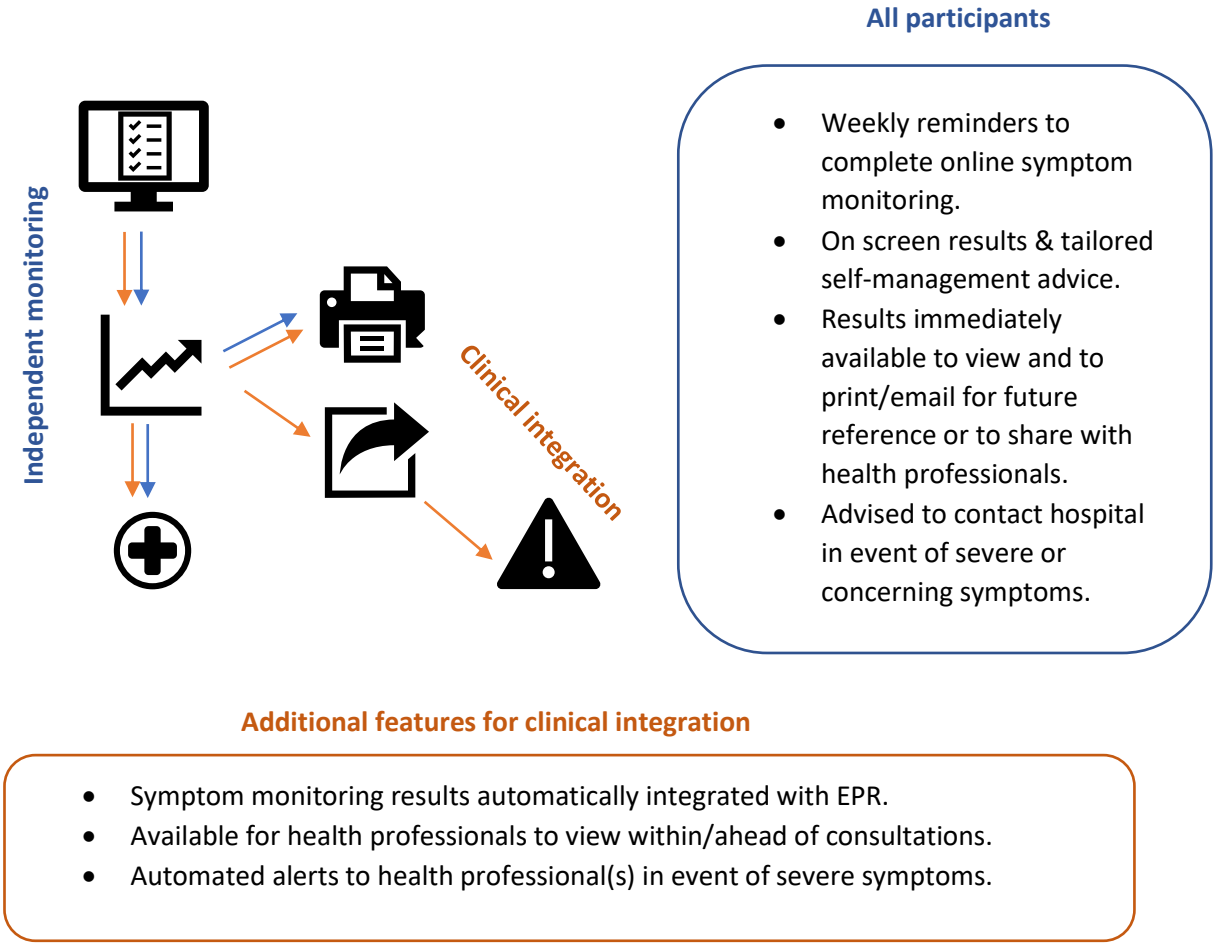
These questionnaires, including severity-dependent responses and grading, were drafted and finalised in Microsoft excel, before being inputted into the QTool online system.

6.6.2.4 Algorithms, advice and alerts

An established 5 level clinical algorithm, developed and trialled within the eRAPID programme of research, was applied to the LIBERATE questionnaires, with expert, ongoing IT and health informatics support from members of the research group (RC & JD). QTool's in-built functionality for dependency scoring allows questionnaires to be scored in accordance with user responses, and for this algorithm to be applied in line with pre-defined scores and levels of severity. These enabled users to receive on-screen automated advice which was tailored to the severity of symptoms or side-effects reported. Levels of severity corresponded to CTCAE grading and the UK Oncology Nursing Society Acute Oncology Initial Management Guidelines (both categorising symptom severity as level 1, mild, level 2, moderate and level 3, severe).[362, 365] To apply these hierarchical algorithms, questionnaire items (both validated eRAPID items and newly developed LIBERATE items) needed to be prioritised and ranked in order of clinical urgency, to ensure that the correct level of advice and/or alert would be provided to the user across different levels of symptom severity. This was achieved through ongoing consultation with the group's clinical experts (GV, AG). The algorithm applied (with wording adapted to fit the LIBERATE intervention and adaptations made in line with the results of usability testing) is discussed further in chapter 8.

On-screen messages alerting users to seek medical attention for severe symptoms and side-effects represent a crucial component of this system. Indeed, this feature is fundamental to the ethical and safety standards for any intervention harnessing such patient reported outcomes, online or otherwise, to ensure that the information collected is appropriately acted upon.[366] Whilst all users receive on-screen alert messages to contact their hospital in the event of severe symptoms being reported, Figure 6.13 illustrates the key differences between the 'clinically integrated' and 'independent monitoring' versions.

Figure 6.13 Key differences between clinically integrated & independent monitoring versions of the symptom monitoring component.



6.6.3 Website design & development

The main intervention website was developed using WordPress. This comprises all 5 intervention components, houses all content and is the platform from which users are directed to complete symptom monitoring questionnaires via QTool. The LIBERATE website can be accessed at:

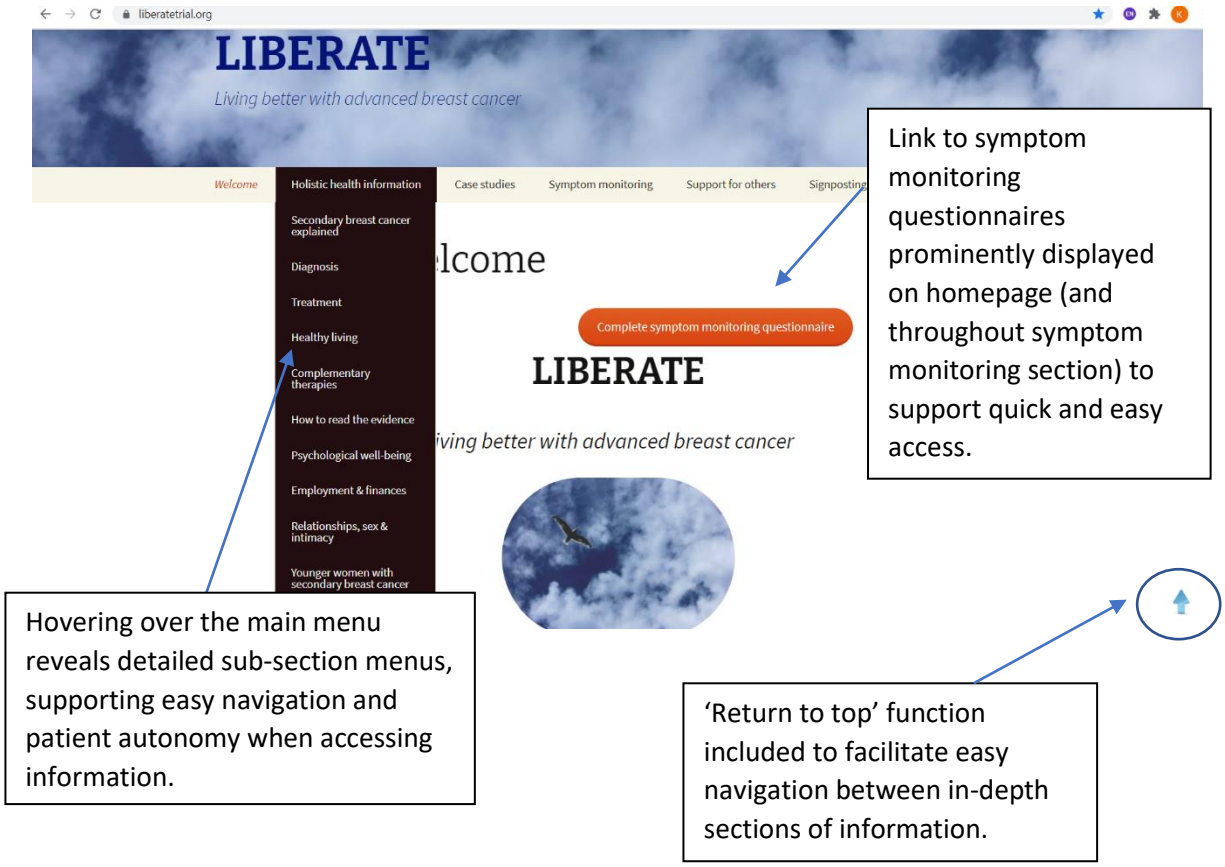
www.liberatetrial.org

Figure 6.14 displays a number of key features. Throughout website design, care was taken to ensure clear navigation between the 5 established components. For example, a prominent main menu with integrated drop-down menus facilitated easy location of specific information and smooth transition between web pages. Different sections and sub-sections were also clearly signposted to support user autonomy in encountering information which may be of a sensitive nature, or which they feel is not relevant to their stage of the disease trajectory, such as content relating to death, dying and advance care planning. This provided a level of tailoring relating to the individual users' preferred style of accessing and coping with information, whether preferring to see all available information ('monitoring') or to avoid any which may

cause unwanted distress or worry ('blunting').[367] In recognition of these varying needs, preferences and 'readiness' for information, some sections also included the option for more in-depth information to be revealed by selecting 'further information', for example in the 'treatment' section. Furthermore, users were regularly provided the option of seeking further information through links to additional, external sources.

Following informal feedback relating to the widespread use of the colour pink in primary breast cancer messaging and campaigns, which some women found was at odds with their own experiences, an alternative colour palette was chosen for the website design.

Figure 6.14 Key design features of the LIBERATE website



6.7 Reflections

The final LIBERATE intervention was built upon a strong foundation of evidence and theory, enabling the selection of the most appropriate approaches to meet the LIBERATE intervention goals. However, some methodological decisions, taken in line with the pragmatics of the tight timeframe for intervention design, testing and development, may have introduced limitations. The modified approach to consensus, for example, fell short of the more traditional and

rigorous approaches such as the Delphi method. Similarly, development of the symptom monitoring questionnaire items was done so on an accelerated basis.

Furthermore, it must also be recognised that, whilst strongly grounded in the available evidence, the LIBERATE intervention alone may not meet all of the needs of women living with SBC. For the women interviewed, despite widespread internet use, health professional expertise remained highly valued and sought after. This mirrors the findings of research exploring preferences and health seeking behaviours in both cancer survivors and patients more generally.[368, 369] Additionally, whilst the case studies may go some way to guiding learning through shared experience, for those seeking interaction and peer-peer support, these may not suffice. However, the intention of the feasibility evaluation (outlined in the next chapter) is to assess whether the LIBERATE intervention is able to bridge the identified gaps in support, as well as supplementing and signposting towards existing resources and services.

Rather than looking to replace health professionals in the delivery of support, the design of online supportive resources such as LIBERATE must seek to facilitate this vital collaboration. Where elements such as interactive peer-peer support are lacking, signposting represents a key strategy for targeting support and harnessing the strengths of readily available resources and services.

6.8 Summary

This chapter has outlined a wide range of evidence and theory which has been applied to the design and development of the LIBERATE intervention. Reflecting on phase I findings, as well as the wider evidence bases across fields of self-management, cancer survivorship and intervention development, a theory and evidence-based approach has been presented, ultimately guided by and embedded within an over-arching target-population based approach. This placed key stakeholders at the centre of intervention design. Furthermore, key stages in the development of the LIBERATE intervention have been outlined, providing a clear overview of how the various components have been shaped. In line with the MRC Framework for the Development and Evaluation of Complex Interventions, the next chapter will focus on outlining the methods for feasibility evaluation of the LIBERATE intervention.

Chapter 7: Planning for feasibility evaluation

7.1 Chapter overview

Usability testing is widely recognised as a pivotal step in the development of information technology to safely and effectively support health, whether information websites, mobile applications, electronic medical records, patient portals or other digital devices.[370] In the health setting, usability considerations are closely related to the ehealth literacy and supportive needs of the intended audience.[371] Any technology designed for consumers of health information must not only be usable, but also comprehensible, relevant and of perceived value if it is to achieve the desired uptake and efficacy.[371, 372] Ensuring that the LIBERATE intervention meets these foundational standards is therefore an essential prerequisite to any feasibility evaluation. Following on from this, the design and planning of feasibility evaluations is as crucial as the results themselves. Researchers must ensure that such studies are designed to effectively and rigorously apply the methods and measures chosen to determine feasibility, providing a sound evidence-basis to inform further research.[116, 373]

This chapter will first explore the usability testing undertaken to assess the readiness of the intervention to progress to the next stage of the MRC Framework. Following on from this, the study designs applied as part of the overall feasibility evaluation will be outlined.

Returning to the research overview (Figure 2.1, chapter 2) these next steps fall under phase II of the LIBERATE project.

7.2 Chapter aims

- To detail the methods, results and outcomes of usability testing, performed to assess the appropriateness of progression to the feasibility evaluation stage.
- To outline and provide rationale for the design and mixed methods approach of a randomised controlled feasibility trial and a single arm pre-post feasibility sub-study.

7.3 Usability testing

Following intervention development, a range of usability testing was conducted. Encompassing both expert and user-led methods, this aimed to:

- Assess the intervention's usability and functionality.
- Gather early indications of acceptability, relevance and comprehensibility.

In order to achieve these aims, a range of outcomes were collected, with the intention of guiding final modifications to the intervention ahead of feasibility evaluation.

7.3.1 Expert testing

Initial expert-based testing was performed to assess functionality and navigation, harnessing aspects of both 'walk-through' and 'usability inspection' methods. Collectively, these aimed to identify any potential system errors or usability issues before the intervention was shared with its target population.[374]

A formal testing plan was followed to evaluate the functionality and accuracy of the symptom-monitoring questionnaire algorithms, ensuring that the different severities and combinations of symptoms generated the correct levels of advice and alerts. This included exploring a number of combinations of symptoms, encompassing all levels of the algorithm, 'walking through' the user's process from start to finish. Minor amendments to the questionnaires, and to the underlying scoring functionality within QTool, were made on the basis of this exercise.

Systematic inspection of navigational aspects of the website itself, which included testing all internal and external links, was also performed. It was recognised that, due to the breadth of external links, users could frequently be navigated away from the LIBERATE website and may find it difficult to return to the section they had be reading. External links were therefore amended to open within a new browser tab, allowing for smoother navigation.

7.3.2 User-based usability testing

A small-scale usability study was conducted to evaluate the intervention from the perspective of the 'end users': women living with SBC. User-based usability methods centred around principles of heuristics and problem discovery.

The identification of issues relating to the usability of a system is referred to as 'problem discovery'.[375]A heuristic evaluation is a lab-based usability testing technique. This involves the use of pre-specified principles of system usability (so-called 'heuristics'), against which a small number of participants evaluate a particular system.[376, 377] These recognised principles comprise the following:[376]

1. Dialogue should be simple and naturalistic.
2. Language and terminology should be familiar to users.
3. The user should not be expected to memorise information or instructions.
4. Dialogue, actions and functions should be consistent throughout the system and between other related systems which share user populations.
5. The system should provide appropriate and timely feedback.

6. The user should be able to move easily and freely though the system with the use of clearly marked 'exit' functions.
7. Well thought out short-cuts should be incorporated and cater for both experienced and inexperienced users.
8. Error messages should be informative and provide a solution.
9. The system should be designed in a way that considers and prevents potential errors.

To meet the aims of this usability evaluation, elements of these principles were harnessed in the testing methods applied.

7.3.2.1 Participants

Patients were recruited from the breast oncology clinics at St James's University Hospital, in accordance with the following eligibility criteria:

- Women diagnosed with SBC, on any form of cancer treatment.
- Able to read and understand English.
- Have access to the internet.
- Not exhibiting any signs of cognitive dysfunction.

7.3.2.2 Sampling

The usability study aimed to purposively sample approximately 5-10 patients across varying treatment pathways (chemotherapy +/- monoclonal antibodies, and hormone therapy +/- targeted therapy, in line with questionnaires A and B respectively, to allow for testing across both groups).

There is extensive debate as to the most appropriate sample size for usability testing, with some long-standing research specifying samples as small as 5 participants as being sufficient.[378, 379] Others argue against this assertion, citing the risk of variation between individual users. They look to statistical calculations highlighting a high percentage of missed findings at lower sample sizes.[380] Appraising such evidence, Macefield advises looking towards a 'middle ground'. Generally, it is acknowledged that sample size must increase in line with the complexity of a study. Therefore, it must be determined on a study by study basis, guided by the overall aims and context.[381] Given the relative simplicity of LIBERATE's home-based testing and the combination of brief self-report questionnaires and informal telephone feedback, a smaller sample may be justified. A study by Faulkner estimates that 5-10 participants will be able to identify between 86% - 95% of problems within the system they are evaluating.[380] As problem discovery is one aspect of the overall exploratory nature of this particular usability study, this level of accuracy was deemed to be sufficient.

Contextually, recruitment took place during the start of the COVID-19 pandemic, and therefore needed to be halted after two weeks. Additional time and resources to recruit further participants via alternative methods was considered unnecessary at this stage.

7.3.2.3 Study procedure

(i) Approval

Permission was obtained from the research governance office at LTHT for LIBERATE's usability testing to be conducted as a service evaluation. This therefore fell outside of the definition of 'research' and did not require Research Ethics Committee (REC) or Health Research Association (HRA) review. However, as part of good clinical and research practice, processes for obtaining informed consent were followed. Participants were provided with a participant information sheet (PIS) and asked to sign a consent form to ensure that they understood how their data would be used and stored.

(ii) Recruitment

Women attending outpatient breast oncology clinics were identified from clinic lists and screened for eligibility by a clinical member of the research team (GV), who briefly explained the study and directed those interested to the researcher in clinic. At the end of their appointment, the researcher (KK) provided further information and gave the participant a demonstration of the intervention and its various features. Participants were given the opportunity to ask any questions before signing the consent form. Brief clinical and demographic information (e.g. age, time since diagnosis, site(s) of metastases, current treatment, frequency of computer use etc.) was collected. Participants were then provided with a full user guide and the researcher's contact details, in case they encountered any issues or had any further questions. Their personal login details (for accessing the symptom monitoring component via QTool at home) were emailed to them later that day.

(iii) Data collection

During the 1-2 week usability period, participants were encouraged to navigate through the website's various features and components, considering where content or usability may be in need of modification or improvement. They were asked to complete and return a number of paper-based questionnaires.

A general usability questionnaire asked participants to rate aspects of the intervention's usability, acceptability and relevance across various Likert scales, as well as giving them the option to provide additional written feedback. Questions focused on 'using the LIBERATE website', 'completing the symptom monitoring questionnaires', 'symptom management advice' and 'general feedback'. Elements of the aforementioned heuristics were incorporated

with the use of the Health Information Technology Usability Evaluation Scale (Health-ITUES), adapted to suit this intervention specifically. The Health-ITUES is a customizable questionnaire consisting of a 20-item scale and a four-factor structure (impact, perceived usefulness, perceived ease of use and user control).[382] In line with previous studies which customized and applied this scale, only the most relevant of the original 20 items were included.[383] The 15-item Health-ITUES adapted for LIBERATE is presented in Table 7.1 below.

Table 7.1 Health ITUES adapted for the LIBERATE intervention

Please circle one number against each statement below **1 = STRONGLY DISAGREE, 5= STRONGLY AGREE**					
Impact					
1. I think LIBERATE would be a positive addition for people living with secondary breast cancer.	**1**	**2**	**3**	**4**	**5**
2. I think LIBERATE would improve the quality of life of people living with secondary breast cancer.	**1**	**2**	**3**	**4**	**5**
3. LIBERATE is an important part of meeting my information needs related to self-management.	**1**	**2**	**3**	**4**	**5**
Perceived usefulness					
4. LIBERATE is useful for the self-management of secondary breast cancer.	**1**	**2**	**3**	**4**	**5**
5.Using LIBERATE enables me to self-manage my symptoms and supportive needs more quickly.	**1**	**2**	**3**	**4**	**5**
6. I am satisfied with LIBERATE for my self-management needs.	**1**	**2**	**3**	**4**	**5**
7. Using LIBERATE increases my ability to self-manage my secondary breast cancer.	**1**	**2**	**3**	**4**	**5**
8. I am able to self-manage my secondary breast cancer related symptoms and supportive needs whenever I use LIBERATE.	**1**	**2**	**3**	**4**	**5**
Perceived ease of use					
9. I am comfortable with my ability to use LIBERATE.	**1**	**2**	**3**	**4**	**5**
10. Learning to operate LIBERATE is easy for me.	**1**	**2**	**3**	**4**	**5**
11. I find LIBERATE easy to use.	**1**	**2**	**3**	**4**	**5**
12. I can always remember how to log on and use LIBERATE's online questionnaire system (QTool).	**1**	**2**	**3**	**4**	**5**
User control					

13. LIBERATE gives error messages that clearly tell me how to fix problems.	**1**	**2**	**3**	**4**	**5**
14. Whenever I make a mistake with LIBERATE, I always recover easily and quickly.	**1**	**2**	**3**	**4**	**5**
15. The information (such as on-screen messages and user guide) provided with LIBERATE is clear.	**1**	**2**	**3**	**4**	**5**

Similar to a heuristic style of evaluation, users are asked to evaluate the system against the statements presented, rating them on a 5-point Likert scale from strongly disagree (1) to strongly agree (5). The overall Health-ITUES score is calculated as the mean of all (equally weighted) items, with a higher value indicating greater usability.[382]

(iv) Qualitative feedback

After 1-2 weeks, the researcher telephoned each participant, as planned, and asked for any further feedback relating to their use of the website. Discussions encompassed users' acceptability of the questionnaire items (content and wording) and thoughts on the value of the user guide, as well as more general considerations relating to usability, navigation, content and overall impressions of the website. Verbal feedback was summarised and collated within an excel spreadsheet, along with users' written feedback from 'free text' sections of the usability questionnaire. This data was then narratively synthesised, with topics of discussion grouped together under key 'themes' to inform points of action ahead of the next stage of evaluation. Potential future considerations, outside the scope of the current research, were also identified.

7.3.3 Results of user-based usability testing

In total, 9 participants agreed to take part, of which 2 were lost to follow up. The remaining 7 participants used the website over a period of 1-2 weeks. All 7 participants provided some form of feedback; 6 participants returned the usability questionnaires, whilst all 7 provided verbal feedback. Overall, the sample comprised women aged 52-73 years old (mean 60.7 years), with no women under the age of 50 represented. The vast majority (n=6, 85.7%) had an initial primary diagnosis (between 3 and 17 years ago) and most were currently being treated with chemotherapy and/or MAB therapy (n=5, 71.4%). Metastasis was predominantly to the bones (n=6, 85.7%), though single or multiple sites of metastasis were also diagnosed across the lungs, liver, brain, lymphatics and soft tissues. The amount of time since women had received their secondary diagnosis varied greatly, from 2 months to 7 years ago. Similarly, length of time on treatment ranged from 1 month to 2 years, with a mean of 14 months (SD

9.5). Computer usage was fairly evenly distributed across those using such technology daily (n=2, 28.6%), weekly (n=3, 42.9%) or monthly (n=2, 28.6%).

7.3.3.1 Health ITUES scores

The mean score for the 4 Health-ITUES subscales was calculated for each participant, alongside a total score (the mean of all 15 items). To provide an overview of the group as a whole, pooled mean scores were also calculated. Results are displayed in Table 7.2 below.

Table 7.2 LIBERATE usability assessed using the Health ITUES

Participant	**Health-ITUES scores, mean (SD)**				
	Impact	Perceived usefulness	Perceived ease of use	User control	**Total score**
001	2.00 (1.00)	1.80 (0.45)	3.00 (0.00)	4.00 (0.00)	**2.38 (0.87)**
004	4.33 (1.15)	3.20 (0.45)	4.00 (0.00)	3.00 (0.00)	**3.60 (0.73)**
005	5.00 (0.00)	5.00 (0.00)	4.50 (0.58)	4.33 (0.58)	**4.73 (0.45)**
006	4.00 (1.00)	3.80 (0.84)	5.00 (0.00)	5.00 (0.00)	**4.40 (0.83)**
008	1.67 (0.58)	1.00 (0.00)	4.00 (0.82)	3.00 (0.00)	**2.33 (1.35)**
009	4.33 (0.58)	3.40 (0.55)	4.00 (0.00)	4.00 (1.00)	**3.87 (0.64)**
Overall group	3.56 (1.38)	3.03 (1.43)	4.08 (0.66)	3.89 (0.78)	**3.55 (1.01)**

**Scores ranging from 1-5; higher scores indicate greater usability.*

The data presents a mixed picture for the impact and perceived usefulness subscales, whereas ease of use and user control were generally rated more highly. Whilst scores for impact and perceived usefulness were relatively high for most participants (between 3 and 5), 2 participants (001 and 008) rated these areas noticeably lower (between 1 and 2). Verbal feedback and questionnaire data supported and provided further contextual insights in relation to these figures.

7.3.3.2 Usability questionnaire

(i) Using the LIBERATE website

The majority of participants (n=5, 83%) reported that the LIBERATE website was easy or very easy to find and to learn how to use. None of the participants reported any difficulty in accessing the different sections and all but one found it easy or very easy to locate the information they needed. For 4 of the participants, the amount of information provided on the

LIBERATE website was ‘about right’. One participant felt that there was too much information, whilst another would have preferred more.

Half of the participants (n=3) found all of the information on the website useful, whilst 2 were unsure as to how useful it was for them overall. One participant found it not at all useful, commenting that it did not add anything new when compared to other available websites.

(ii) Completing the symptom monitoring questionnaires

For 4 of the participants, accessing and logging in to the QTool website was easy (1 found it neither easy nor difficult, whilst another had difficulty). The majority (n=5, 83%) found completing the symptom questionnaires to be easy or very easy. Most participants (n=4, 67%) indicated that the length of the symptom monitoring questionnaire was about right, whilst 2 participants felt that there were too many questions.

One participant commented that the questionnaire had made her realise the range of symptoms which could be attributed to her cancer and treatment, prompting her to seek help. Another added that it would be useful to include a free text box, to ensure that users can report any additional symptoms not featured. Only 1 participant cited any questions which did not feel relevant, specifically referencing those relating to sexual health and well-being.

(iii) Self-management advice

Those who felt the questionnaires were of the appropriate length (n=4, 67%) also reported finding the self-management advice both useful and relevant. This was not the case for the participants (n=2) who reported that the questionnaires were too long (of note, these were the same participants who scored lower for the Health ITUES). However, all participants found these summaries easy to read. Most (n=5, 83%) followed the links from these summaries to the self-management information provided on the main website (either always or sometimes). Notably, the participant who did not follow the links indicated that this was due to being restricted to her mobile phone data limit. Of the 5 participants who followed the links, 2 found the information and advice here very useful, 1 was uncertain, whilst another found it not at all useful (the remaining participant did not respond).

7.3.3.3 Qualitative feedback

Table 7.3 highlights and summarises the key areas of discussion. Furthermore, identified ‘problems’ warranting action ahead of feasibility evaluation were listed, alongside issues to be considered as part of any future development.

Table 7.3 Usability feedback, actions and future considerations

Area of discussion	Summary of feedback & problems discovered	Short/medium terms actions	Future considerations
Ease of use *"Laid out very well, easy to follow…" U03* *"I don't usually use the computer much, I'm not the best on the computer but it was a pleasure." U05* *"Easy to use but very poor search function."U08*	Feedback surrounding navigation and usability was generally very positive, though one user felt that the website search function was too limited. Others found it easy to navigate and helpful to have all information in one place, whilst also being guided to resources elsewhere. Potential barriers were discussed in relation to older age groups, who may have lower levels of ehealth literacy, and difficulties navigating the intervention on a mobile phone. One user did not have access to a computer or Wi-Fi at home and (with libraries closed due to COVID-19) was limited to the data available on her mobile phone.	To assess functionality on mobile phones as opposed to computer/laptop/tablet screen and to consider recommending use on the latter where possible. To consider offering demonstration on mobile phone if this is the device participants will use to access intervention. To explore potential age-related barriers to intervention use within feasibility setting.	More advanced search function (currently limited to the level of functionality provided within WordPress platform). At this stage, clear and detailed main menu, as well as signposting within each section, seeks to strengthen the basic search function. Potential for mobile phone/app specific future development. Larger scale trials may have the resources to provide necessary technology to overcome potential socio-economic barriers.
General impression *"Overall, very good." U04* *"I don't know how you could change it for the better." U05*	Users were polarised in this area of discussion; some had a very positive overall impression whilst others (001U and 008U) felt that the intervention did not stand out from other similar resources in terms of what it offered e.g. Macmillan website. One user suggested that improvements could be made aesthetically.	Incorporation of additional relevant images to break up large sections of text. Acceptability of intended 'novel' elements (e.g. multi-level tailoring and clinically integrated symptom reporting) to be further explored in feasibility setting.	Potential for collaborative research efforts with other organisations to streamline resources in the future.

"Very similar to what's currently available." U01			
Functionality *"I found no problems at all" U06* *"The links to other websites were fantastic and all worked." U05* *"I was expecting something different, interactive." U01*	With the exception of search function, all feedback on functionality was positive, with key examples of good functionality relating to the widespread use of external links, signposting and QTool. One user would have preferred a more interactive style of intervention (e.g. blogs, forums) but reported no issues with the level of functionality available.		Potential further development to encompass interactive and Web 2.0 technology.
Content *"If I read it on a website like this, I know I can trust it." U05* *"Family do worry so it's good to have the 'support for others' section." U03*	A range of content was highlighted as particularly useful, including 'healthy living', 'support for others' and the symptom monitoring questionnaires. One user highlighted the case studies as helpful, whilst another would have preferred an interactive alternative. Suggested gaps in content included information relating to dental health during treatment and guidance relating to the unfolding COVID-19 pandemic. One user felt that stylistic improvements could be made to content wording to improve its readability.	Addition of content and signposting relating to dental health & COVID-19. Additional proof reading of all content ahead of feasibility studies. Further exploration of the acceptability and perceived value of case studies as an alternative to interactive features within feasibility setting.	
Usefulness	Several factors appeared to have a potential mediating effect on usefulness, including time since diagnosis and time available to access the intervention. One user felt the intervention would	Intervention period (i.e. length of time women will be able to access intervention) to be a significant	Recommendations for a longer period of study in the usability setting for future intervention development research.

"I've already read everything that's going" U01 *"Especially helpful for someone like me…I do as my consultant says, I don't interact." U05* *"I found out things I didn't know." U03* *"Not at all helpful, lots of words but nothing new." U08*	have been more useful earlier on in her disease trajectory, whilst a recently diagnosed user felt she needed predominantly face-to-face support with a clinician. It was also suggested that having a longer period of time to access the intervention would have heightened its usefulness. Others described significant benefits, particularly in relation to symptom monitoring support. For several women, whilst useful, face-to-face support remained their preference. One user did not find the intervention at all useful and felt that she would have been able to access the information independently via Google.	consideration in feasibility study design. Potential mediating factors of diagnostic timeframe and level of ehealth literacy/computer expertise to be further explored across a more diverse sample. Influence of clinical integration of intervention on women's face-to-face supportive needs/clinical encounters to be explored within an RCT.	
Relevance and acceptability *"…some of it could be upsetting for some people, but then it is par for the course. It was certainly helpful for me." U03* *"Too long…and the messages could wrongly induce panic." U08*	Feedback in this area largely related to the symptom monitoring component. Several users disagreed with the alert messages advising them to contact the hospital; they felt they knew their ongoing symptoms better. One user disagreed with some of the CTCAE-guided questionnaire response wording e.g. whilst she experienced chronic severe pain, 'not being able to get out of bed' was not an option for her. She also queried the appropriateness of being questioned about severe symptoms. Views were mixed with regards to the length of the questionnaires; some would have preferred shorter whilst for others they were 'about right'. Some	Changes to the algorithm, alert messages and questionnaire structure to reflect users' treatment across a chronic as opposed to acute trajectory. This included removal of the branching question asking whether symptoms were 'ongoing or resolved'. Adaptation of 'severe' option response wording to be more inclusive of those continuing day to day life with chronic/ongoing symptoms. Users to still have the option to report severe symptoms	More in-depth user involvement in the development and wording of questionnaire items specific to the chronic/metastatic cancer setting.

"It wasn't flagged as serious but it is something I'm anxious about." U09	users felt further tailoring was needed, suggesting inclusion of a free text box to report any symptoms not listed and appreciation that clinical advice may still be needed for symptoms which are concerning to them, whether graded as 'severe' or not. More generally, one user commented that some women may find aspects of the intervention upsetting, though this wasn't the case for her.	for safety and to ensure clinical advice is sought where needed. Acceptability of questionnaire length to be explored in greater detail in feasibility setting. Addition of a free-text box for any additional symptoms to be reported.	

7.3.4 Reflections

Methodologically, it is clear that the outlined testing could have been strengthened with a longer recruitment period, perhaps allowing for women across a broader range of age and treatment groups to be sampled. This was an acknowledged limitation and significant challenge, given the need to halt recruitment as COVID-19 restrictions were implemented. For those who had agreed to take part, care was needed to ensure that their ongoing participation was not adding to any distress likely felt with the uncertainty brought by the pandemic and national lockdown. The researcher was also keenly aware of the unknown impact this situation could be having on women's treatment and access to care, as well as worries they may have been having in relation to their safety (and that of their loved ones) and prognosis. This may have been the reason for two participants being lost to follow up. Such added uncertainty brought home the (likely intensified) need for psychological and other support for these women, with remote, online access suddenly even more pertinent.

Findings also gave the opportunity to reflect further on the notion of there being differing stages and experiences along an extremely varied and individualised disease trajectory. Whilst much emphasis has thus far been placed on tailoring support to women across all stages of the disease trajectory, here it became clear that some women did not perceive much value from this sort of support. Indeed, those further along the disease trajectory would have valued the intervention closer to their initial SBC diagnosis, whilst a recently diagnosed participant would have liked to use the intervention for longer. Yet earlier qualitative findings highlighted a breadth of unmet needs for women, regardless of how long they had been living with SBC. The ongoing research will be key to further exploring these underlying contextual determinants for the LIBERATE intervention. More generally, it became clear that some users' expectations of the intervention may have been at odds with the reality of what was possible within the remit of the research, available resources and skills. Going forwards, it was emphasised to participants that the project was small-scale, led by a PhD student and carried out without any formal web-design involvement. Furthermore, participants were made aware that the intervention was in its earliest stages and that their involvement would help to assess how feasible, acceptable and appropriate the intervention would be in a larger scale evaluation setting.

7.3.5 Summary

This usability testing informed crucial aspects of intervention design and delivery which could be refined and improved, ensuring that both usability and acceptability was optimised ahead of feasibility evaluation. Furthermore, expert testing provided the opportunity to run through key functionalities, identifying very few errors which were easily reconciled. From a user-based

perspective, this small sample demonstrated a mixed impression of usability and acceptability (specifically relating to impact and perceived usefulness), with some feedback and results polarised. Whilst observed within a very small sample, the range of data suggests a potential negative correlation between the usefulness and impact of the intervention and the participant's level of experience (both of navigating SBC and navigating computers and health information). This suggested that both contextual and individual determinants may have some part to play in how users interact with the intervention. This hypothesis warranted further investigation amongst a larger group of women sampled using more rigorous methods.

As highlighted in Table 7.3, across these varying results, a number of key actions were highlighted as having the potential to enhance usability and acceptability. These were therefore implemented ahead of the feasibility evaluation.

7.3.4.1 Actions taken ahead of feasibility evaluation

- Addition of a 'free-text' box to allow users to report additional symptoms.
- Removal of the branching question asking whether each reported symptom is 'ongoing or resolved', in recognition of the chronic nature of symptoms for some women with SBC.
- Amendment of safety-netting information to advise (rather than alert) women to seek expert medical advice for any new onset, severe symptom or (at their discretion) any ongoing symptom which has worsened, changed or is causing them concern.
- Amendment of response wording for symptoms graded as severe (originally guided by the CTCAE) from 'I was not able to care for myself (e.g. getting out of bed, bathing, dressing)' to 'this has had a significant impact on my normal daily life.'
- Assessment of overall functionality and readability on a mobile phone in order to advise future participants on the most appropriate device (where the choice is available).

Notably, some considerations warranted further investigation, as opposed to an immediately implementable change, and were outside of the remit and capacity of this PhD research. However, the subsequent feasibility evaluation provided the opportunity to explore these further, alongside potential barriers and determinants relating to impact and perceived usefulness, amongst a larger, more diverse group of women. Overall, the results of this usability testing supported the need for (and appropriateness of) further evaluation of the LIBERATE intervention in the feasibility setting.

7.4 Feasibility evaluation: Design and methods

7.4.1 Rationale

To allow for the evaluation of both iterations of the LIBERATE intervention (clinically integrated and independent monitoring), phase II of the project was designed to encompass two feasibility studies running in parallel, as will be outlined in the rest of this chapter. This multi-faceted approach aimed to look beyond the experimental context of the traditional RCT, applying principles of realistic evaluation in seeking to explore not just whether the intervention works (and is feasible) but also *how*, for *whom* and in what *circumstances*. This was further supported through the use of mixed methods, harnessing both quantitative and qualitative data to gain a more complete picture of intervention feasibility.

7.4.2 Aims & objectives

The overarching goal of this phase of research was to establish the feasibility and acceptability of the LIBERATE intervention and methods for its evaluation across two distinct contexts. To achieve this, a number of research aims were identified.

7.4.2.1 Primary aim

- To assess the feasibility and acceptability of the LIBERATE intervention as a clinically integrated resource for women living with SBC and accessing care at St James's University Hospital, Leeds (clinically integrated group).

7.4.2.2 Secondary aims

- To explore the feasibility and acceptability of the LIBERATE intervention in the absence of clinical integration, delivered as a self-monitoring, self-management resource to women living with SBC and accessing care elsewhere in the UK (independent monitoring group).
- To guide the selection of outcome measures and gather data for the estimation of effect sizes, informing potential future larger scale evaluation.

7.4.2.3 Study objectives

To achieve the identified research aims, several study designs encompassed a range of objectives, as outlined in Table 7.4 below.

Table 7.4 Cross-context study objectives for the LIBERATE feasibility evaluation

	LIBERATE: clinically integrated	LIBERATE: independent monitoring
1.	Determine rates of recruitment in both the clinical and online settings.	
2.	Determine the rate of attrition in the presence of active follow-up by clinicians.	Determine the rate of attrition in the absence of active follow-up by clinicians.
3.	Assess the acceptability of randomisation with a waiting list control group.	Assess the acceptability of online recruitment methods.
4.	Evaluate the integrity and usability of the protocol and data collection forms.	
5.	Evaluate the acceptability, uptake and adherence to the LIBERATE intervention.	Evaluate the acceptability, uptake and adherence to the intervention in the absence of clinically integrated symptom monitoring.
6.	Select the most appropriate outcome measures and assess the feasibility of their collection.	
7.	Determine the optimal frequency of data collection.	
8.	Gather patient reported outcome data for QoL and self-efficacy in managing cancer.	

7.4.3 Study design

In order to achieve the cross-context research aims, two separate study designs were harnessed, each applying repeated measures and a mixed methods approach to analysis. Table 7.5 summarises the key contextual distinctions across the studies.

Table 7.5 Matching study design to the intervention context, features and delivery

	Study design	Context	Summary of intervention features & delivery
Clinical integration	Two-arm randomised waiting list controlled trial.	Women recruited in the clinical setting in Leeds.	➢ Access to the LIBERATE website. ➢ Personal login details for symptom monitoring component with weekly reminders to encourage engagement. ➢ Symptom monitoring results integrated with EPR for clinician review. ➢ Alerts to clinician where severe symptoms reported.
Independent monitoring	Single arm, pre-test post-test study.	Women recruited online from across the UK.	➢ Access to the LIBERATE website. ➢ Personal login details for symptom monitoring component with weekly reminders to encourage independent engagement. ➢ Option to print/email symptom monitoring results for personal monitoring or to share with health professionals.

7.4.3.1 Randomised controlled trial

An RCT, applying a prospective, two-arm parallel group, pre-test, post-test design, was planned to assess the LIBERATE intervention in the context of clinical integration. A waiting list was chosen as the control condition. These elements of study design will be explored in greater detail.

(i) Randomisation

In clinical trials, randomisation provides participants with an equal and unbiased chance of receiving either the treatment (or, in the context of this research, the intervention) or the control (i.e. usual care).[384] Furthermore, it seeks to ensure that participants' varying characteristics are randomly distributed across the intervention and control groups, allowing results to be more clearly attributed to what is being trialled (as opposed to any other potential influencing factors e.g. age, disease stage etc).[384, 385] This latter goal is strengthened through the use of stratification, allowing for randomisation on the basis of clinical and/or demographic characteristics (so called co-variates), so that the resulting study groups are as similar and as balanced as possible.[385, 386] This is particularly valuable to smaller trials, where imbalance is more likely given the smaller number of participants.[386]

Stratified randomisation is usually performed with numerous co-variates, leading to multiple subgroups ('strata'). In this patient group, for example, it is clear that both age and time since diagnosis (of SBC) could potentially influence the feasibility and acceptability of the intervention. However, in small-scale trials such as the LIBERATE RCT, stratification on the basis of several strata is not effective.[386, 387] Instead, there is widespread consensus as to the value and efficacy of an alternative approach for small samples: minimisation.[388, 389] Using this method, the first participant is allocated by simple randomisation. All subsequent participants are then allocated according to the balance of the specified variables within each group (in this case, age and time since diagnosis). In other words, allocation is determined by what will lead to the most balanced distribution (or minimise the imbalance) across groups.[387]

Whilst there is an inherent risk of bias (where the same individual performs both minimisation and recruitment) in that it may be possible for the allocation sequence to be predicted, on balance, this is the best available alternative to stratified randomisation for small scale RCTs.[387, 388]

(ii) Waiting list control design

A waiting list control design aims to ensure that all participants have the opportunity to access the intervention under evaluation, whilst also providing a valid comparator/control condition against which to assess intervention efficacy.[390]

Though not always deemed essential at the feasibility stage (given studies are not usually powered for or focused on definitive evaluation of efficacy), applying randomisation with a waiting list control group allows for the acceptability and practicalities of these elements of the study to be assessed. Randomisation to the waiting list control arm, for example, may prove unacceptable to participants, potentially impacting upon adherence and retention.[162] Using a waiting list control design is advantageous, however, in that it overcomes ethical concerns relating to withholding the intervention from eligible and interested research participants, who may derive benefits from its use in the trial setting.[391] Though their access to the intervention is delayed, leading some to question the potential harms for such participants,[392] a relatively short study period, alongside the provision of care (and support) as usual, was considered to mitigate against these in this instance. The study design also encompassed plans to explore the acceptability of this design feature both qualitatively and quantitatively, as a key contextual factor with the potential to impact upon the internal causal mechanisms driving the outcomes under investigation.

Whilst widely applied in trials of behavioural and psychological interventions, there is increasing evidence suggesting that waiting list control designs can lead to over-estimation of effect sizes. This may be due to control participants' efforts to perform a targeted behaviour change being 'put on hold' as they await the intervention, or their expectations of decline/lack of improvement in the absence of the intervention.[391, 393] Though the evaluation of efficacy is not the primary goal of this study, this must be acknowledged when estimating effect sizes and making any recommendations for future further evaluation.

(iii) Blinding & allocation concealment

Within RCTs, the use of blinding describes methods to ensure that participants' allocation status remains unknown to key individuals involved in the study, minimising the potential for bias. Such individuals include the participants themselves and any research personnel (and, in the clinical setting, health professionals) involved in key activities such as intervention delivery and the assessment and scoring of outcomes.[394]

As is frequently the case for behavioural interventions,[395] the nature of the LIBERATE intervention meant that it was not possible for the participants, health professionals or researcher to be blinded to group allocation. Furthermore, given the involvement of the

researcher in all aspects of trial conduct, blinded assessment of outcome measures (a feasible form of blinding to minimise bias in studies of behavioural interventions)[395] was not possible.

Allocation concealment, on the other hand, refers to methods which ensure that the researcher recruiting participants does not have prior knowledge of the allocation sequence.[396, 397] This was possible thanks to the use of the minimisation software (QMinim), which randomly allocated participants on the basis of their characteristics and those of the subjects already recruited.[398] Whilst some argue that, theoretically, subsequent allocations may be predicted, this is much less likely than with stratified randomisation using blocks of known sizes.[396] Allocation was also performed prior to the collection of outcome data, ensuring that these results did not inadvertently influence or introduce bias to the process of group allocation.

The absence of any form of blinding is acknowledged as a limitation and is one which could potentially be mitigated against within a future larger scale setting.

(iv) Two-group pre-test post-test measures

Repeated measures refers to a range of study designs in which a dependent variable is measured across two or more timepoints.[399] For the RCT, this was applied in the form of a two-group pre-test post-test design, with outcome measures assessed for the same subjects, under different conditions (intervention and control), at the start (T0) and end of the defined study period (T1). The inclusion of two groups means that results can be compared across timepoints both within and between groups, with the control condition aiding internal validity.[400] For example, whilst there is still the possibility that factors (other than the intervention) will influence the outcome variables over time, this will be true for both groups. A between-group difference can therefore more strongly support an intervention effect.[400]

7.4.3.2 Single arm pre-test post-test sub-study

The feasibility and acceptability of the intervention as an independent, patient led self-monitoring resource was evaluated within a separate sub-study, applying a single arm, pre-test post-test design. This study design is widely applied across the social and behavioural sciences to assess the implementation and efficacy of interventions. Whilst stronger designs undoubtedly exist, these simple studies provide useful insights where a control group is not appropriate and can be a complementary element of, or stepping-stone towards, further rigorous experimental research.[401]

(i) Single arm

This simple design was chosen in light of the sub-study's overall explorative purpose, seeking to gather evidence relating to acceptability and potential efficacy within an alternative context

(absence of clinical integration). It also had the additional explorative aim of assessing the feasibility of online recruitment methods. Whilst the RCT drew from a known population of women living with SBC, the number of women likely to be recruited via online channels was unknown, hence inclusion of a control arm was not deemed appropriate. Though the absence of a control group represents a threat to internal validity,[400] the strength of this design lies in its supportive insights (supplementing the RCT) into both feasibility and contextual factors.

(ii) One-group pre-test post-test measures

Outcome measures were again assessed pre-test and post-test, this time to compare the dependent variables across two points within a single study group (i.e. before and after exposure to the intervention in its independent monitoring form). These pre-test post-test measurements also provided direct points of comparison with those measured at the same timepoints within the RCT.

7.4.4 Study documents

Core study documents (Participant Information Sheets and study questionnaires, including a PDF copy of the online symptom monitoring questionnaires) are available to view on the LIBERATE section of the Patient Centred Outcomes Research group's website. (https://pcor.org.uk/liberate-living-better-with-advanced-breast-cancer-symptom-monitoring-self-management-and-sign-posting-support-for-women-living-with-secondary-breast-cancer/)

7.4.5 Intervention duration and frequency

A range of evidence suggests that a longer intervention duration (i.e. participants being exposed to the intervention over a longer period of time), both online and 'offline', across chronic diseases, is likely to support efficacy.[329, 402] Originally, a 16 week intervention period was planned. This was considered to be the longest possible duration due to the research timeline, the need to allow for the same period of intervention use post-study for waiting list control participants, and the time needed to analyse results and formulate recommendations. However, this was later refined to 12 weeks due to delays in both the ethical/R&I approvals and the impact of the COVID-19 pandemic on research activity.

Participants were encouraged to use the website as often as was beneficial for them during the 12 weeks. They were, however, asked to complete at least one symptom monitoring questionnaire per week to ensure that this component could be adequately assessed. This was encouraged through weekly reminders to all participants. For those recruited to the RCT, reminders were sent via PROMPT and could be via either email or SMS. For sub-study participants, the researcher sent weekly email reminders manually, on their preferred day of the week.

7.4.6 Selection of outcome measures

As explored in detail in chapter 5, a number of key theoretical constructs are pivotal to this research: self-efficacy and QoL. Their measurement was therefore crucial to both understanding and evaluating the LIBERATE intervention.

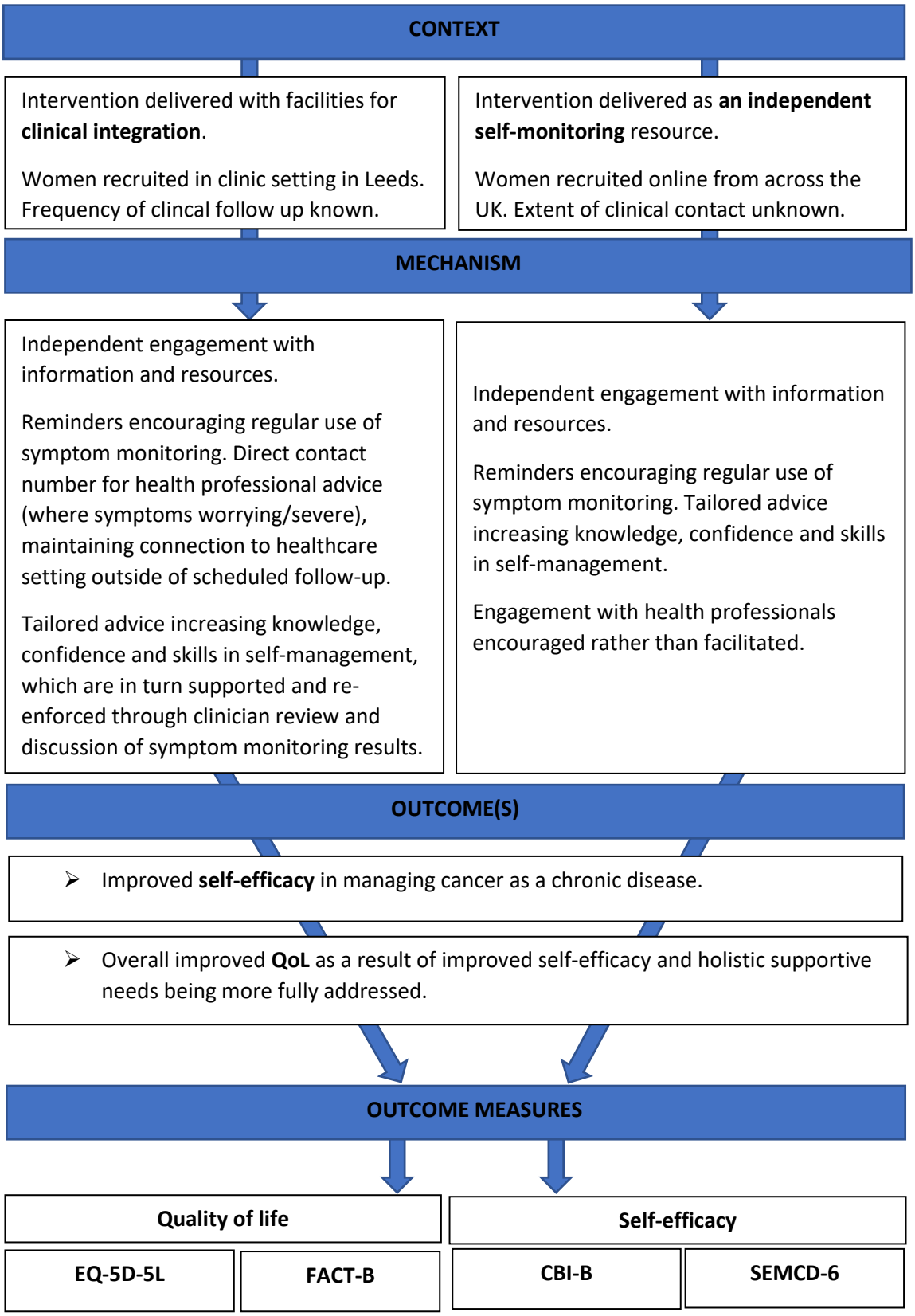
Numerous validated PROMs were selected to capture these crucial constructs, before and after intervention use, from the participants' perspective. Selection was guided by their brevity and content in terms of how comprehensively and succinctly the outcome in question (self-efficacy and QoL) was measured. Several were chosen for each of the outcomes, allowing for comparisons as to their acceptability and appropriateness, as determined qualitatively (end of study interviews) and quantitatively (assessing for missing data and floor and ceiling effects). Collectively, their application to the study designs supports the core realistic evaluation principle of seeking to understand the underpinning mechanisms and surrounding context of the intervention. Figure 7.1 situates the chosen outcome measures, detailed below, within the distinct contexts and theorised mechanisms of the LIBERATE intervention.

7.4.6.1 Functional Assessment of Cancer Therapy scale – Breast (FACT-B)

This 37-item questionnaire measures multi-dimensional QoL in breast cancer. It comprises the four subscales (physical well-being, emotional well-being, social well-being and functional well-being) of the general measure (Functional Assessment of Cancer Therapy scale – General, 27 items), alongside the Breast Cancer Subscale (BCS, 10 items). Its relevance for use across both research and clinical settings has been confirmed through evidence of its validity, reliability (Cronbach's alpha 0.9) and sensitivity to change, first demonstrated by Brady and colleagues and since replicated across a breadth of contexts.[403-405]

The FACT-B Trial Outcomes Index (TOI) accounts for the BCS and the physical and functional well-being subscales. This is generally considered to be a valuable index of physical and functional domains and, since social and emotional outcomes are less likely to vary over shorter timeframes, is frequently applied in the clinical trial setting.[406] Given the relatively short timeframe of the LIBERATE studies, this was also an outcome of interest in this context.

Figure 7.1 Situating outcome measures in the Context, Mechanism, Outcome realist evaluation framework



7.4.6.2 EuroQoL-5D-5L (EQ-5D-5L)

The EQ-5D-5L is a standardised, self-report instrument developed by the EuroQol Group, providing a measure of health status across a range of health conditions and treatments. Each of the 5 dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) have 5 response levels, ranging from no problems to extreme problems, with a higher score relating to more perceived problems. A scale (EuroQol Visual Analogue Scale, EQ-VAS) is also included for patients to rate their health from 0 (the worst health you can imagine) to 100 (the best health you can imagine); the higher the rating, the better their perceived health.[407] This version of the questionnaire (EQ-5D-5L) has been shown to have significantly improved properties when compared to the shorter EQ-5D-3L, demonstrating greater discriminant validity, convergent validity and reduced ceiling effects.[408] Furthermore, this superiority has been further evidenced within the cancer context specifically.[409]

7.4.6.3 Brief version of the Cancer Behaviour Inventory (CBI-B)

This 14-item questionnaire is derived from the original 33-item CBI (CBI-L). It seeks to measure patients' self-efficacy for coping with cancer by asking them to rate their confidence to perform certain behaviours on a scale of 1 (not at all confident) to 9 (totally confident).[295, 410] Psychometric analysis of the CBI-B has shown a high level of internal consistency and validity, with scores positively correlated with QoL, coping and optimism, and negatively correlated with depression and the impact of sickness. Furthermore, the brief version is strongly correlated with the original CBI-L and has demonstrated adequate assessment of the core factors underling the process of coping, such as 'maintaining independence and positive attitude'.[410]

7.4.6.4 Self-Efficacy for Managing Chronic Disease Scale (SEMCD-6)

This 6-item scale measures self-efficacy to manage chronic disease, asking patients to rate their confidence in performing a range of self-management tasks on a scale of 1 ('not at all confident') to 10 ('totally confident').[411, 412] Overall, the scale encompasses a range of domains relevant to a breadth of chronic diseases, such as emotional functioning, symptom management and communicating with health professionals. Internal consistency has been demonstrated (Cronbach's alpha 0.88-0.95) amongst individuals with chronic disease, yet it has also been successfully applied within the cancer setting.[413, 414]

The scoring and analysis of these outcome measures will be discussed in detail in chapter 8.

7.4.7 Study methods

7.4.7.1 Ethics

Ethical approval for the outlined feasibility studies was granted by the Yorkshire and The Humber (Leeds East) Research Ethics Committee and the Health Research Authority.

7.4.7.2 Target sample size

On the advice of the ethics committee, in line with the research timeline, PhD context and what was considered to be a standard sample size for pilot and feasibility studies, the initial target sample size (of 84 participants, outlined in the study protocol) was reduced.

A formal sample size calculation was not appropriate for this small-scale feasibility evaluation.[415] Instead, a revised recruitment target for the main trial of 30 participants (15 per arm) was in line with Julious' statistical rule of thumb for determining the sample size of pilot studies. This rule states that 12 participants per group is justified on the basis of feasibility (12 per group permitting a range of block sizes in a parallel group trial design) and precision about the mean and variance.[416] The latter justification relates to the finding that, for small sample sizes, there is a marked gain in precision with each increase of 1 up to a sample size of 12. Beyond this, the gain in precision with increasing sample size is much less marked.[416, 417] Furthermore, a larger sample size is not justified given the trial's primary objective is to determine feasibility as opposed to efficacy. Recruiting further participants may also be judged unethical since they would be unnecessarily exposed to potential burden and the study itself would require additional resources beyond those needed to sufficiently determine feasibility.[418] The final recruitment target of 30 (15 per arm) accounts for the high rate of attrition widely encountered in trials of e-health interventions.[419, 420]

For the single arm sub-study, a target sample of 15 was also set. However, given its exploratory nature, a convenience approach to sampling was deemed appropriate.

7.4.7.3 Eligibility criteria

Across both studies, participants were targeted for recruitment according to the eligibility criteria outlined in Table 7.6 below.

Table 7.6 Study participant eligibility criteria

	RCT (clinically integrated)	Sub-study (independent monitoring)
Inclusion Criteria	✓Adult females (aged 18 and over).	
	✓ Clinically confirmed diagnosis of SBC.	✓Self-reported diagnosis of SBC.
	✓Accessing care/follow-up within LTHT (St James's University hospital).	✓Accessing care/follow up outside of LTHT
	✓Have access to the internet.	
	✓Able and willing to take part, following informed consent.	
	✓Able to read and understand English.	
Exclusion criteria	× Exhibiting signs of overt psychopathology or cognitive dysfunction.	
	× Current involvement in other clinical trials involving completion of QoL or other patient reported outcome measures.	

7.4.7.4 Recruitment & study procedures: RCT

(i) Identifying & approaching potential participants

Participants were recruited from breast oncology outpatient clinics at St James's University Hospital. A member of the clinical team (GV) screened clinic lists in order to identify those eligible to participate. An appropriate health professional (the patient's assigned clinician or a member of the clinic's nursing team) sought patients' permission for the researcher to approach them, in order to explain the study and to provide them with a participant information sheet (PIS). Initially, this interaction was planned to be face-to-face, immediately following the patient's appointment. Patients could then choose to consent at this point in clinic, to opt to take more time to consider their decision, or to decline participation.

In light of the restrictions and additional safety measures in place due to the ongoing COVID-19 pandemic, study procedures were modified (in line with ethical approvals in place). The PIS was attached to all eligible patients' clinic documentation ahead of their appointment. Their clinician then asked if they would be interested in finding out more about the study. If so, they were provided with the PIS and their permission was sought for the researcher to follow up with them via telephone, several days after their appointment, minimising close contact and giving them the opportunity to consider whether they would like to participate.

A study note was added to all eligible patients' clinic documentation and clinicians were asked to indicate whether patients were happy to consider taking part and receive a follow-up phone call. For those who declined to participate, clinicians were asked to indicate any reason provided. The researcher was also present in all clinics to greet those who had expressed an interest, briefly introduce the study and arrange a suitable time for telephone follow up. If interested, they were provided with baseline documentation (consent form, sociodemographic questionnaire, baseline outcome questionnaire booklet and a stamped addressed envelope) to

take away with them and to discuss during their upcoming telephone call. If the researcher did not have the opportunity to meet the patient before they left clinic, they checked with the clinician (or via the attached study note) that permission for telephone follow up had been given and contacted them several days later. Baseline documentation was subsequently posted to the participant.

(ii) Informed consent

Prospective participants were provided with the PIS which detailed all aspects of study participation, as well as an additional information sheet providing further detail relating to data collection, use and storage (in line with General Data Protection Requirements, GDPR 2018).[421] They were encouraged to take as much time as they needed to consider this information and to ask any questions they had.

For those who had the opportunity to read through the consent form ahead of telephone follow-up, they were offered the choice of providing verbal consent (following the University of Leeds protocol for verbal consent).[422] In these instances, the researcher answered any questions the participant had before reading through the consent form and asking them to confirm whether they agreed with each statement. This was documented using an encrypted audio-recorder and a copy of the completed consent form (initialled and signed on their behalf) was sent to the participant. Where participants had not read the consent form ahead of telephone follow-up, or preferred to provide written consent, they also had the opportunity to have any questions answered before completing and returning the form alongside the baseline questionnaires, using a stamped, addressed envelope provided.

For several patients who requested to consent in clinic, this was facilitated following both national and trust-level guidance for social distancing, with both the researcher and the patient wearing the appropriate personal protective equipment (PPE).

(iii) Study arm allocation

Using the freely available, specially designed online minimisation software 'QMinim',[398] LIBERATE participants were randomly allocated, at a ratio of 1:1, to either the intervention arm or the waiting list control arm on the basis of the factors outlined below.

- Age: 50< and 50≥
- Diagnosis: newly diagnosed (<12 months) vs longer term diagnosis (≥12 months).

Minimisation did not account for treatment group, since it was unlikely that sufficient numbers would be achieved across all strata within the available timeframe and with the intended recruitment target. Furthermore, on the basis of the above factors alone, it was anticipated

that women across diverse treatment pathways would be sampled. The researcher performed random allocation prior to receiving the participants baseline questionnaires.

On completion of the consent form and baseline questionnaires, the participant was informed of their study allocation via their preferred means of contact.

7.4.7.5 Recruitment & study procedures: Sub-study

(i) Identifying & approaching participants

Women were recruited from across the UK to the sub-study of the independent monitoring LIBERATE intervention via Breast Cancer Now's and Breast Cancer Haven's online channels. These included social media platforms, dedicated sections of their websites and forums accessed by women living with SBC. A recruitment advert was shared, giving a brief overview of the study and directing those interested to contact the researcher via email. The researcher responded to all interested potential participants, attaching copies of the PIS and the additional (GDPR) information sheet. For those confirming their interest at this stage, a suitable date and time was arranged for a recruitment telephone call, during which the study was explained in further detail and participants had the opportunity to ask any questions.

(ii) Informed consent

Verbal consent was recorded as per the approved procedure outlined above.

Figure 7.2 displays both studies running in parallel, within the overall feasibility evaluation.

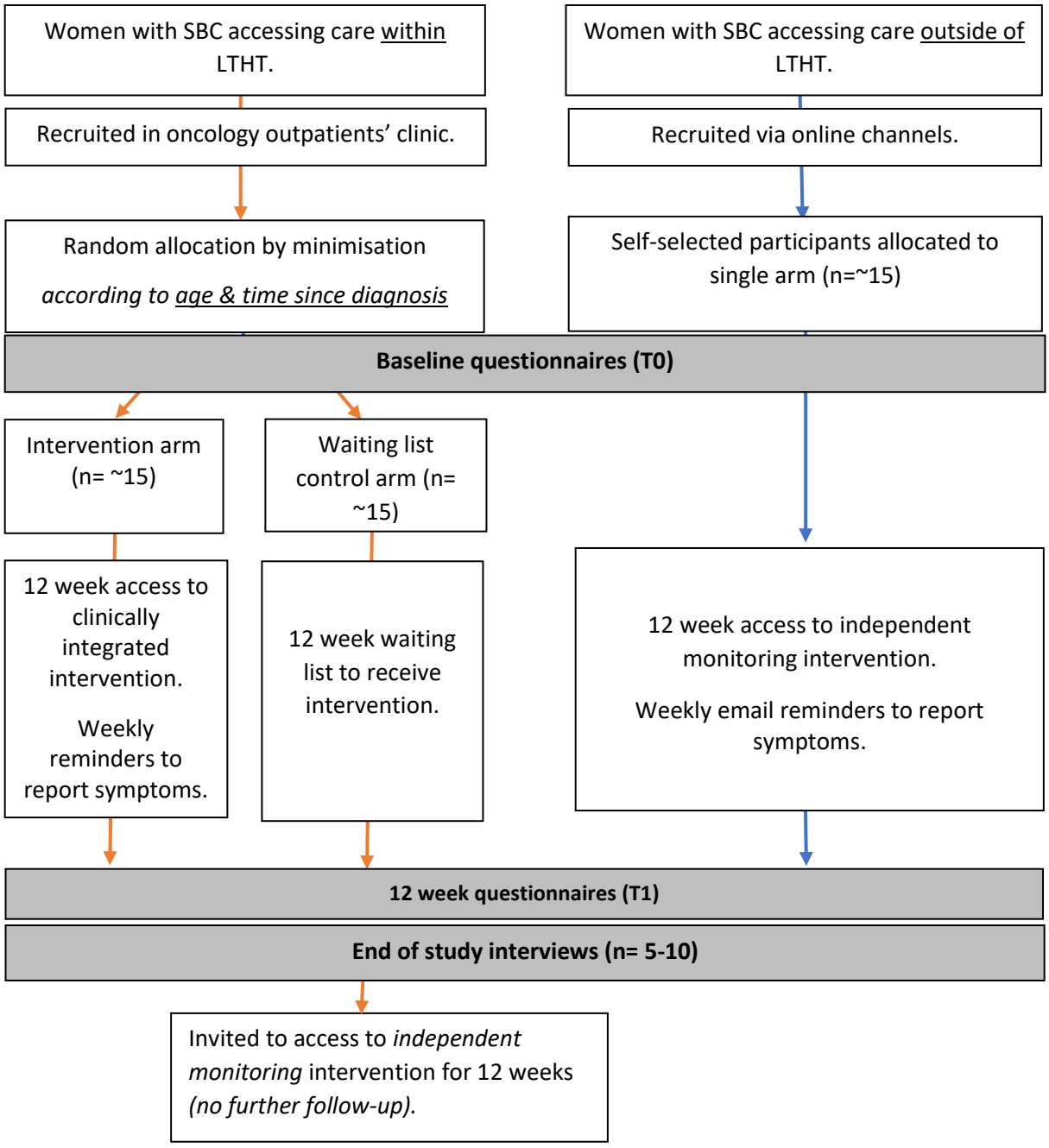
7.4.7.6 Data collection & outcome assessment

Both studies gathered clinical and sociodemographic (including computer usage, breast cancer history, SBC diagnosis and treatment, and general health) data at baseline. For RCT participants this was collected (with their prior consent) from their EPR. For sub-study participants, self-reported information was gathered during the initial recruitment telephone call. All participants completed PROMs (FACT-B, EQ-5D-5L, CBI-B and SEMCD) via a paper-based questionnaire booklet at baseline (T0) and 12 weeks (T1, end of intervention period). For intervention arm (RCT) and sub-study participants, there was also an end of study feedback questionnaire to complete at 12 weeks.

A selection of participants from across both studies were interviewed at the end of the study period to further explore feasibility and acceptability of the intervention and methods of evaluation. A selection of health professionals involved in supporting the recruitment and review of participants trialling the clinically integrated intervention were also interviewed. Their involvement was intended to provide additional contextual insights relating to the feasibility of both study methods and intervention delivery. Written informed consent was

obtained from participating health professionals. Semi-structured interviews were conducted via telephone or Microsoft Teams video conferencing software, guided by interview schedules tailored to each group (RCT participants, sub-study participants and health professionals). The researcher transcribed all interviews verbatim and the resulting data sets were managed using NVivo software. Thematic analysis was then conducted and themes were identified and interpreted in the context of the surrounding data. As with the first phase of research, a reflexive approach to thematic analysis was applied from a critical realist perspective, with codes identified and themes generated inductively from the data set. In this way, this qualitative research sought to describe a reality which is reflected in the data itself.[177, 183]

Figure 7.2 The LIBERATE Feasibility Evaluation: RCT and single arm sub-study



7.4.7.7 Intervention training

For those allocated to the intervention arm of the RCT, and for all sub-study participants, a suitable date and time was arranged for a brief demonstration to be conducted via telephone (unless clinic-based participants preferred a face-to-face demonstration, following the necessary safety measures). This involved a run-through of the LIBERATE website features and completion of symptom monitoring questionnaires via QTool. Participants were then provided with their personal login details and a user guide to refer to. If preferable, brief instructions, login details and the user guide were sent via email. Participants were encouraged to contact the researcher if they encountered any issues.

Training for those clinicians who would be reviewing participants was initially planned. Due to the COVID-19 restrictions and the increased work pressures for health professionals, this was not possible. Brief instructions detailing how and where to access results were instead attached to all intervention participants' clinic notes, at each of their appointments, and the researcher was present in all clinics to provide any additional support and reminders.

7.4.7.8 Intervention delivery

(i) Intervention arm

Participants were able to freely access all components of the LIBERATE website from home. They were reminded via email to complete a symptom monitoring report each week (though there was no restriction on the number of reports patients were able to complete) over the 12 weeks.

(ii) Waiting list control arm

The waiting list control arm continued to receive care as usual, with routine follow up, support and treatment (though an increasing amount of follow-up was conducted via telephone due to COVID-19 and, for some women, treatment was disrupted). The frequency of their appointments with health professionals was dependent on their current treatment regime and the status of their disease.

At the end of the waiting list period, these participants were then provided with access to the intervention in its independent monitoring form, alongside a user guide and instructions for use (as well as the offer of a demonstration via telephone). They were free to use the intervention as much or as little as they liked over a period of 12 weeks and the researcher was available to provide any technical support. However, due to timing and funding constraints, there was no further follow up of these participants.

(iii) Risk of contamination between trial arms

To safeguard against contamination between the intervention and waiting list control arms of the main trial, at the time of study entry, the intervention was only made available to those in the intervention group. The risks of contamination was emphasised during patients' training and they were asked not to share the resource with others, who may or may not be involved with the LIBERATE feasibility evaluation, for the duration of the study.

(iv) Sub-study (independent monitoring group)

The LIBERATE website was freely available to all sub-study participants. They also received email reminders to complete weekly symptom monitoring questionnaires, though without clinical integration or review. These participants instead had the option of reporting for self-monitoring purposes and the ability to print and discuss with their healthcare professionals (e.g. GP, Clinical Nurse Specialist etc.) as they wished.

7.4.8 Reflections

Methodologically, there are weaknesses in the design of each of the individual studies. The absence of any form of blinding in the RCT, for example, risks introducing a range of biases, whilst the lack of a control arm in the single arm sub-study compromises internal validity. Both of these factors would cast doubt on any definitive determinations of efficacy. However, the evaluation of efficacy is not the overarching aim in the feasibility setting. Collectively, the studies offer methodological strength in the range of design features and feasibility outcomes which they are able to assess, supporting a realist evaluation centred not only on the intervention, but also on the contextual factors and causal mechanisms in which it is embedded.

When it came to implementing these study designs, a range of challenges to recruitment were encountered. These were largely as a result of the ongoing COVID-19 pandemic and the impact this had on both health service delivery and research activity. Following significant delays, the researcher was able to adapt to the circumstances, modifying study procedures as necessary whilst remaining within the bounds of the ethical approvals in place. This was largely iterative and guided by the evolving circumstances and the participants themselves. As with the usability testing stage, the researcher was aware of the significant additional personal and health related stresses that women may have been experiencing in the context of COVID-19, as well as concerns surrounding their own safety. Great care was therefore taken to ensure that the research posed the minimum possible burden to participants, and that they were made to feel safe and comfortable. For example, where possible, recruitment was conducted over the telephone and, later in the recruitment pathway, written website 'demonstrations'

were offered via email rather than scheduling in an additional phone call. This was readily accepted by many of the participants, particularly those working and those who felt confident in the use of computers and technology. This suggests that such remote methods could and should be offered, even in the absence of COVID-19.

Significant barriers to communication in clinic made it difficult to build a rapport, demonstrate the website or discuss the study in detail. These related to the necessary PPE and social distancing requirements, as well as the added anxieties of the patients, clinical teams and researchers alike.

Undoubtedly, these wider contextual factors, as well as the challenges and learning points encountered during recruitment, represented vital considerations to be taken forwards in the analysis and interpretation of results.

7.4.9 Summary

This section has outlined the study designs applied as part of a multi-faceted approach to the feasibility evaluation of the LIBERATE intervention.

Harnessing the methods and design features discussed, and incorporating the results of initial usability testing, these studies set out to explore the feasibility and acceptability of the intervention across contexts. Outcome measures were chosen in line with the intervention's underlying theory and justified with reference to both the wider context and proposed causal mechanisms. Applying a mixed-method approach, both studies were designed to gather a range of qualitative and quantitative data, the analysis and interpretation of which will be discussed in the next chapter.

Chapter 8: Feasibility Evaluation (I) - quantitative analysis & results

8.1 Chapter overview

The results of feasibility studies are crucial to the onward trajectory of complex interventions, allowing researchers to determine the appropriateness of progressing to future pilot studies. Furthermore, the application of feasibility findings is essential to guide any further intervention development or refinement of evaluation methods, with the goal of ensuring that intervention efficacy can be both assessed and achieved on a larger scale.[423]

With this in the mind, this chapter will outline the steps taken as part of a mixed-methods approach to analysing the feasibility of the LIBERATE intervention. The results of these analyses will be presented and explored in order to determine the feasibility and acceptability of the intervention, as well as the methods for its evaluation across contexts. Across the following two chapters, qualitative and quantitative results from both strands of the evaluation will be integrated and interpreted, drawing on earlier hypothesised programme theory, to guide the development of robust, evidence-based recommendations for potential future further evaluation and implementation.

8.2 Chapter aims

- To outline the analysis conducted to achieve the identified aims and objectives.
- To present the results of quantitative analysis across the contexts of clinical integration and independent monitoring.
- To recommend outcome measures and explore the potential for efficacy in line with the proposed programme theory.

8.3 Analysis

As outlined in chapter 7, the aims and objectives for the LIBERATE feasibility evaluation were achieved through a mixed-method approach, centred upon a range of primary and secondary endpoints. These encompassed the feasibility of recruitment strategies and methods of evaluation, as well as the feasibility of the intervention itself, across clinically integrated (RCT) and independent monitoring (online sub-study) contexts. For the purposes of this chapter, quantitative results gathered from both feasibility studies will be analysed and presented in parallel for ease of comparison and to aid integration. Qualitative data, which sought to draw out collective perspectives from participants across study settings, will be analysed and presented in chapter 9.

8.3.1 Endpoints

8.3.1.1 Recruitment, follow-up and attrition

The feasibility of recruitment strategies was assessed through indicators of recruitment, follow up and attrition across both study settings. A consort diagram mapped the progression of participants from identification to study completion. Recruitment and attrition rates were calculated and, for the RCT, compared across study arms.

(i) Withdrawals and non-return of outcome questionnaires

Study completion was defined by the return of both baseline and 12 week outcome questionnaires, alongside completion of at least 1 online symptom monitoring questionnaire (for those in the intervention arm of the RCT and all sub-study participants). Across both studies, missing data was defined as the number of questionnaires not returned by consenting participants at baseline and 12 weeks. Missing data was further classified as the proportion of missing items within outcome questionnaires.

(ii) Sociodemographic, computer usage and clinical data

Sociodemographic, computer usage and clinical characteristics were compared for completers versus non-completers to explore potential reasons for attrition or non-usage. Baseline characteristics of all participants were also analysed to determine the balance of samples achieved through the varying recruitment strategies (and through use of minimisation randomisation in the RCT).

8.3.1.2 Intervention engagement: symptom monitoring questionnaire completion

The feasibility of the intervention itself was assessed through a range of indicators of participant engagement, largely centred upon the completion of symptom monitoring questionnaires.

(i) Compliance

Participants allocated to the intervention were asked to complete a minimum of 1 symptom monitoring questionnaire per week. Given the known heterogeneity across this disease group, it was anticipated that this rate may be too frequent (or, indeed, too infrequent), depending on participants' current disease status and factors relating to treatment (e.g. treatment type, length of time on treatment, point in treatment cycle). The feasibility of this specified frequency, in terms of both intervention delivery and study design, was therefore assessed. A compliance score was calculated (n/12 where n = number of actual completions and 12 = expected number of completions), providing a key indicator of engagement with this core component of the intervention. A compliance score of 1 therefore equated to weekly completions over the course of 12 weeks.

(ii) Alerts & algorithms

The number and frequency of clinician (RCT) or on screen (sub-study) alerts generated, as well as the proportions of algorithms activated (A, B, C and D), were calculated and compared across studies.

(iii) Symptoms reported

The types, frequency and severity of symptoms were analysed by treatment group (A: Monoclonal Antibodies (MABs) +/- chemotherapy and B: hormone therapy +/- targeted therapy) within and between studies.

8.3.1.3 Intervention engagement: website analytics

Website analytics data was also gathered and analysed to assess engagement with the wider LIBERATE intervention. This was supplemented by qualitative data (gathered across end of study interviews and written end of study feedback), guiding the overall assessment of engagement and acceptability. These qualitative insights are reported in chapter 9.

8.3.1.4 Intervention delivery: clinical process measures

For the RCT, a range of clinical process measures were collected across study arms by assessing participants' electronic medical records within Patient Pathway Manager (PPM). These measures provided insight into the feasibility of delivering LIBERATE as a clinically integrated intervention and any associated impact on cancer service delivery and health professional workload. Over the 12 week trial period, the number of additional contacts outside of routine scheduled appointments were counted for each participant. A distinction was made between 'contacts outside of consultation' and 'attendances outside of consultation'. Contacts outside of consultation referred to any telephone, email or (non-routine) face-to-face contact participants had with their nurse, doctor or other (secondary care based) health professional in addition to and outside of their regular follow up appointments. These were further categorised according to whether the contact was initiated by the participant themselves, or by their health professional. Additionally, attendances outside of the consultation referred to hospital admissions, visits to the acute oncology assessment unit, non-routine (urgent re-staging) scans and other (non-oncology) hospital appointments. Routine scheduled (telephone and face-to-face) appointments were also counted, to give an overall picture of participants' healthcare activity. All of these were compared between intervention and control groups.

8.3.1.5 Integrity of intervention and study procedures

The integrity and functionality of the LIBERATE and QTool websites was assessed through a log of reported issues recorded across the study period, as well as end of study questionnaire data relating to usability. The integrity of study procedures (protocol & data collection forms) was

explored by assessing documented deviations from the planned study procedures, alongside the amount and type of missing data. Qualitative data on the time taken to complete data collection forms and the acceptability of study procedures was also gathered through end of study interviews and questionnaires (as reported in chapter 9).

8.3.1.6 Outcome scores

Both study designs incorporated pre-test, post-test measures in order to determine the feasibility and acceptability of the methods and means of data collection, as well as to guide the selection of appropriate outcome measures for any future larger-scale evaluation. Scores for all 4 outcome measures (described in chapter 7) were computed in accordance with scoring guidelines and analysed descriptively, exploring their range and change over time.

(i) FACT-B

For the FACT-B questionnaire, scores are calculated for each of the four subscales (physical well-being, emotional well-being, social well-being and functional well-being) of the general measure (Functional Assessment of Cancer Therapy scale – General), alongside the Breast Cancer Subscale (BCS). Scores for the FACT-G subscale are combined with the 'additional concerns' (BCS) to give an overall score, with higher scores reflecting better QoL.[406] Where answers are missing, an overall prorated subscale is calculated using the following:

[Sum of question scores] x [No. questions in subscale] ÷ [No. questions answered]

For this prorated score to be considered valid, it is specified that >50% of questions in each subscale (equating to a minimum of 4 of 7 questions) must be answered. All subscales must be valid for the overall score to be considered valid. The administration and scoring guideline also specifies that an overall raw response rate of 80% for the whole questionnaire (equating to 22/27 questions) is needed.[406]

(ii) EQ-5D-5L

For the EQ-5D-5L, results are displayed as a simple descriptive profile and a single index value.[424] Participants were asked to rate the various dimensions of health by placing a tick in the box next the corresponding level. Level 1 is coded as '1', level 2 as '2' etc. For the purposes of this small-scale study, analysis of EQ-5D-5L outcome data was descriptive, providing an overview of the percentage of participants reporting levels 1 (no problems) to 5 (extreme problems) for each of the subscales, giving an overall descriptive profile. For the EQ-VAS scale, participants were asked to rate their health by placing a cross on a 20cm long horizontal line (labelled 0-100) and to write the corresponding number in a box. The higher the rating, the better their perceived health. All missing answers are left blank. Where there are multiple or ambiguous answers for a particular dimension, this data is classed as missing. In the case of a

discrepancy between the number written in the box and where the 'X' has been placed on the EQ-VAS, the number in the box is used.[424]

(iii) CBI-B

The CBI-B is a single score measure with higher scores indicative of greater self-efficacy.[410] As the overall score is taken as the sum of individual items, any missing item may provide a misleading, underestimated total score in that missing items are taken to be zero. However, the CBI-B scoring manual does not outline specific instructions for the handling of missing data. Processes established and trialled within the eRAPID RCT were therefore followed.[425] If a participant answered >50% of the items (i.e. 8/14), the score was taken as the mean value of the items answered. As researchers highlighted in the previous programme of work, this method is not without its limitations. Indeed, imputation using the mean value does not account for variability in participants' responses. In light of this being a small-scale, largely exploratory study, and in the absence of instructions for missing data, this method is felt to be acceptable.

(iv) SEMCD-6

For the SEMCD-6, a final score is calculated as a mean of the 6 items (each scored from 1-10), with higher scores indicating greater self-efficacy.[412] Where scores for more than 2 of the 6 items are missing, the scale should not be scored. In the case of multiple response options being circled, the lowest response (equating to lower self-efficacy) should be taken.[411]

(v) Floor & ceiling effects

Floor and ceiling effects were also assessed for, in order to determine the ability of each individual measure to adequately distinguish between participants scoring at the highest and lowest ends of the scale.[426] A ceiling effect is defined as a high proportion of participants scoring at the maximum level for a scale or measurement, whilst a floor effect describes a large proportion of participants scoring at the lowest possible level.[427, 428] Across studies exploring psychometric properties of PROMs applied in wider fields of health, this proportion is usually set at ≥15%.[428-431] The presence of floor and ceiling effects is a limitation since these suggest that a measure cannot discriminate, or accurately assess, highest functioning or lowest functioning individuals.[428, 429]

For the EQ-5D-5L, the presence of floor and ceiling effects were assessed for within each individual dimension and for the overall measure across timepoints. In line with the methods of Greene et al, a ceiling effect was defined as any participant scoring 1 (i.e. reporting no problems) in a particular dimension, whilst an overall ceiling effect referred to a participant scoring 1 across 5 dimensions. A floor effect was defined as being present where participants

scored 5 (i.e. reporting extreme problems) in a particular dimension or (overall) across all five dimensions.[432]

(vi) Estimates of effect size

For the RCT, estimations of intervention effect size for QoL and self-efficacy were calculated to further support the selection of an appropriate measure, providing insight into the strength and direction of the relationship between intervention use and these variables.[433] Mean change scores for each of the measures were also calculated (i.e. the mean of the pre-test, post-test difference for each group). Using the formula below, estimates of effect size based on the standardised difference between groups were calculated.

$$[\text{Mean change score}_{I}] - [\text{Mean change score}_{WL}] \,/\, \text{pooled Standard Deviation}$$

Following calculation of the standard error, 95% confidence intervals were constructed for each effect size.

8.3.2 Data validation

The accuracy of data input and scoring from across a random selection of all 4 outcome questionnaires was self-validated by the researcher (20% of baseline and 20% of 12 week questionnaire data for both RCT and sub-study participants). From this, very little error was detected, hence further independent validation was not conducted. Validation of data collected for the purpose of evaluating clinical process measures was also performed by the researcher. As data was collected across two stages (following an iterative approach to analysis and in response to emerging results), this presented an opportunity for in-depth validation, during which there were few instances of error. Queries relating to the definitions and categorisations of data, e.g. 'number of additional contacts', were discussed and agreed with the wider research team, supporting validation and ensuring accurate and consistent measurement.

8.3.3 Statistical analysis

In keeping with the aims, scale and power of the studies, analysis of quantitative data was descriptive and explorative, guiding the assessment of feasibility and looking to inform future inferential statistical methods to be applied within a larger scale setting.

All statistical analysis was conducted using SPSS v.26. Descriptive data is presented using cross-tabulations, comparing between study arms (RCT) and across studies. Frequencies, means, medians and standard deviations are reported to 1 decimal place, whilst effect sizes and confidence intervals are reported to 2 decimal places.

8.4 Results

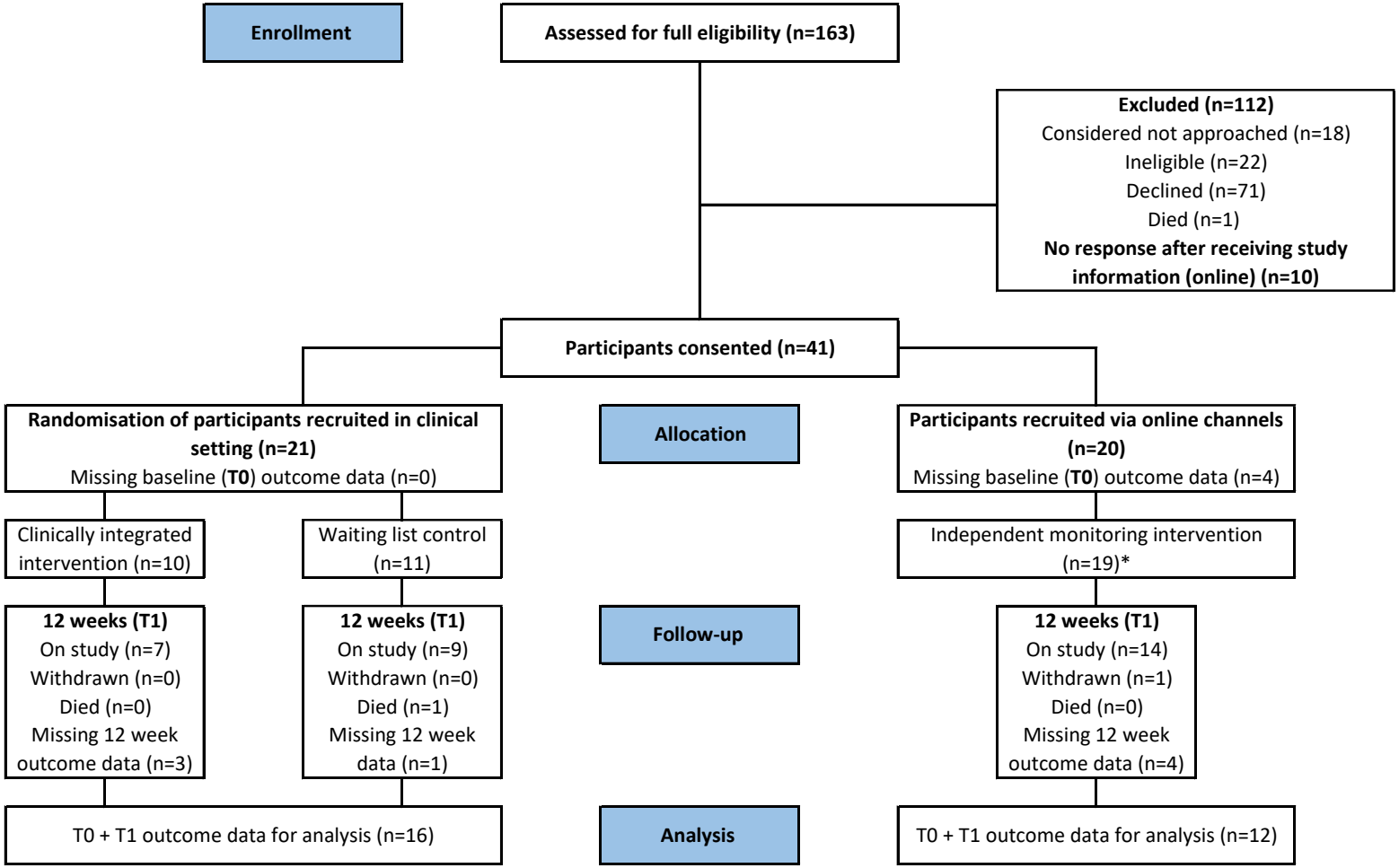
8.4.1 Recruitment, follow-up and attrition

The CONSORT diagram (Figure 8.1) displays the processes of screening and recruitment across both feasibility studies in full.

Recruitment to the LIBERATE feasibility RCT was conducted from 3rd August – 9th December 2020 within breast oncology outpatient clinics at St James's University Hospital.

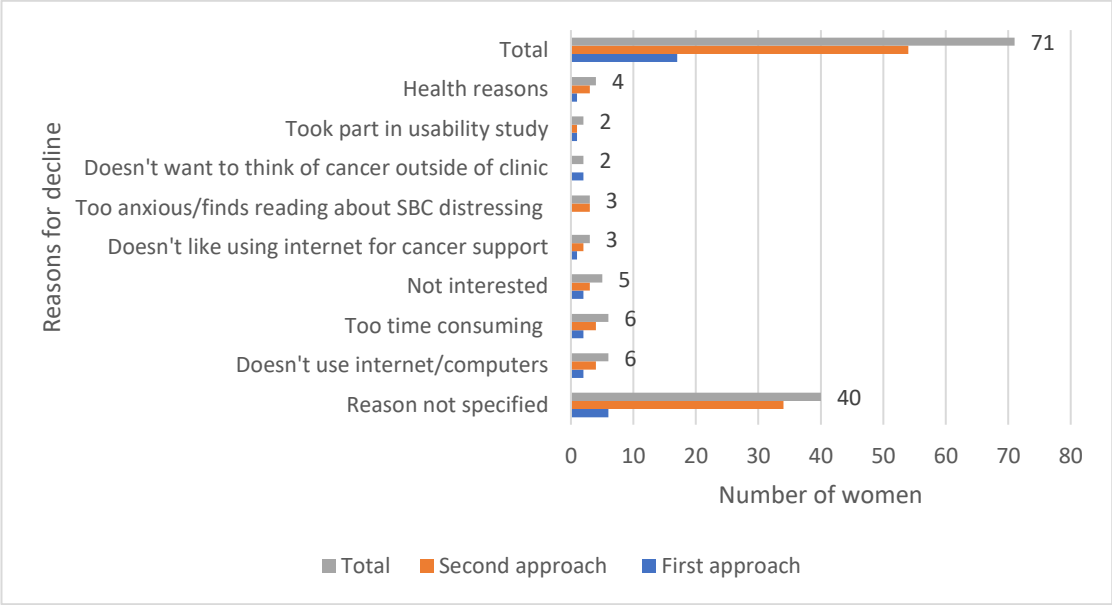
Over the recruitment period, 133 women were identified as potentially eligible. Of these, 95 were confirmed as eligible and were approached. A total of 71 women declined to participate due to the reasons highlighted in Figure 8.2 (though, of significance, 56.3% of those declining did not provide a reason). For those who did provide a reason, this was most frequently due to not using the internet or computers and concerns relating to the time burden of participation.

Figure 8.1 CONSORT diagram of recruitment and study involvement: LIBERATE feasibility RCT & sub-study



**n=1 participant consented but did not return baseline questionnaires or progress to intervention uptake.*

Figure 8.2 LIBERATE feasibility RCT: Number and reasons for decline



'Second approach' relates to women who took study information away for further consideration but went on to decline at subsequent follow-up.

In total, 21 women were consented and recruited, giving an overall recruitment rate of 22.6%. This equated to 70.0% of the original recruitment target (30). The rate of recruitment (Figure 8.3) was closely monitored on a month by month basis and continued to remain below the anticipated level. Recruitment was therefore extended beyond the initially proposed 16 weeks. The challenges encountered across this period were likely to be reflective of the rising COVID-19 cases and reduced face-to-face contacts in the clinical setting. The final participant was recruited and consented on the 7th December 2020, completing the 12 week study period on the 1st March 2021. Figure 8.1 displays all patients who were identified and approached, subsequently consenting or declining, as well as those deemed ineligible or considered but not approached.

Figure 8.3 LIBERATE feasibility RCT: Rate of recruitment

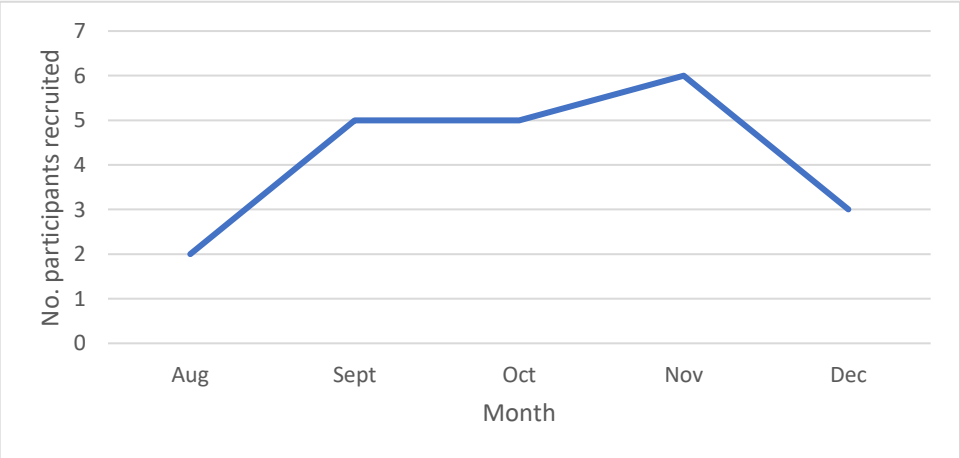


Table 8.1 highlights the balance which was achieved (through use of the specialist software, QMinim)[398] across both of the RCT study arms for the selected co-variates of diagnosis and age. Overall, 10 participants were allocated to the intervention group and 11 to the waiting list control group.

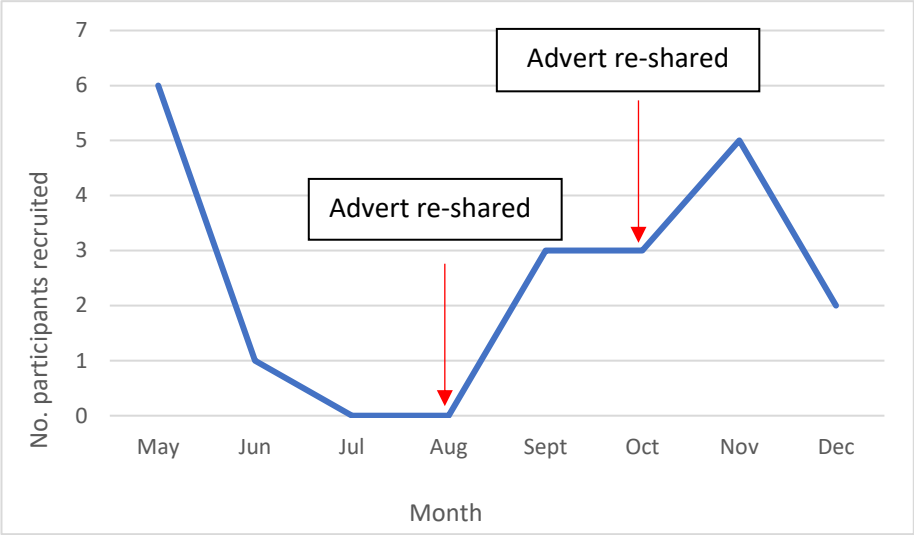
Table 8.1 Randomised study arm allocation using minimisation: balance across groups

	Diagnosis		Age		Total
	12m or less	>12m	50 and over	Under 50	
Intervention	3	7	7	3	10
Control	4	7	8	3	11
Total	7	14	15	6	21

Whilst all NHS based recruitment activity was on hold during early summer 2020 due the COVID-19 pandemic, the remote, single arm sub-study had the approvals and means to continue, therefore commencing recruitment earlier than the RCT. Online recruitment was conducted between 19th May – 6th December 2020. The recruitment advert was shared via a number of Breast Cancer Now's online channels (including the 'Voices' email newsletter, SBC forum and research forum) and on the Breast Cancer Haven website. The wider research team also shared the recruitment advert via Twitter and it later featured on the NIHR's 'Be Part of Research' website. All participants reported encountering the study via the Breast Cancer Now forums or the 'Voices' email newsletter.

After an initially high rate of recruitment (Figure 8.4), interest slowed in subsequent months. In response, the advert was re-shared on Breast Cancer Now forums (this time within a more general SBC private group, as well as the forum specific to research and studies) generating further interest. Once the original target of 15 participants was achieved, the decision was made to exceed this figure in order to supplement the lower rate of recruitment of the RCT running in parallel. Recruitment was therefore extended until the point at which the RCT closed to recruitment. The final participant was recruited on the 4th of December 2020, completing the 12 week study period on the 26th February 2021. In total, 20 of the 30 women who expressed an interest in the research consented to take part, giving an overall recruitment rate of 67%. Notably, this was 3 times the recruitment rate achieved in the clinical setting and 33% above the original recruitment target (15).

Figure 8.4 LIBERATE feasibility sub-study: Rate of recruitment



Online recruitment seems to have been most successful when conducted via more interactive means, such as the forums and email newsletter (as opposed to the study being advertised on static webpages) and when reaching out to a broader range of women, targeting those who may encounter the recruitment advert incidentally, as well as those actively seeking out research.

8.4.2 Withdrawals and non-return of outcome questionnaires

Of the 21 women consented to the RCT, 23.8% (n=5) did not complete the trial. Of these 'non-completers', one participant (allocated to the waiting list control arm) died during the course of the study, whilst the remaining four (n=3 intervention arm, n=1 waiting list control arm) did not return the 12 week outcome questionnaires. In addition to missing outcome measure data, those in the intervention arm did not complete any symptom monitoring questionnaires at any point over the 12 weeks, potentially suggesting informal withdrawal. This will be explored further as part of the analysis of intervention engagement (section 8.4.4).

Comparing between study arms, the rate of attrition was higher for the intervention group (30%) than the waiting list control group (18.2%), but it was still in line with the anticipated rate (20-30%) widely predicted for trials of online interventions.[419]

Of the 20 women who consented to take part in the sub-study, 14 returned the 12 week outcome questionnaires, giving an overall attrition rate of 30%. Full study completion status was only achieved by 12 participants overall, although data was available for n=16 at T0 and n=14 at T1.

For those participants who did not achieve full sub-study completion status (n=8), this was due to a number of different reasons. One participant was lost to follow-up; baseline

questionnaires were not returned following the initial recruitment telephone call and they did not respond to an email reminder. For several women (n=3), baseline questionnaires were not received, though they reported having posted them and requested further instructions for progressing onto the next stage of the trial (website demonstration and personal login details). This was suspected to be due to postal or delivery issues, given the questionnaires were posted to the hospital during the height of the pandemic. These 3 women proceeded with the trial and 12 week questionnaires were received for 2, whilst the other participant (despite completing regular online symptom monitoring questionnaires) did not return the 12 week questionnaires or respond to an email reminder. Non-return of 12 week questionnaires was also the case for 3 other participants, who had otherwise completed all other aspects of the study. The final participant who did not achieve full completion status withdrew formally due to difficult personal circumstances. The researcher therefore felt that it was not appropriate to ask them to complete a withdrawal feedback form. The participant did, however, provide feedback within an email, alongside consent for this used in any subsequent analysis.

As the sociodemographic questionnaires were returned by post, those missing baseline outcome measure questionnaires were also missing this data (though date of birth was provided by all participants). Where available, the clinical, sociodemographic and computer usage characteristics of those completing versus those not completing the study were compared.

8.4.2.1 Comparing characteristics: completers vs non-completers

Within the RCT, descriptive data for sociodemographic characteristics generally highlighted similarities across 'completer' (n=16/21) and 'non-completer' (n=5/21) subgroups, with no notable differences in age, ethnicity, marital status or level of educational attainment. A higher proportion of non-completers (60%) reported living alone, with one of these participants also identifying as a carer. All non-completers were retired or unable to work, whilst some women with full completion status worked full time (12.5%, n=2), were studying (6.3%, n=1) or currently looking for work (6.3%, n=1). Most women reported daily computer use, though 40% of non-completers (n=2) reported less regular, weekly use and one participant who completed the trial cited infrequent, monthly use at baseline. Notably, just one of the non-completers reported using the internet to access health information (compared to 93.8% of completers, n=15). Furthermore, the non-completers generally appeared to have received their breast cancer diagnoses over a shorter trajectory; the mean time between primary and secondary diagnoses was much shorter (2.8 years, SD 1.0) when compared to the completers (8.9 years, 7.0). Several of the completers had, however, received a de novo diagnosis (2/16, 12.5%). Progression was generally more widespread (with lymphatic involvement and metastases diagnosed across a wider range of sites) for the completers.

For the sub-study, completion status was defined by the return of the 12 week questionnaire alone, due to the noted postal difficulties resulting in some baseline questionnaires not being received. Of n=14/20 who completed 12 week questionnaires, n=3 were missing baseline and sociodemographic data. For the n=6/20 who did not complete 12 week questionnaires, n=1 was missing baseline and sociodemographic data.

Few differences were evident when comparing the sociodemographic characteristics by completion status within the sub-study, though a higher proportion of the non-completers were unable to work due to ill health (40% vs 27.3% for completers) or retired (40% vs 18.2%). Notably, the latter may have encompassed ill health retirement. The mean age was largely similar, though the range of ages was lower for those not completing (with a maximum age of 56 compared to 72 in the completers group). Notably, a higher proportion of non-completers reported using the internet for health information (100% vs 81.8%). Comparing across baseline clinical data, a substantial proportion (35.7%, n=5) of completers had been diagnosed as de novo metastatic, whilst 100% of those missing 12 week data received a primary diagnosis. For those who had experienced primary breast cancer, mean time to secondary diagnosis was similar for completers (6.23 years, SD 5.5) versus non-completers (7.4 years, SD 6.2 years). Little difference was observed in the extent and sites of metastasis, though those completing were more recently diagnosed (57.1%, n=8 ≤ 12 months) than those not completing (66.7%, n=4 > 12 months).

8.4.3 Baseline characteristics: all participants

8.4.3.1 Sociodemographic & computer usage characteristics

As displayed within Table 8.2, for the RCT, the intervention and waiting list control groups varied little across sociodemographic characteristics. The mean age for the overall sample was 59.8 years (SD 12.7) and the vast majority of women were white (95.2%) and married or in a civil partnership (61.9%). A higher proportion of women in the waiting list control group were unable to work due to their health (36.4%), whilst the intervention group were predominantly retired (70%, though this may have included participants who had retired due to ill health). Overall, the sample was highly educated, with most women (90.4%) educated beyond school leaving age, 71.4% of whom also had a degree or professional qualification. Just two women across the whole sample identified as carers and the majority (81%) did not live with children under the age of 18 (likely due to the average age of the sample).

Table 8.2 Baseline sociodemographic characteristics: comparing across studies

	RCT						*Sub-study*	
	Intervention (n=10)		**Waiting list (n=11)**		**Overall group (n=21)**		**Single arm (n=16)§**	
Age							(n=20)	
Mean (SD)	60.4 (13.5)		59.3 (12.5)		**59.8** (12.7)		**51.5** (8.6)	
Range	34.0		32.0		36.0		36.0	
Min, max	40, 74		44, 76		40, 76		37, 73	
	N	**%**	**n**	**%**	**n**	**%**	**N**	**%**
Ethnicity								
Black/Black British	0	0.0	1	9.1	1	4.8	1	6.3
White	10	100.0	10	90.9	20	**95.2**	15	**93.8**
Marital status								
Married/civil partnership	6	60.0	7	63.6	13	61.9	10	**62.5**
Cohabiting	1	10.0	1	9.1	2	9.5	3	18.8
Single	3	30.0	1	9.1	4	19.0	2	12.5
Divorced/separated	0	0.0	2	18.2	2	9.5	1	6.3
Household occupancy								
Adults ≥18								
1	3	30.0	2	18.2	5	23.8	3	18.8
2	5	50.0	8	72.7	13	61.9	8	50.0
≥3	2	20.0	1	9.1	3	14.3	5	31.3
Children <18								
0	8	80.0	9	81.8	17	**81.0**	12	**75.0**
1-2	2	20.0	2	18.2	4	9.1	4	25.0
Caring responsibilities								
Yes	1	10.0	0	0.0	1	4.8	2	12.5
No	9	90.0	11	100	20	95.2	14	**87.5**
Education								
To school leaving age	1	10.0	1	9.1	2	9.5	3	18.8
Beyond school leaving age	2	20.0	2	18.2	4	19.0	1	6.3
To degree/professional level	7	70.0	8	72.7	15	**71.4**	12	**75.0**
Employment status								
Working full time	1	10.0	1	9.1	2	9.5	3	**18.8**
Student	1	10.0	0	0.0	1	4.8	3	18.8
Unable to work due to health	1	10.0	4	**36.4**	5	23.8	5	**31.3**
Unemployed and looking for work	0	0.0	1	9.1	1	4.8	1	6.3
Retired	7	**70.0**	4	36.4	11	52.4	4	**25.0**
Other	0	0.0	1	9.1	1	4.8	0	0.0

§Data missing for n=3 participants whose baseline and sociodemographic data was not received, but who went on to progress through study.

The overall sub-study sample also comprised women who were predominantly white, married or co-habiting, most living without children (75%) and reporting no caring responsibilities (87.5%). Participants were generally highly educated, 81.3% beyond school leaving age and

75% to a degree or professional level, with the majority either retired or unable to work due to ill health (56.3%). This overall picture very much mirrored the RCT sample, yet several key distinctions were also evident. The mean age of sub-study participants was notably younger than the overall RCT sample (51.5 years, SD 8.6 compared to 59.8 years, SD 12.7) Furthermore, a significant proportion of women recruited to the sub-study (37.6%) were actively employed or looking for work (compared to just 14.3% in the RCT).

There were also few notable differences between RCT study arms for computer usage characteristics (Table 8.3). The vast majority of women were experienced computer users (90.5% having used a computer for five years or more) and 85.7% had access to a personal computer. Women reported using multiple forms of technology; 66.7% used a tablet and the same proportion used a smartphone. Smaller yet substantial proportions reported using a desktop (33.3%) and/or laptop computer (47.6%). Though the overall sample can largely be regarded as frequent computer users, 100% of waiting list control participants accessed a computer daily whilst in the intervention group, some women reported less regular use (20% weekly, 10% monthly). For both groups, experience was widespread across a diverse range of internet activities.

For the sub-study, computer usage data once again evidenced a highly computer literate sample, with a high level of experience and access to a range of devices. All participants reported frequent (daily) use of computers and enjoyment in doing so. Again, the internet was used for a wide range of activities, with 87.5% reporting accessing health information online.

Table 8.3 Baseline computer usage characteristics: comparing across studies

	RCT						***Sub-study***	
	Intervention (n=10)		**Waiting list (n=11)**		**Overall group (n=21)**		**Single arm (n=16)§**	
	n	**%**	**N**	**%**	**N**	**%**	**n**	**%**
Computer experience: No. years using computer								
2-5 years	0	0.0	1	9.1	1	4.8	0	0.0
More than 5 years	9	90.0	10	90.9	19	**90.5**	16	**100.0**
Only with support	1	10.0	0	0.0	1	4.8	0	0.0
Computer access: Main computer used								
Personal computer	7	70.0	11	100.0	18	**85.7**	11	**68.8**
Work computer	1	20.0	0	0.0	1	4.8	3	18.8
Public computer	0	0.0	0	0.0	0	0.0	1	6.3
Family member's computer	2	10.0	0	0.0	2	9.5	1	6.3
Type(s) of computer used								
Desktop	4	40.0	3	27.3	7	33.3	7	43.8
Laptop	5	50.0	5	45.5	10	47.6	12	75.0
Smartphone	7	70.0	7	63.6	14	66.7	13	81.3
Tablet	5	50.0	9	81.8	14	**66.7**	13	81.3

Computer frequency of use								
Daily	7	**70.0**	11	**100.0**	18	85.7	16	**100.0**
Weekly	2	20.0	0	0.0	2	9.5	0	0.0
Monthly	1	10.0	0	0.0	1	4.8	0	0.0
Computer enjoyment								
Yes	8	80.0	7	63.6	15	71.4	16	100.0
No	0	0.0	0	0.0	0	0.0	0	0.0
Sometimes	2	20.0	4	36.4	6	28.6	0	0.0
Computer activities								
Internet	10	100	11	100.0	21	100	16	100.0
Word/data processing	6	60.0	5	45.5	11	52.4	11	68.8
Games	3	30.0	4	36.4	7	33.3	4	25.0
Other	2	20.0	2	18.2	4	19.0	1	6.3
Internet activities								
Banking	8	80.0	9	81.8	17	81.0	16	100.0
Email	10	100	11	100.0	21	100.0	15	93.8
Games	0	0.0	6	54.5	6	28.6	6	37.5
Health information	7	**70.0**	9	**81.8**	16	76.2	14	**87.5**
News	7	70.0	6	54.5	13	61.9	13	81.3
Shopping	7	70.0	10	90.9	17	81.0	16	100.0
Social networking	6	60.0	7	63.6	13	61.9	12	75.0
Streaming	4	40.0	4	36.4	8	38.1	10	62.5
Other	2	20.0	3	27.3	5	23.8	0	0.0

§Data missing for n=3 participants whose baseline and sociodemographic data was not received, but who went on to progress through study.

8.4.3.2 Clinical characteristics

Overall, the RCT was also largely balanced across study arms in terms of clinical characteristics (Table 8.4), though with several notable distinctions. One participant in each arm was diagnosed as de novo metastatic whilst the remaining sample (90.5%) had an initial primary diagnosis. For women in the intervention group, however, primary breast cancer was mostly diagnosed in its earlier stages, whilst for the waiting list control group, this was more variable (30% diagnosed at stage 3, 20% initially diagnosed as having DCIS). The mean time between primary and secondary diagnoses appeared similar for intervention (8.0 years, SD 7.6) and waiting list control participants (6.6 years, SD 5.9), both demonstrating significant within-group variation. Similarly, time since secondary diagnosis appeared largely similar across groups, with a mean of 2.3 years (SD 2.6) for the sample overall. Looking more closely, the waiting list control group had a higher proportion of women diagnosed within the last 12 months (54.5%), whilst 70% of intervention participants had been diagnosed more than 12 months ago. Across both arms, the majority of those falling under the '> 12 months' category (n=12) had lived with their secondary diagnosis for significantly longer, with n=7 diagnosed more than 2 years ago (of which n=4 were diagnosed between 3.5 – 9 years ago).

Those in the intervention group had predominantly single site metastasis (60%), whilst all but one participant in the waiting list control group had multi-site metastases (90.9%), potentially indicating more progressive disease. The bones were the most frequent site of metastatic spread at diagnosis, regardless of study arm allocation (diagnosed in 61.9% of the sample overall) and a high proportion of women in both groups had early metastases to the lungs and lymphatics (diagnosed in 33.3% of the overall sample in both cases). Over half of the waiting list control group had liver metastases at diagnosis (54.5%), whilst this was rare for the intervention group (10%). For both groups, disease progression was most frequently to the bones and liver, whilst the waiting list control group also had relatively high proportions with spread to the lymphatics (36.4%, n=4), lungs (27.3%, n=3) and brain (27.3%, n=3). Very few of the overall group (n=2) had two or more co-morbidities; 60% of the intervention group had one reported co-morbidity whilst just over half (54.5%) of the waiting list control group had no co-morbidities.

Table 8.4 Baseline clinical characteristics: comparing across studies

	RCT						***Sub-study***	
	Intervention (n=10)		**Waiting list (n=11)**		**Overall group (n=21)**		**Single arm (n=20)***	
	N	**%**	**N**	**%**	**N**	**%**	**n**	**%**
Diagnostic history								
De novo metastatic	1	10.0	1	9.1	2	9.5	5	**25.0**
Previous primary BC	9	**90.0**	10	**90.9**	19	90.5	15	75.0
Stage of previous primary BC	(n=9)		(n=10)		(n=19)		(n=15)	
DCIS	0	0.0	2	20.0	2	10.5	2	13.3
Stage 1	4	44.4	2	20.0	6	31.6	1	6.67
Stage 2	4	44.4	3	30.0	7	36.8	4	**26.7**
Stage 3	0	0.0	3	**30.0**	3	15.8	8	**53.3**
Unknown	1	11.1	0	0.0	1	5.3	0	0.0
Years to secondary diagnosis	(n=9)		(n=10)		(n=19)		(n=15)	
Mean (SD)	8.0 (7.6)		6.6 (5.3)		7.3 (6.6)		6.7 (5.6)	
Range	19.2		18.6		19.5		16.0	
Min, max	0.6, 19.8		0.3, 18.8		0.3, 19.8		1, 17	
Extent of metastasis								
Single site	6	**60.0**	1	9.1	7	33.3	7	35.0
Multiple sites	4	40.0	10	**90.9**	14	66.7	13	**65.0**
Site(s) of metastases								
Initial secondary diagnosis								
Bone(s)	6	**60.0**	7	**63.6**	13	**61.9**	16	**80.0**
Lung(s)	3	30.0	4	36.4	7	33.3	6	30.0
Liver	1	10.0	6	**54.5**	7	33.3	3	15.0
Brain	1	10.0	0	0.0	1	4.8	0	0.0
Lymphatics	2	20.0	5	45.5	7	33.3	4	20.0

Other	2	20.0	0	0.0	2	9.5	1	5.0
Disease progression								
Bone(s)	2	20.0	6	**54.5**	8	38.1	4	20.0
Lung(s)	0	0.0	3	27.3	3	14.3	0	0.0
Liver	4	**40.0**	5	45.5	9	**42.9**	6	**30.0**
Brain	0	0.0	3	27.3	3	14.3	0	0.0
Lymphatics	1	10.0	4	36.4	5	23.8	3	15.0
Other	1	10.0	0	0.0	1	4.8	1	5.0
Years since secondary diagnosis								
Mean (SD)	2.4 (2.4)		2.2 (2.9)		2.3 (2.6)		1.72 (1.5)	
Range	8.4		8.8		8.8		7.0	
Min, max	0.3, 8.7		0.2, 9.0		0.2, 9.0		0.0, 7.0	
≤ 12 months	3	30.0	6	**54.5**	9	42.9	8	40.0
> 12months	7	**70.0**	5	45.5	12	57.1	12	**60.0**
Co-morbidities								
0	3	30.0	6	**54.5**	9	42.9	6	30.0
1	6	**60.0**	4	36.4	10	47.6	10	50.0
2	0	0.0	1	9.1	1	4.8	4	20.0
≥3	1	10.0	0	0.0	1	4.8	0	0.0

*Baseline clinical data available for all consenting sub-study participants.

The sub-study sample comprised a significant proportion of women diagnosed as de novo metastatic (25%, n=5 compared to 9.5%, n=2 in the RCT). Those who experienced a primary breast cancer were predominantly diagnosed at more progressed stages (80% at stage 2-3). Whilst this was also the case in the RCT, the overall proportion was much lower (52.6%), with a substantial number of women receiving DCIS and stage 1 diagnoses. However, the mean time to secondary diagnosis was largely similar for those in the sub-study (6.7 years, SD 5.6) and RCT (7.3 years, SD 6.6). Metastasis was predominantly multi-site (65%) and most frequently diagnosed in the bones (80%) and lungs (30%), with any reported progression confined to the bones (20%, n=4) liver (30%, n=6) lymphatics (15%, n=3) and endometrium (5%, n=1). At first glance, the sample appeared to be evenly split between recent and longer-term diagnoses. However, in contrast to the RCT, a significant proportion of those falling under the '> 12 months' category were still very recently diagnosed. Overall, 85% of the sample were diagnosed with SBC between 2018 and 2020. Of the remaining 15% (n=3), 2 participants were diagnosed in 2017 and the other in 2013, representing the longest-term diagnosis of the group. Most women reported 1-2 co-morbidities (70%, n=14); the remaining reported no other significant health problems.

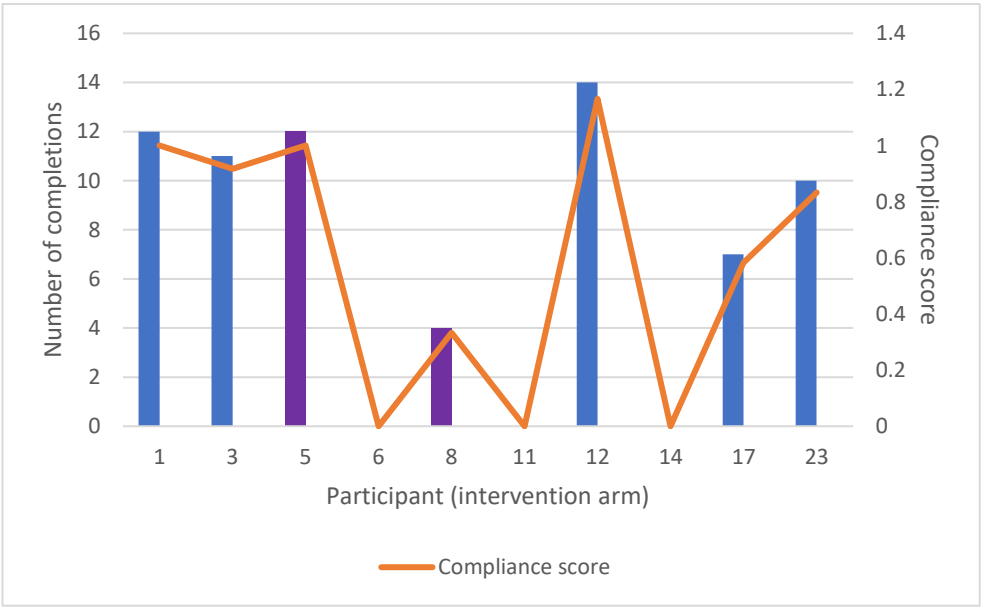
8.4.4 Intervention engagement: symptom monitoring questionnaire completion

8.4.4.1 Compliance

The mean number of completions across the 12 weeks for all 10 RCT intervention participants was 7.0 (SD 5.6), equating to an average compliance score of 0.6. The number of symptom monitoring questionnaires completed per participant is displayed in Figure 8.5.

Overall, 3 participants did not meet the requirement of completing a minimum of 1 online symptom monitoring questionnaire. Notably, 1 participant completed above the specified weekly frequency, with a total of 14 completions (and 2 further completions outside of the study period, though these were not included in the analysis).

Figure 8.5 Number of symptom monitoring questionnaires completed (RCT)



Treatment group A (chemo +/- MABs) *Treatment group B (hormone +/- targeted therapy)*

Data regarding sub-study participants' engagement and interaction with the independent monitoring intervention was also collected. This was a crucial indicator of the feasibility and acceptability of delivering the LIBERATE intervention in the absence of clinical integration. Overall, there was a higher level of compliance for online symptom monitoring questionnaire completion in the sub-study than in the RCT. All participants (excluding those who formally withdrew and were lost to follow up at baseline, n=2) completed a minimum of 4 and maximum of 13 online symptom monitoring questionnaires, regardless of whether or not they had returned the baseline and/or 12 week outcome questionnaires. The mean number of completions for the overall group (n=20) was 8.8 (SD 3.4), giving an average compliance score of 0.73.

The total number of symptom monitoring questionnaires completed is displayed in Figure 8.6. Notably, 2 participants completed 13 symptom monitoring questionnaires (equating to a compliance score of 1.1) and, overall, 60% of the group completed 10 or more. Even for those participants who did not return 12 week outcome questionnaires, the completion rate was relatively high (ranging from 5 to 11 completions over the 12 week period).

Figure 8.6 Number of symptom monitoring questionnaires completed (sub-study)

Treatment group A (chemo +/- MABs) *Treatment group B (hormone +/- targeted therapy)*

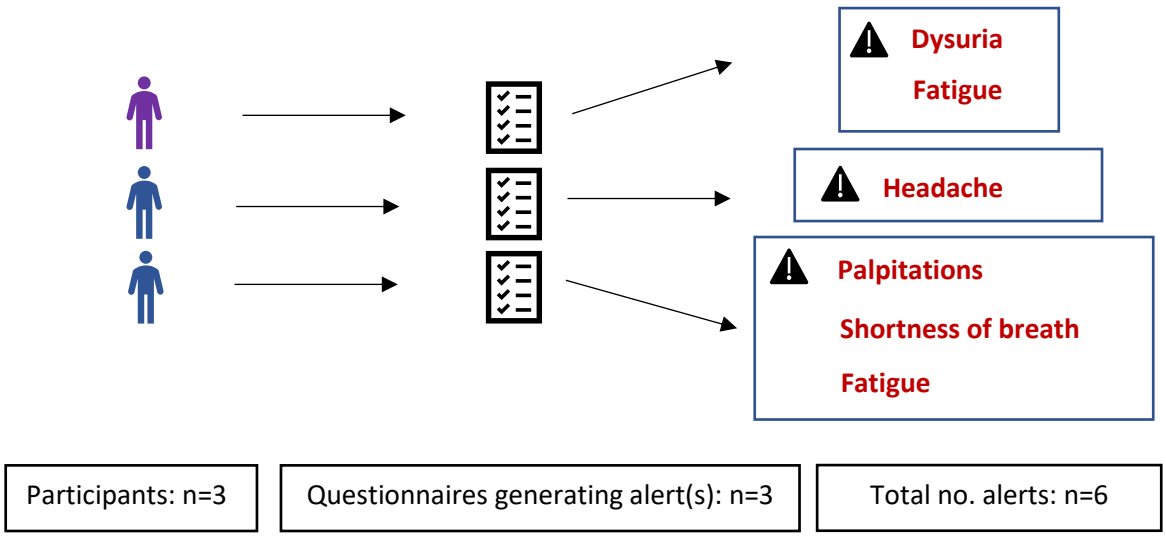
8.4.4.2 Alerts and algorithms

Out of 70 symptom monitoring questionnaires completed by 7 RCT intervention participants, just 3 (4.3%) resulted in the generation of alerts to clinicians due to the reporting of one or more severe symptoms. From these 3 questionnaires (completed by 3 separate intervention participants), a total of 6 alerts were generated. This is displayed in Figure 8.7.

In all cases, a clinician (GV) followed up these alerts to ensure that the participant had sought medical attention (i.e. had called the acute oncology assessment unit) or was due to be seen in clinic imminently. On the advice of clinical experts (GV, AG), moderate dysuria (graded as 2 within CTCAE guidance) warranted clinical review. Therefore, where reported, this scored as a severe symptom, triggering the generation of an alert.

As well as providing insight into how participants engaged with the symptom monitoring component, analysing the number of alerts generated provided an indicator of the feasibility of intervention delivery in the clinical setting. Indeed, this low level of alerts demonstrated that this crucial element of clinical integration resulted in minimal additional burden on the clinical workload. This aspect of feasibility will be explored further in section 8.4.6.

Figure 8.7 Frequency and type of alerts generated across the 12 week study period



As displayed in Figure 8.8, the vast majority of questionnaire completions for the RCT (82.9%) activated algorithm C. This was the case for intervention participants across treatment groups A (87.5%) and B (81.5%). In line with the criteria for algorithm C, this meant that, for most questionnaire completions, participants had reported no severe symptoms and one of the following:

I. Less than 3 moderate symptoms (level 2 scores).
II. Less than 3 moderate symptoms (level 2 scores) and any number of mild symptoms (level 1 scores).
III. Any number of mild symptoms only.

A much smaller proportion of completions activated algorithm B (12.9%), where 3 or more moderate symptoms were reported, whilst (as discussed in relation to the generation of alerts), just 3 completions (6.3% of those for treatment group A and 3.7% of those for treatment group B) included ≥1 severe symptom, activating algorithm A. None of the completions activated algorithm D, meaning that none of the participants reported a complete absence of symptoms.

Overall, participants in the sub-study reported a wider breadth of symptoms at a higher frequency of completion when compared to those in the RCT. Furthermore, an interesting pattern emerged in relation to the reporting of severe symptoms. Whilst participants in the RCT reported very few severe symptoms, a higher proportion of the symptoms reported in the sub-study were severe. Though automated alerts to clinicians were a feature exclusive to the clinically integrated setting, sub-study participants using the independent monitoring

intervention did receive the on screen alert messages to contact their hospital in the event of severe symptoms (and for any new, changing or concerning symptom of moderate severity).

When viewed as the proportion of severe (grade 3) symptoms reported, this is still minority of the symptoms reported across the sub-study overall (5.3%, n=164/3113). However, when viewed as the percentage of completions triggering algorithm A (i.e. a questionnaire in which any one or more symptoms is reported as severe, resulting in an automated message advising the participant to contact their hospital), the contrast with the RCT is much more evident (Figure 8.9). Overall, 22.3% of all completions by sub-study participants (n=39/175) resulted in the activation of algorithm A, compared to 4.3% (n=3/70) of clinically integrated RCT completions. Though algorithm A was activated much more frequently, the same overall pattern in the proportions of algorithms generated (Figure 8.9) was observed across the sub-study as was evident in the RCT, with the highest proportion of questionnaire completions (53.1%) pertaining to mild symptoms and generating self-management advice in line with algorithm C. As was the case in the RCT, algorithm B was the second most frequently activated (24.6%), though this time at a higher frequency due to the higher number of moderate symptoms (≥3 moderate symptoms leading to self-management advice in line with algorithm B). Again, none of the participants used the questionnaire to report an absence of symptoms, meaning algorithm D was not activated.

Figure 8.8 Proportion of algorithms activated across groups (RCT)

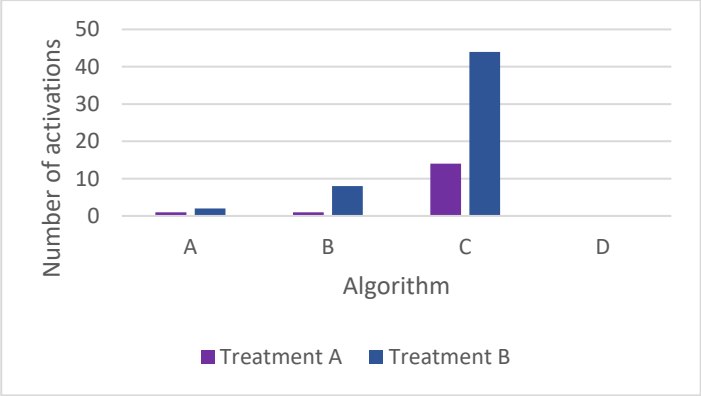
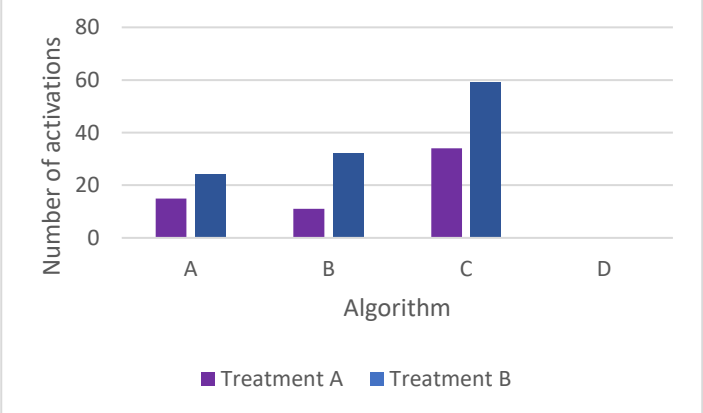


Figure 8.9 Proportion of algorithms activated across groups (sub-study)



8.4.4.3 Symptoms reported

Overall, 2 of the 7 RCT intervention group participants who engaged with online symptom monitoring were in treatment group A, reporting a total of 148 symptom occurrences (relating to 29 individual symptoms) over the 12 week study period. This equated to an average of 74 reported symptom occurrences per participant. The remaining 5 participants were allocated to treatment group B. They reported a total of 607 symptom occurrences (relating to 38 individual symptoms), at an average of 121.4 symptoms per participant. A wider range of symptoms were therefore reported, at a higher average frequency, across treatment group B when compared to treatment group A.

The type and frequency of symptoms reported across all intervention participants are displayed in Figure 8.10. For both treatment groups, this demonstrates a breadth of symptoms reported relatively infrequently, alongside what appears to be a core group of more regularly occurring or ongoing symptoms. For treatment group A, these included fatigue and reduced physical ability, unsteadiness, cough and anxiety. Whilst observed across a very small sub-sample (n=2), this may suggest a wider range of symptoms occurring more transiently with chemotherapy +/- MAB treatment, alongside a smaller subset being experienced more chronically. For treatment group B, more ongoing symptoms included numerous related to pain and physical functioning (pain, fatigue, reduced physical ability, muscular aches, pains or weakness) menopausal or hormone-related side-effects (aching joints, night sweats and hot flushes) and gastrointestinal symptoms (sore mouth and indigestion). Notably, the various questionnaire items relating to pain (general, muscular and joint-related) were collectively the most frequently reported symptom for women on these treatments (hormone +/- targeted therapy), indicating that pain was potentially experienced as more chronic in nature and may not have been resolved or controlled with the simple self-management advice offered.

Regardless of their frequency of occurrence, the overwhelming majority of symptoms reported across treatment group A (91.9%) and B (86.3%) were mild in severity (Figure 8.11). A minority of symptoms were reported as moderate though, proportionately, these occurred at nearly twice the frequency in treatment group B (12.4%) compared to treatment group A (6.8%). Severe symptoms represented a very small minority of those reported overall (1.35% and 1.32% for treatment A and B respectively).

Figure 8.10 Type and frequency of reported symptoms (RCT)

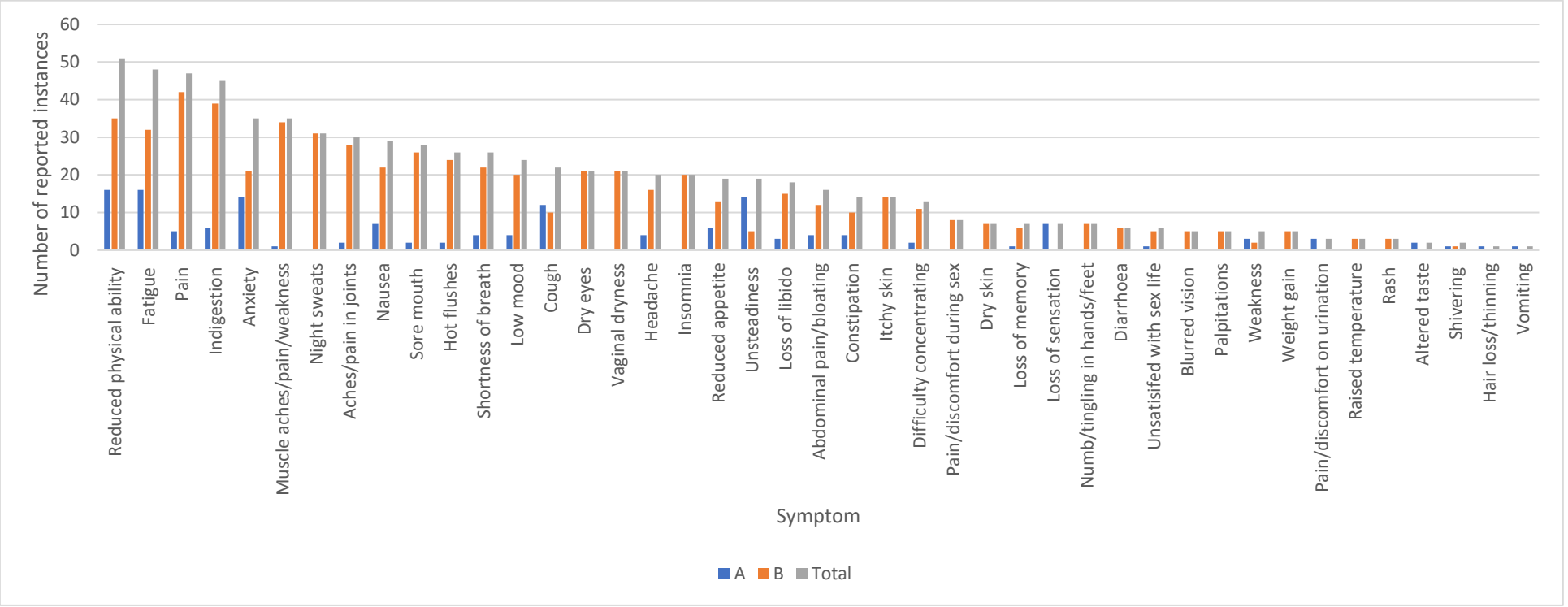
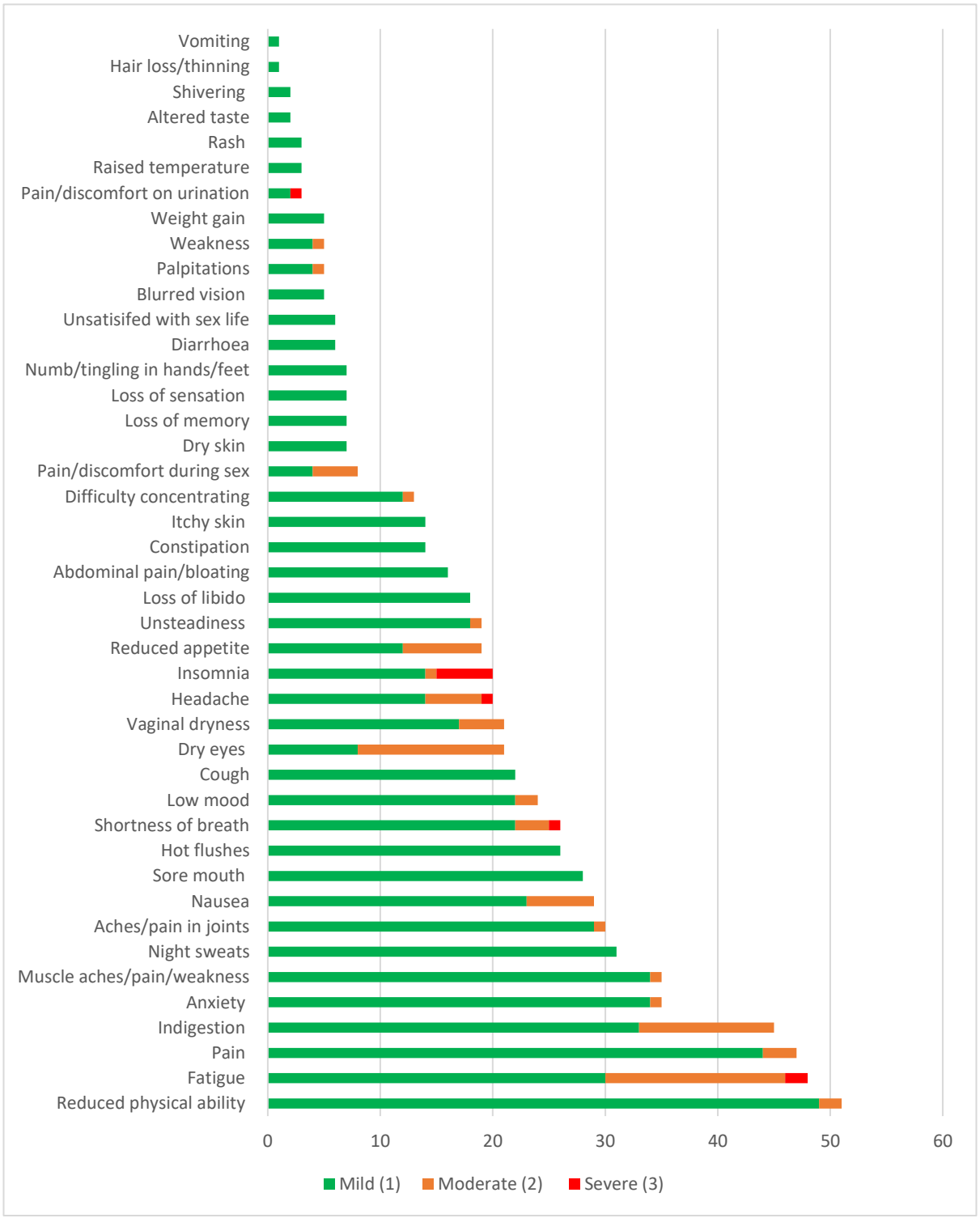


Figure 8.11 Severity of reported symptoms (RCT)



For the 7 sub-study participants in treatment group A, 1037 symptom occurrences were reported over the 12 week period (relating to 43 individual symptoms) at an average of 148.1 symptom occurrences per participant. Comparing to treatment group B, a total of 2076 symptom occurrences were reported by 11 participants, at an average of 188.7 symptoms per participant. As was observed for treatment group A, these were reported across a higher number of completions and encompassed a wider breadth of symptoms (45 individual symptoms) than the equivalent group in the RCT setting.

Figure 8.12 displays the type and frequency of symptoms reported across all questionnaire completions in the sub-study. This again demonstrates a wide range of symptoms reported at lower levels of frequency, amidst what appears to be more regularly occurring or ongoing symptoms. For those in treatment group A, these included fatigue, reduced physical ability, anxiety and indigestion, mirroring the pattern of reporting observed in the RCT. In addition, sub-study participants also collectively reported a high level of pain related symptoms (pain and muscle aching, pain or weakness), alongside low mood, difficulty sleeping, memory loss, shortness of breath, peripheral neuropathy (pain and tingling in the fingers and toes) and nail changes. For those in treatment group B, the most frequently reported symptoms again included a range of physical functioning and pain related symptoms (reduced physical ability, fatigue, pain, abdominal pain/bloating and general muscle aching, pain or weakness) and menopausal symptoms (hot flushes, night sweats, aching and pain in the joints, vaginal dryness, loss of libido and low satisfaction with sex life), this time alongside symptoms related to psychosocial well-being (low mood, anxiety, insomnia), headaches and shortness of breath.

The overall pattern of reporting across groups again alluded to transient symptoms experienced against a background of more chronic, ongoing symptoms.

Figure 8.13 displays the severity of all symptoms reported in the sub-study. As evident in the pattern of algorithms activated, the majority of symptoms reported across treatment group A (65.1%) and B (65.2%) were mild in severity. Alongside these, a much higher proportion of moderate (29.6%) and severe (5.3%) symptoms were observed when compared to participants reporting in the clinically-integrated, RCT setting (11.3% and 1.3% respectively).

Figure 8.12 Frequency of reported symptoms (sub-study)

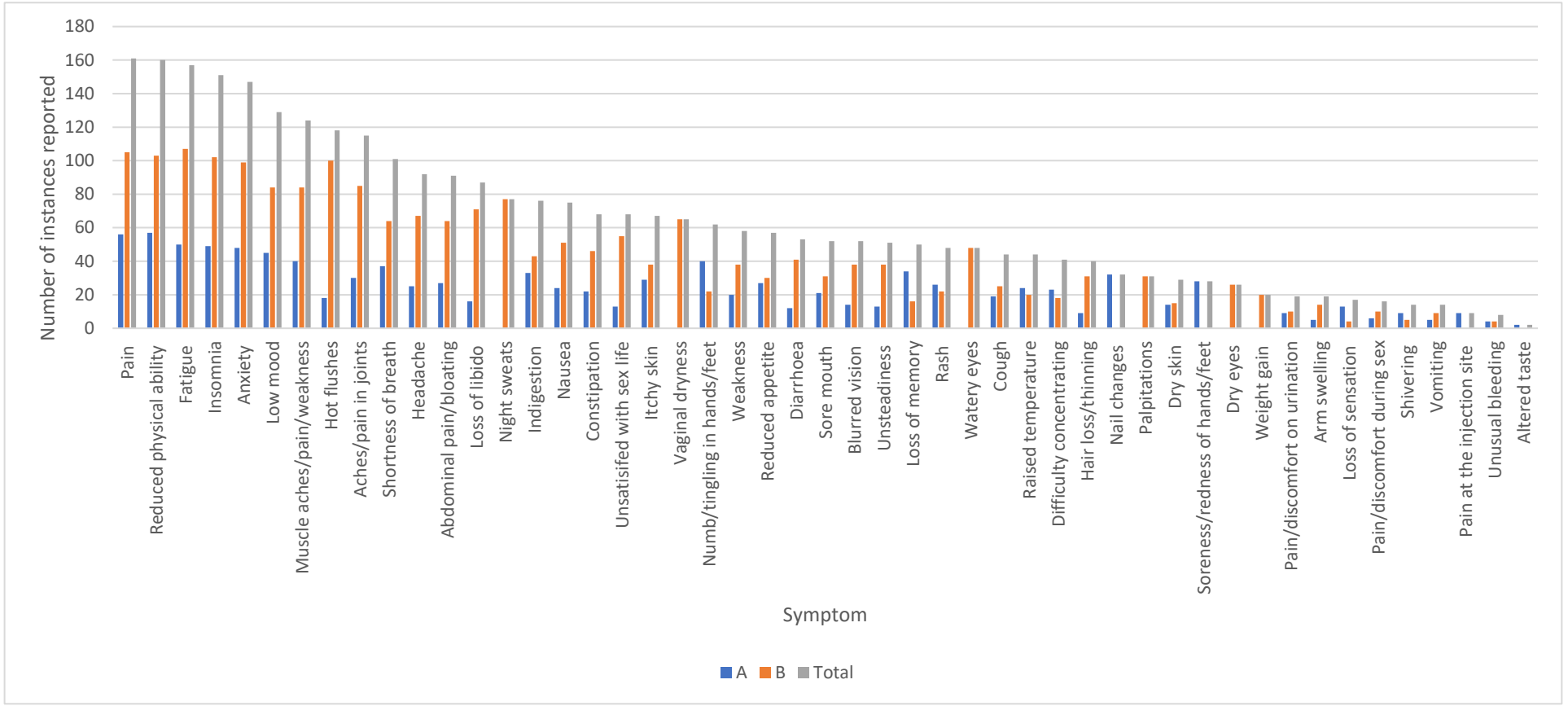
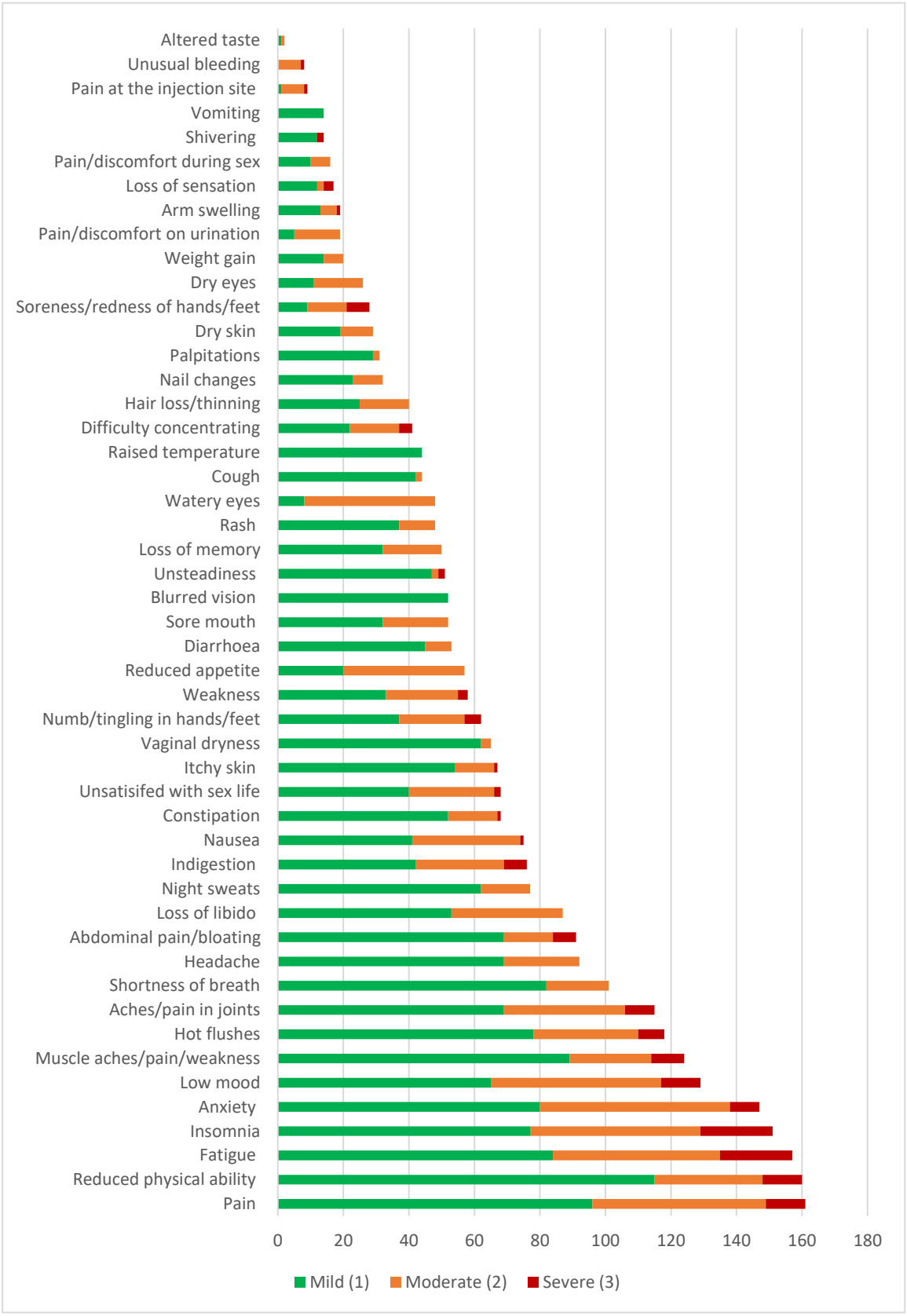


Figure 8.13 Severity of symptoms reported (sub-study)



8.4.5 Intervention engagement: LIBERATE website analytics

Website analytics data was gathered to further explore the level of intervention engagement, given symptom-monitoring questionnaire completion demonstrated use of just one of the five core intervention components. Indeed, participants may have used the LIBERATE website either alongside or in absence of the symptom monitoring feature. The data is limited, however, in that it was not possible to distinguish between individual users or participants from across the RCT and single arm sub-study.

Data was gathered from the first day of recruitment (sub-study recruitment commencing 19th May 2020) up until the point at which the vast majority of waiting list control participants had received 12 weeks access to the website (with final data collected 1st June 2021). Across this time period, there was a total of 1373 unique page views, a breakdown of which is displayed in Table 8.5.

For those sections which comprised a number of sub-sections ('holistic health information' and 'symptom monitoring'), the page views were broken down further to explore the frequency of use of different pages. More general SBC information was most frequently referred to, as well as practical considerations ('looking ahead' and 'finance & employment') and information relating to healthy living. Psychological well-being and complementary therapies comprised a smaller proportion of views, alongside diagnostic and treatment information, and content specific to younger women.

Within the symptom monitoring section, women appeared to predominantly seek out self-management information relating to pain and fatigue, with smaller proportions of views relating to sickness and other gastrointestinal problems (soreness of the mouth and tongue, diarrhoea and constipation, indigestion and heartburn), respiratory problems (breathlessness and coughing) soreness in the hands and feet, hair loss, skin and nail problems and menopausal symptoms. A small number of views were for content related the management of raised temperature, weight gain and 'symptoms in the arms', which included advice surrounding phlebitis (pain and inflammation along the veins) and lymphoedema.

Table 8.5 LIBERATE website analytics: number and proportion of unique page views

Website section/page	Unique page views	
	N	%
Homepage	533	38.8
Holistic health information	376	27.4
Secondary breast cancer explained	139	37.0
Looking ahead	43	11.4
Section homepage	34	9.00
Finance & employment	31	8.2
Healthy living	31	8.2
Psychological well-being	22	5.9
Complementary therapies	21	5.6
Relationships, sex & intimacy	21	5.6
Treatment	20	5.3
Younger women with SBC	8	2.1
Diagnosis	6	1.6
Symptom monitoring	283	28.6
Section homepage	91	32.2
Pain	47	16.6
Tiredness, fatigue & difficulty sleeping	39	13.8
Sickness	15	5.3
Breathlessness & coughing	14	5.0
Soreness of hands & feet	12	4.2
Soreness of mouth & tongue	12	4.2
Menopausal symptoms	12	4.2
Diarrhoea & constipation	11	3.9
Hair loss, skin & nails	9	3.2
Symptoms in the arms	8	2.8
Indigestion & heartburn	6	2.1
Weight gain	5	1.8
Raised temperature	2	0.7
Case studies	59	4.3
Support for others	39	2.8
Signposting	33	2.4
Low mood & anxiety	13	1.0
Memory & concentration problems	11	0.8
How to read the evidence	9	0.7
Homepage (privacy & use of cookies)	6	0.4
Total	1362	99.2

The remaining 11 of the 1373 unique page views (0.8%) related to use of the website search function (n=9) and, importantly, two instances of '404' errors which are likely to be indicative of a broken link.

8.4.5.1 Engagement of waiting list control participants

It is difficult to ascertain whether any of the waiting list control group made use of the wider LIBERATE website once they received access at the end of their study period. However, just 2 of the 11 participants accessed and completed the symptom monitoring questionnaires, using the login details provided to them.

8.4.6 Intervention delivery: clinical process measures

As displayed in Table 8.6, the number of attendances outside of scheduled consultations (during the 12 week study period) varied little across the study arms. The mean number of acute oncology unit attendances and hospital admissions was low for all participants and the highest number of attendances were nurse pre-assessment appointments in line with treatment delivery. 'Other' attendances related to non-oncology outpatient appointments (though often related to women's wider breast cancer care e.g. plastic surgery for breast reconstruction review, orthopaedics for fracture related to bone metastasis, lymphoedema clinic etc.), which were slightly higher for the waiting list control arm.

Table 8.6 Attendances outside of consultation: comparing across study arms

Attendances outside of consultation	**Intervention (n=10)**				**Waiting list control (n=11)***			
	Min	Max	Mean	SD	Min	Max	Mean	SD
Acute oncology unit	0	2	0.5	0.7	0	2	0.4	0.7
Hospital admission	0	1	0.1	0.3	0	2	0.4	0.8
Scans	0	3	1.3	1.2	0	4	1.6	1.4
Nurse pre-assessment	0	9	0.9	2.6	0	6	1.2	2.4
Other	0	1	0.6	0.5	0	4	0.9	1.6
Total attendances	0	12	3.4	3.6	0	12	4.5	4.2

**n=11 including participant who died in week 8.*

Table 8.7 Contacts outside of consultation: comparing across study arms

Contacts outside of consultation	**Intervention (n=10)**				**Waiting list control (n=11)***			
	Min	Max	Mean	SD	Min	Max	Mean	SD
Nurse initiated	0	5	1.7	1.8	0	11	1.6	3.2
Doctor initiated	0	2	0.3	0.7	0	2	0.4	0.7
Patient initiated	0	3	1.0	1.3	0	11	1.3	3.3
Other	0	0	0.0	0.0	0	3	0.6	1.0
Total contacts	0	10	3.0	3.0	0	24	3.8	6.9

**n=11 including participant who died at week 8.*

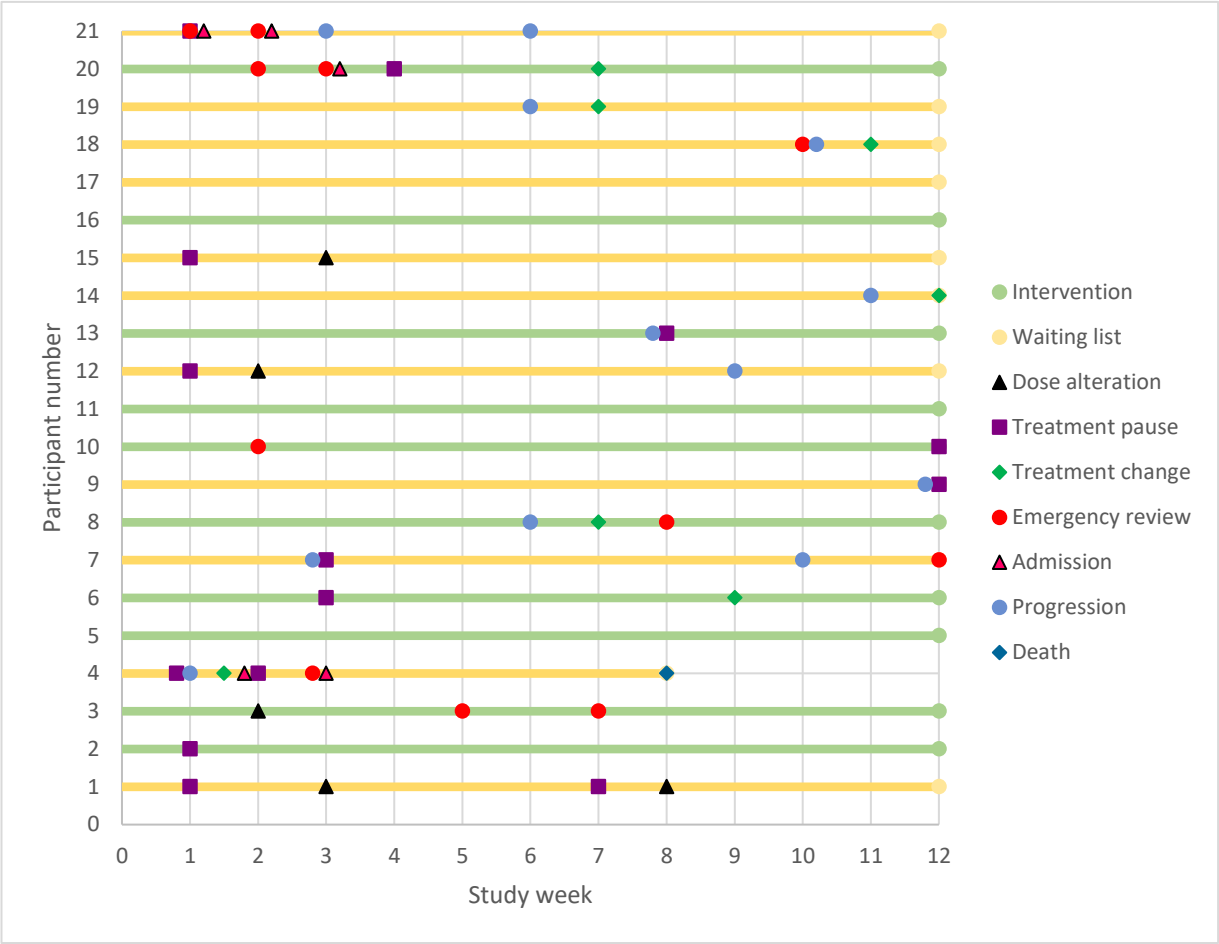
As displayed in Table 8.7, frequencies of all forms of additional contact were also generally very low and appeared largely similar across both study groups. 'Other' contacts refers to non-oncology related interactions (e.g. orthopaedics telephone consultation), which were only observed amongst waiting list control participants. Looking at the maximum number of patient

and nurse-initiated contacts, the notably higher figures for the waiting list control group related to an individual participant. When interpreted in the context of their clinical status, however, it became clear that this was due to significant deteriorations in their physical health, disease progression and several prolonged hospital admissions, as opposed to being attributable to the absence of the intervention. The presence of this outlier therefore highlighted the potential for 'blind spots' in the clinical process measures collected, when interpreted without consideration of the individual participants' surrounding context and any changes to their disease status, treatment and overall health during the 12 week study period.

In order to look to the wider context and explore factors (other than the intervention itself) which may have influenced these figures, further clinical data was explored within a swimmer plot (Figure 8.14). This also provided a crucial opportunity to explore potential reasons behind the extremely low intervention engagement of waiting list control participants when they were given access to the intervention post study.

Clinical process measures relating to treatment changes and disease progression across the trial period provided insight into the participants' overall health and performance status, the stability of their cancer and the course of their disease trajectory. Participants progression through the 12 week study period (whether or not they went on to drop out) was plotted in line with a series of clinical indicators referred to as 'events.' These were related to treatment and management (dose alteration, pause to treatment, change of treatment, emergency reviews and admissions) and the disease trajectory (evidence of progression and death). In analysing this data, a number of different disease 'profiles' became evident, providing contextual insights in support of the wider findings. In this sense, context refers to women's health state and disease stability as factors potentially influencing their interaction with the intervention and engagement with the study overall. Returning to completion status, all those participants (n=5) who did not complete the study (participants labelled as numbers 4, 6, 7, 10 and 13) encountered two or more events during the course of the 12 weeks. For one participant (labelled as 4), multiple events culminated in her death during week 8. For the remaining 'non-completers', events were tracked across their full 12 week study period, since it was not clear at what point they dropped out from the study.

Figure 8.14 Swimmer plot of treatment & disease related events across 12 week study (RCT)



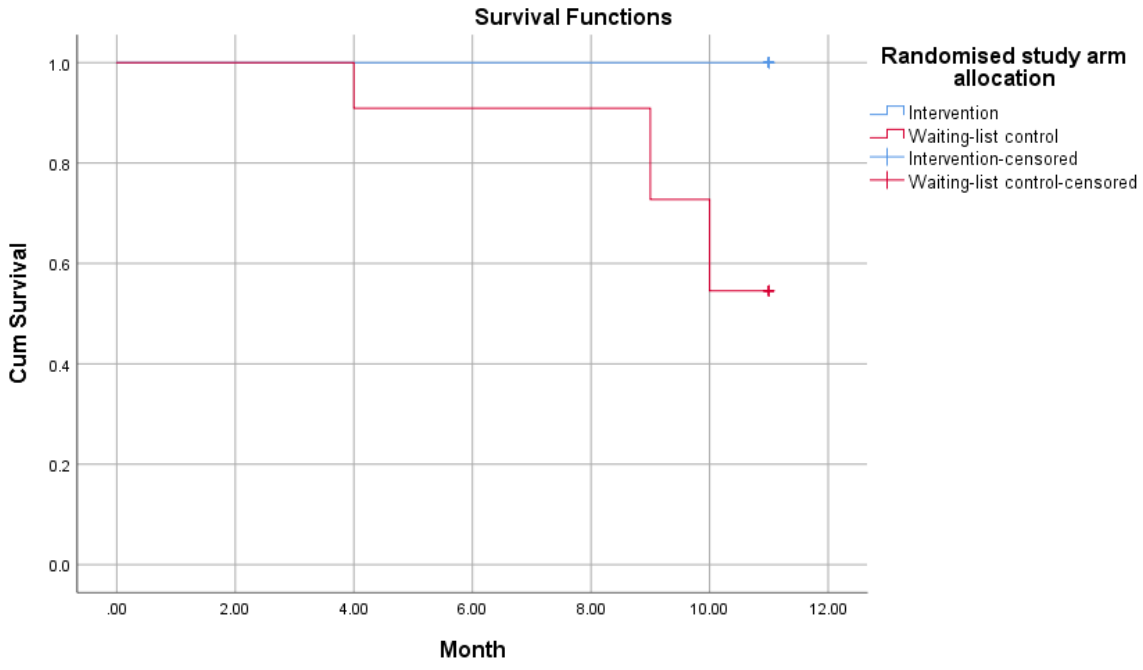
A number of varying 'disease profiles' appear evident. Some women appeared to have a period of prolonged stability, progressing through the 12 weeks without encountering any of the treatment or disease related events. However, this was the case for just 4 of the 21 participants (5, 11, 16 and 17, of whom n=3 were in the intervention arm and n=1 in the waiting list control arm). This highlights the significant complexity of the trajectory, the regularity of fluctuations and the potential rapidity of change amongst the other 17 participants.

Indeed, as demonstrated in Figure 8.14, some experienced what might be referred to as more 'micro' events such as dose alterations and pauses in treatment in order to manage side-effects. For others, these micro events were experienced alongside more 'macro' events, indicating significant disruption or deterioration. This included disease progression, change of treatment, emergency reviews and admissions. For some, a period of stability was maintained between events (e.g. participants 6 and 15) whilst for others, multiple events occurred in close succession (e.g. participants 4, 20 and 21).

Taking this a step further, to provide a more detailed overview of participants' disease trajectories from the time of recruitment to the point of final analysis (a 10 month period overall, from August 2020 – June 2021), a Kaplan Meier curve was constructed. In the oncology setting, this form of survival analysis is widely used to assess and compare the length of time participants survive when treated with a particular drug or treatment regimen (in other words, 'time to death'). The technique is also used more widely to analyse the time it takes for participants to experience a particular event, such as disease progression or remission.[434-436]

In this RCT, in light of the evident disease instability and deterioration experienced within the trial period, a Kaplan Meier curve (Figure 8.15) was used to analyse a specified 'time to death' variable for all study participants. This allowed for the assessment of survival beyond study completion within and between study arms. The curve highlights a significant difference in survival (p=0.02) between the intervention and waiting list control arms, with all five recorded deaths occurring in the waiting list group (n=1 within the 12 week study period, n=4 within 1-3 months post study). However, interpreted in the context of the wider clinical data, it is clear that contextual influences are much more likely to be behind this difference than the intervention itself. Indeed, as displayed in the swimmer plot above, waiting list control participants experienced a higher average frequency of disease and treatment related events across the 12 weeks (3.3) when compared to intervention participants (1.8). Furthermore, earlier baseline data indicated that the waiting list control group had more widely metastasized disease, making a lower rate of survival within or just beyond the study period more likely for these participants (regardless of their lack of intervention use).

Figure 8.15 Kaplan Meier survival estimate for intervention & waiting list control participants



8.4.7 Integrity of intervention & study procedures

8.4.7.1 Intervention delivery

Overall, few issues impeding the integrity of the intervention and its delivery were reported across the study periods of both the RCT and the single arm sub-study. Functionally, these predominantly related to issues encountered with study reminders for RCT participants due to problems with the PROMPT system, or to QTool server downtime (as opposed to issues with the main intervention website). For sub-study participants, as reminders were sent manually by the researcher, these continued regardless of issues with the clinically integrated system. Active RCT participants were informed of PROMPT related issues (of which there were two instances) as soon as they became evident, though this did not appear to change their pattern of reporting. Instances of QTool platform downtime (n=1 planned, n=2 unplanned) prevented access to symptom monitoring questionnaires. However, this was for a short period of time in all cases, during which an issue was reported by a single participant, who was able to log in shortly afterwards. A brief period of sever downtime was encountered for the LIBERATE website itself, though this was resolved within 30 minutes and did not appear to cause disruption to users.

The integrity of the clinically integrated feature (specifically, the viewing of participants' results by clinicians) appeared variable. For one of the health professionals, the integrity of this feature was compromised as they did not use the relevant version of the EPR (PPM+) and were therefore unable to view results. The researcher instead emailed the results of any intervention participants they were seeing, though this did not appear to prompt their use. Further difficulty was encountered with increasing numbers of consultations being performed via telephone. In these instances, paper reminder slips (informing the clinician of their patient's study involvement and providing instructions of how to access their symptom monitoring results) could not always be attached to clinical notes ahead of time. In this way, integrity of delivery was closely linked to challenges engaging health professionals.

8.4.7.2 Protocol & study documents

There were no deviations from the study protocol, though adaptations to planned procedures were made in response to the COVID-19 pandemic, as detailed in chapter 7. This meant that more of the planned face-to-face procedures were performed remotely (i.e. follow up discussions, consenting and intervention demonstrations via telephone), though this did not compromise overall study designs or the achievement of the objectives outlined. The acceptability of such adaptations, and any potential influence on study outcomes, was explored within end of study interviews (chapter 9).

A number of observations were made throughout the study period in relation to the integrity and completeness of the data collected using the study documents. More detailed clinical information was required than the data collection form initially gathered (though further collection was possible given participants had consented to their EPRs being accessed for any relevant medical information to support the study). Furthermore, the computer usage data collection form lacked insight into competency and confidence in using computers and technology, instead focusing on frequency and experience of use (e.g. respondents who reported using a computer for 'more than 5 years' were assumed to be competent as a result of experience, though this may not necessarily have been the case). The addition of further questions to explore how confident and competent participants are in various aspects of computer use would strengthen any future evaluation. Similarly, the sociodemographic data collection form required more nuanced responses in relation to employment status. For example, 'unable to work due to illness' potentially encompassed those unable to work long-term as well as those who may currently be signed off from work but planning to return. Also, participants self-reporting as 'retired' may have done so at the age they planned or earlier due to ill-health. One participant who selected the 'other' option for employment status (without further information) may have been referring to the government's furlough scheme, introduced in response to the COVID-19 pandemic, which would have been a useful update to include. Distinctions between these various categories would have provided useful contextual information.

Otherwise, study documentation was fit for purpose from a data collection perspective. Acceptability of documentation completed by the participants themselves was further explored in the end of study interviews (chapter 9).

8.4.8 Outcome measures

8.4.8.1 Missing item data

The amount and type of missing data was assessed at both timepoints across all 4 outcome measures. As highlighted in Table 8.8, there was a very small amount of missing item data overall and this was confined to the FACT-B measure. For the RCT, this predominantly related to one participant omitting four of the five subscales at baseline. Otherwise, across both studies, these few instances of missing items most frequently related to the item, '*My work (including work at home) is fulfilling'* (FACT-B functional well-being subscale). This may have been due a perceived lack of relevance, given a large proportion of participants were not in active employment. Also categorised within this missing item data were instances of the 'prefer not to say' option being selected in response to '*I am satisfied with my sex life'* (FACT-B social well-being subscale).

Table 8.8 Missing item data across outcome measures

	Missing item data (%)			
	RCT		Sub-study	
Outcome measure	T0 (n=21)	T1 (n=16)	T0 (n=16)	T1 (n=14)
FACT-B	5.3	1.7	0.3	1.2
EQ-5D-5L	0	0	0	0
CBI-B	0	0	0	0
SEMCD-6	0	0	0	0

8.4.8.2 Scoring

(i) FACT-B

All 3 summary scores were calculated, applying all 5 subscales, with higher scores indicative of greater QoL. Scoring guidelines specify that all subscales must be valid (i.e. ≥50% of items scored) for the overall score to be considered valid. One participant did not complete 4 of the 5 subscales of the FACT-B measure at baseline. They were therefore excluded from the analysis for this outcome. Their available data across all other outcome measures at baseline, however, was analysed. Descriptive data is presented in Table 8.9.

Table 8.9 Pre and post-test FACT-B scores across studies*

	RCT				**Sub-study**	
	Intervention		**Waiting list**		**Single arm**	
	T0 (n=10)	**T1 (n=7)**	**T0 (n=10)**	**T1 (n=9)**	**T0 (n=16)**	**T1 (n=14)**
FACT-B total score *(score range 0-148)*						
Mean (SD)	103.1 (20.0)	104.1 (14.7)	104.0 (17.4)	100.0 (22.4)	89.4 (20.4)	82.6 (22.7)
Min	67	89	58.0	55	52	45
Max	67, 131	89, 135	58, 118	55, 118	131	130
Median	103.0	101.0	108.5	111.0	87.5	81.5
FACT-G total score *(score range 0-108)*						
Mean (SD)	75.6 (17.2)	76.0 (11.9)	75.5 (14.2)	72.7 (16.3)	67.3 (15.5)	61.4 (16.6)
Min	42	64	43	45	41	36
Max	100	101	95	85	95	92
Median	74.0	72.0	76.5	80.0	69.0	61.5
FACT-B Trial Outcome Index (TOI) *(score range 0-96)*						
Mean (SD)	67.7 (13.2)	65.4 (10.7)	66.4 (13.3)	63.6 (18.6)	56.9 (15.7)	50.4 (17.5)
Min	54	49	33	26	25	17
Max	87	85	77	80	86	88
Median	64.5	65.0	70.5	71.0	54.5	49.0

**Higher score denotes greater QoL.*

For RCT participants, the FACT-B total mean score was relatively high, and varied little, across both groups and timepoints (between 100-104.1 in all instances). However, individual scores

were across a wider range in the waiting list control group (55 – 118 at T1), with lower minimum and maximum scores compared to the intervention group (89 – 135 at T1). From the descriptive data, there appeared to be a very small improvement in the mean score for the intervention group (103.1 to 104.1, change of +1.0) versus a small deterioration for the waiting list control group (104.0 to 100.0, change of -4.0) post intervention period.

The FACT-G mean scores were again largely similar across study groups and timepoints. The intervention group demonstrated minimal improvement in the mean score from baseline to 12 weeks (75.6 to 76.0, +0.4) whilst the waiting list control group had a more notable deterioration (75.5 to 72.7, change of -2.8). Though the intervention group (I) had a slightly lower minimum score at baseline (score ranges 42-100 vs 43-95 for waiting list controls, WL) this demonstrated a much higher increase at 12 weeks (64-101) when compared to the waiting list control (45-85).

Overall, FACT-B TOI scores ranged from 26 – 87, with a wider range of scores and lower minimum and maximum values observed for the waiting list control group at baseline (WL 33 - 77 vs I 54 - 87) and 12 weeks (WL 26 - 80 vs I 49 – 85). Both groups demonstrated a similar deterioration in mean scores from baseline to 12 weeks, though this was slightly larger in the waiting list control group (66.4 to 63.6, change of -2.8) than in the intervention group (67.7 to 65.4, change of -2.3). The maximum score was highest for the intervention group across all three measures at both baseline and 12 weeks. However, as an overall group, all mean scores (FACT-B total, FACT-G and FACT-B TOI) deteriorated over time.

In light of the small sample sizes and the potential for skewness in the distribution of the data, median scores were also calculated. As the median is less influenced by the presence of outliers, this presented a more accurate indication of the central tendency of the data (Table 8.9). This in fact highlighted a pattern of overall deterioration in FACT-B and FACT-G median scores for the intervention group, compared to overall improvement in these scores for the waiting list control group. FACT-B TOI scores, on the other hand, demonstrated minimal improvement across both arms. As an overall group (RCT), the pattern of deterioration observed across mean scores over time was on the whole mirrored in the median scores (except for median FACT-G which demonstrated an improvement of +1, from 75.5 – 76.5).

There was no evidence of floor or ceiling effects for FACT-B total, FACT-G total or FACT-B TOI; none of the participants scored the minimum or maximum value for any of these measures.

Looking to the sub-study, descriptive data for FACT-B scores (displayed in Table 8.9) demonstrated a similar pattern of overall deterioration in mean scores (FACT-B total, FACT-G and FACT-B TOI), though this time change scores illustrated more substantial reductions.

Overall, across timepoints, mean scores were lower for all three measures in the sub-study when compared to the RCT. Furthermore, in the sub-study, minimum scores reduced across timepoints for each of the measures. For the FACT-B total score, the score range was similar at baseline (52-131) and 12 weeks (45-130). However, the mean score reduced from 89.4 to 82.6 (change of -6.8). For the FACT-G, the range again increased slightly due to a lower minimum score at T1 (41-95 vs 36-92), whilst there was a notable reduction in mean scores (67.3 to 61.4, change of -5.9). In the case of FACT-B TOI scores, the pattern of lower minimum scores (25 to 17) and deterioration in the mean score from baseline to 12 weeks (56.9 to 50.4, change of -6.5) continued, yet this time the maximum score increased slightly (86-88).

Floor and ceiling effects were not present across any of the FACT-B measures. For the FACT-B TOI, one participant (6.3%) scored the maximum possible score, though this fell far short of the 15% cut-off.

(ii) EQ-5D-5L

Baseline EQ-5D-5L data was available for all 21 RCT participants. As displayed in Table 8.10, this demonstrated a predominance of either no problems or slight to moderate problems, across all domains, for both study groups.

Overall, RCT participants functioned most highly in the self-care domain, with the vast majority experiencing no problems or slight problems in this area across both timepoints. Whilst the waiting list control group had a higher proportion of mobility problems at baseline, these remained relatively constant across the intervention period, with a slight increase in participants with severe problems after 12 weeks (from n=1 to n=2). Problems relating to usual activities were also largely absent or slight. The intervention group reported a higher proportion of moderate problems, yet these fluctuated little across timepoints. One participant progressed from extreme to severe problems with usual activities; this was the only reported instance of extreme problems. Pain and discomfort were predominantly absent or slight for the intervention group, with a small proportion of moderate problems reported; this pattern remained largely the same across timepoints.

For the waiting list control group, there was a lower proportion of moderate problems, alongside a small proportion of severe problems with pain and discomfort. Whilst the proportion of waiting list control participants with absent, slight or moderate anxiety and depression remained constant over the study period, a higher proportion of intervention participants reported no problems at 12 weeks (71.4%) than they did at baseline (20%).

Table 8.10 Pre and post-test descriptive profiles of EQ-5D-5L scores across studies*

	Intervention				Waiting list				Single arm sub-study			
	T0 (n=10)		T1 (n=7)		T0 (n=11)		T1 (n=9)		T0 (n=16)		T1 (n=14)	
EQ-VAS												
Mean (SD)	68.9 (16.1)		69.4 (16.0)		70.0 (12.2)		61.3 (29.5)		64.4 (16.2)		56.1 (17.8)	
Min, max	50, 99		50, 99		45, 80		10, 92		35, 90		20, 80	
Mobility	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**N**	**%**	**n**	**%**
1: No problems	6	60.0	3	42.9	4	36.4	4	44.4	9	56.3	7	50.0
2: Slight	2	20.0	3	42.9	4	36.4	1	11.1	2	12.5	3	21.4
3: Moderate	2	20.0	1	14.3	2	18.2	2	22.2	5	31.3	3	21.4
4: Severe	0	0.0	0	0.0	1	9.1	2	22.2	0	0.0	1	7.1
5: Extreme	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Self-care	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**N**	**%**	**n**	**%**
1: No problems	7	70.0	5	71.4	10	90.9	8	88.9	9	56.3	9	64.3
2: Slight	3	30.0	2	28.6	0	0.0	1	11.1	6	37.5	3	21.4
3: Moderate	0	0.0	0	0	1	9.1	0	0.0	1	6.3	1	7.1
4: Severe	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	7.1
5: Extreme	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Usual activities	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**N**	**%**	**n**	**%**
1: No problems	3	30.0	2	28.6	2	18.2	3	33.3	6	37.5	3	21.4
2: Slight	3	30.0	2	28.6	7	63.6	4	44.4	3	18.8	6	42.9
3: Moderate	4	40.0	3	42.9	1	9.1	1	11.1	5	31.3	3	21.4
4: Severe	0	0.0	0	0.0	1	9.1	0	0.0	2	12.5	2	14.3
5: Extreme	0	0.0	0	0.0	0	0.0	1	11.1	0	0.0	0	0.0
Pain & discomfort	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**N**	**%**	**n**	**%**
1: No problems	4	40.0	3	42.9	2	18.2	2	22.2	3	18.8	2	14.3
2: Slight	4	40.0	3	42.9	5	45.5	3	33.3	7	43.8	5	35.7
3: Moderate	2	20.0	1	14.3	4	36.4	2	22.2	6	37.5	5	35.7
4: Severe	0	0.0	0	0.0	0	0.0	2	22.2	0	0.0	1	7.1
5: Extreme	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	7.1
Anxiety & depression	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**N**	**%**	**n**	**%**
1: No problems	2	20.0	5	71.4	6	54.5	4	44.4	3	18.8	2	14.3
2: Slight	7	70.0	2	28.6	4	36.4	3	33.3	8	50.0	5	35.7
3: Moderate	1	10.0	0	0.0	1	9.1	2	22.2	5	31.3	7	50.0
4: Severe	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
5: Extreme	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

**1=No problems, 2=slight problems, 3=moderate problems, 4=severe problems, 5=extreme problems.*

The mean EQ-VAS score increased slightly in the intervention group (68.9 to 69.4, change of +0.5), whilst for the waiting list control group there was a more substantial deterioration (70.0 to 61.3, change of -8.7).

Significant (≥15%) ceiling effects were evident across all five domains, with a large number of participants reporting no problems (i.e. scoring 1) across domains and timepoints. This was most evident for the self-care domain (81.0% at T0 and 81.3% at T1), closely followed by the mobility domain (47.6% at T0 and 43.6% at T1) and the anxiety domain (38.1% at T0 and 56.3% at T1). Ceiling effects were less marked (though still substantially above the 15% cut-off level) across the domains of pain (28.6% at T0 and 31.3% at T1) and usual activities (23.8% and 31.3%), suggesting the presence of more varied responses (and, in this sense, the presence of problems). Overall ceiling effects (i.e. participants scoring 1 across all 5 dimensions) were present at much lower levels and fell below the cut-off for significance. These were evident in 4.7% (n=1) of cases at T0 and 12.5% (n=2) of cases at T1. Floor effects were not present (with only a single participant scoring at the extreme end of the scale for the usual activities domain).

Looking to the sub-study, scores across all domains were again largely reflective of no, slight or moderate problems, with minimal change across timepoints. Participants predominantly reported having no problems with their mobility at T0 and T1, with fewer reporting slight to moderate problems and one participant reaching severe problems by T1. Again, the majority of participants reported no problems in the self-care domain across timepoints. Where they did, these were slight to moderate, with just one instance of severe problems at 12 weeks. There was a higher proportion of slight problems with pain and discomfort at T0, yet this reduced at T1, with a small proportion of participants reporting severe (n=1) or extreme (n=1) problems. At T0, the majority of participants reported slight problems with anxiety and depression. By T1, this reduced, and a higher proportion reported moderate problems.

There was a notable reduction in the mean EQ-VAS score from baseline to 12 weeks (64.4 to 56.1, change of -8.3).

As with the RCT, ceiling effects were evident across all 5 domains and were, again, most significant in domains of self-care (56.3% at T0 and 64.3% at T1) and mobility (56.3% at T0 and 50% at T1), with the usual activities domain also demonstrating substantial ceiling effects across timepoints (37.5% at T0 and 21.4% at T1). Effects were equal across pain and anxiety domains, reaching the necessary cut-off of 15% at T0 (18.8%) but not at T1 (14.3%). Again, floor effects were not present (with only a single participant scoring at the extreme end of the scale for the pain domain).

(iii) CBI-B

With no missing item data for CBI-B measures across either timepoint, a total score was calculated for all participants returning questionnaires at baseline and/or 12 weeks. As displayed in Table 8.11, the actual score range for the overall group was 70-119 at T0 and 41-126 at T1. The sizeable reduction in the minimum score post intervention related to the score range for the waiting list control group (41-126).

The baseline mean CBI-B score was higher in the waiting list control group (97.1) compared to the intervention group (92.3). However, in the waiting list control group this reduced by 12 weeks (97.1 to 93.9, change of -3.2), whilst for the intervention group this increased (92.3 to 94.6, change of +2.3). Across the overall group, the median score deteriorated very slightly over the 12 weeks (95.0 to 94.0, change of -1.0). The pattern of change in median scores across intervention arms and the overall group mirrored that observed with the mean scores.

Table 8.11 Pre and post-test CBI-B total scores across studies*

	Intervention		**Waiting list**		**Sub-study**	
	T0 (n=10)	**T1 (n=7)**	**T0 (n=11)**	**T1 (n=9)**	**T0 (n=16)**	**T1 (n=14)**
Mean (SD)	92.3 (15.9)	94.6 (18.7)	97.1 (13.0)	93.9 (25.4)	83.4 (21.7)	81.1 (14.7)
Median	87.0	92.0	99.0	96.0	80.5	79.0
Min, max	70, 117	70, 124	75, 119	41, 126	41, 120	65, 115

** Potential total scores range from 14-126; higher scores relate to greater self-efficacy.*

Comparing to the sub-study, a small deterioration in the mean (and median) scores was also evident. In this case, however, the range of scores was wider, with a lower minimum score at T0 as opposed to T1 (as was observed in the RCT). This indicated a lower baseline self-efficacy for sub-study participants. A minimum score of 41 was again observed (41-120), this time increasing by 24 points at T1 (65-115).

(iv) SEMCD-6

A total mean score was calculated for all RCT participants who returned questionnaires at T0 and/or T1 (Table 8.12). At T0, the minimum score amongst RCT participants did not fall below 5.0 (with score ranges of 5.3-9.5 and 5.0-9.7 for the intervention and waiting list control groups respectively). For the waiting list control group, the mean score deteriorated across timepoints (7.3 to 6.8, a change of -0.5, with the median score remaining largely the same). For the intervention group, the increase in mean score observed over time (7.2 to 7.6, change of +0.4) was not reflected in the median scores, which demonstrated a slight deterioration (7.1 to 7.0, change of -0.1).

Table 8.12 Pre and post-test SEMCD-6 total scores across studies

	Intervention		Waiting list		Sub-study	
	T0 (n=10)	**T1 (n=7)**	**T0 (n=11)**	**T1 (n=9)**	**T0 (n=16)**	**T1 (n=14)**
Mean (SD)	7.2 (1.3)	7.6 (1.4)	7.3 (1.3)	6.8 (2.6)	6.2 (2.4)	5.2 (1.9)
Median	7.1	7.0	7.7	7.8	6.4	5.7
Min, max	5.3, 9.5	6.2, 10.0	5.0, 9.7	1.0, 9.0	1.0, 9.0	2.5, 8.0

Possible scores could range from 1-10, with a higher score indicating greater self-efficacy.

Comparing to the sub-study, there was notable deterioration over time in both the mean scores (6.2 to 5.2, change of -1.0) and the median scores (6.4 to 5.7, change of -0.7).

8.4.8.3 Estimation of effect size: RCT

Using the formula below, estimations of effect size based on the standardised difference between groups were calculated. Mean change scores are displayed in Table 8.13, with effect sizes calculated in Table 8.14.

$$[\text{Mean change score}_{I}] - [\text{Mean change score}_{WL}] \,/\, \text{pooled Standard Deviation}$$

Effect sizes were interpreted in line with the widely applied 'benchmarks' set out by Cohen (1988).[437] These state that a small effect size (*d*) lies in the region of 0.20, medium 0.50, whilst a large effect size equates to *d*= 0.80.

Table 8.13 Mean change scores across outcome measures for RCT participants

Mean change scores (SD)			
	Intervention	Waiting list	Overall group
	(n=7)	**(n=8)**	**(n=15)**
FACT-B total	0.6 (13.8)	-5.3 (10.7)	-2.5 (12.1)
FACT-G	0.0 (12.8)	-5.3 (8.5)	-2.8 (10.6)
FACT-B TOI	-2.0 (10.3)	-3.4 (7.3)	-2.7 (8.5)
	(n=7)	**(n=9)**	**(n=16)**
EQ-VAS	3.9 (11.7)	-8.7 (23.6)	-3.2 (19.9)
CBI-B	1.7 (12.3)	-3.1 (25.1)	-1.0 (20.1)
SEMCD-6	0.4 (0.7)	-0.6 (1.7)	-0.20 (1.4)

Table 8.14 Estimations of effect size

Measure	Effect size	Confidence interval (95%)	
		Lower	Upper
FACT-B	0.49	-0.78	1.29
FACT-G	0.50	-0.77	1.30
FACT-B TOI	0.16	-0.93	1.10
EQ-VAS	0.65	-0.68	1.36
CBI-B	0.23	-0.87	1.11
SEMCD-6	0.73	-0.65	1.42

In accordance with this guidance, the SEMCD-6 and EQ-VAS might be said to have the strongest relationships to intervention use (though of moderate effect size), with the FACT-B total score and FACT-G total score also estimated as having a small-moderate effect size. The CBI-B just about reached the threshold to be considered a small effect size, whilst the FACT-B TOI fell short of this. However, significant caution is warranted with any interpretation of these effect size estimations in light of the very small sample sizes and likely skewed distribution of the data. As such, these estimations and interpretations are purely explorative, to be considered in the context of the wider data, providing insight as to the potential strength of the relationship between variables (use of the intervention and the outcome measure in question). For larger sample sizes, and in contexts other than the feasibility setting, estimations of efficacy using inferential statistical techniques, supported by the calculation of effect sizes, would be appropriate.

8.5 Preliminary interpretations

Before moving on to analyse and interpret qualitative data gathered across the feasibility studies, some preliminary interpretations can be made on the basis of these quantitative findings.

➢ The feasibility of the recruitment strategy

Recruitment in the clinical setting fell short of target and expectations, achieving a rate of 22.6% over a five month period. The strategy was, however, supported by successes in online recruitment, evidencing the benefit of this hybrid approach to recruitment. The high level of

attrition potentially relating to participant characteristics may be difficult to overcome, making successful recruitment of larger samples of women living with SBC all the more important.

➢ The feasibility of the online recruitment strategy

Recruitment via online channels was much more feasible and effective, achieving a recruitment rate nearly three times greater than the traditional clinic-based approach (67%). Indications of self-selection bias, however, alongside plateauing interest, support a hybrid strategy which encompasses both online and 'off-line' sources of recruitment.

➢ The selection of appropriate outcome measures

The potential for women living with SBC to be highly functioning whilst also managing significant clinical burden must be considered when choosing appropriate outcome measures. Given the high percentage of ceiling effects across domains, the EQ-5D-5L may not be appropriate for distinguishing between highly functioning individuals. On the basis of explorative estimations of effect size, absence of missing data and near absent floor and ceiling effects, the SEMCD-6 may be the most appropriate of the measures assessed. However, a general pattern of deterioration for waiting list controls, particularly in the SEMCD-6 is notable. Whilst the potential for a 'waiting list control' effect has been touched upon,[391, 393] this observation may be more likely related to the progressive disease and clinical deterioration evident in this group. Yet it is difficult to draw conclusions in such a small and likely skewed dataset; determinations of efficacy are beyond the scope of this feasibility setting.

➢ The feasibility of delivering the clinically integrated intervention

Features for clinical integration did not pose additional burden to service delivery. However, the integrity of this component may well have been compromised due to challenges engaging health professionals.

➢ The integrity of study procedures

All study procedures outlined during study design were largely adhered to, though adjustments were made in line with COVID-19 restrictions and the need for more remote contact and follow-up. Greater specificity within the data collection forms (in terms of more in-depth sociodemographic and clinical information) would allow for improved contextual analysis across study arms and study settings. Use of software to perform minimisation randomisation was highly effective, resulting in a balanced sample across several stratification factors, despite its small size. Though not formally explored, allocation to the waiting list control group appeared to be acceptable to participants, evident in their discussions with the researcher at the point of allocation and in subsequent correspondence.

➢ The integrity and functionality of the LIBERATE and QTool websites

Few issues relating to the integrity and functionality of the LIBERATE website were reported. However, the external QTool website (hosting the symptom monitoring questionnaires) did encounter a number of technical issues. Though short term and easily resolved, these highlighted the difficulties of hosting a website across two domains.

8.6 Reflections

In terms of the next steps, key areas warranting further qualitative exploration include the high rate of declines encountered in the clinical setting, with health professionals potentially able to provide insights into barriers to recruitment. Furthermore, given the challenges engaging health professionals, the integrity of delivery of the clinically integrated intervention needs to be determined through patients' and health professionals' experiences. Whilst a relatively high rate of compliance was observed across both settings, these figures provide little information as to participants' acceptability of this component. Similarly, the website analytics data, whilst a valuable overview, requires further insight in order to determine how useful and relevant the various components were for women across varying trajectories. In the next chapter, qualitative data will be presented and interpreted in the context of the outlined quantitative findings. These will be integrated to provide an overview of feasibility which is informed by mixed methods and multi-perspectives.

Limitations and reflections on the overall feasibility evaluation will be explored.

8.7 Summary

Using a range of descriptive statistics, this chapter has presented key quantitative findings for the LIBERATE feasibility evaluation. To provide a definitive interpretation of the overall feasibility and acceptability of the intervention and its methods of evaluation, these must now be taken forwards and interpreted in the context of wider, qualitative findings.

Chapter 9: Feasibility Evaluation (II) - qualitative perspectives & integration of findings

9.1 Chapter overview

As is recognised throughout this thesis, the strength of multiple and mixed methods research lies in its ability to draw upon a variety of data and perspectives. For realist evaluators, qualitative data offers rich insights into wide reaching aspects of an intervention's feasibility and its surrounding context, which may not be uncovered through quantitative methods alone.

Having compared findings between studies using a quantitative 'lens', this chapter will now explore the collective perspectives of participants from across both study contexts, gathered through qualitative interviews and questionnaires. As part of the MMMR approach, these will then be integrated with the quantitative findings, providing further context and insights in support of the overall feasibility evaluation.

9.2 Aims

- To further explore feasibility and acceptability through qualitative and questionnaire data, providing a collective perspective from across study settings.
- To support and further the quantitative findings presented in the previous chapter.
- To provide a more informed overview of intervention feasibility through the integration of findings.

9.3 Analysis

9.3.1 End of study feedback

The results of the feasibility questionnaire, sent to all intervention group and sub-study participants at the end of their study period, were collated (using SPSS and Microsoft Excel) and analysed collectively. Where questions allowed for additional written feedback, responses were collated within an excel spreadsheet and narratively synthesised. The remaining questions assessed usability, feasibility and acceptability across various Likert scales. The results of these were collated and analysed graphically, supporting the interpretation of qualitative data and of the wider results.

9.3.2 End of study interviews

Across end of study interviews, distinct interview schedules for women and professionals guided an overall semi-structured approach to interviewing. Flexibility in the scope of topics

discussed permitted insights into the surrounding context as well as the intervention itself. For the health professionals, questions were focused on their areas of involvement (support in providing recruitment information to participants and their experiences and attitude towards clinical integration of results). All interviews were transcribed verbatim by the researcher and the data was collated and managed using NVivo v.12. A reflexive approach to thematic analysis was conducted, as detailed previously (chapters 3 and 6).[178, 183] Given the small size of the overall sample, transcripts from across participant and health professional interviews were viewed as a single data set, providing varying perspectives and exploring shared areas of discussion from differing angles. A single coding framework was therefore developed, with codes identified iteratively from the data. This inductive approach was taken to ensure that the reality of the intervention and its surrounding context was reflected, rather than being viewed through the lens of prior theoretical hypotheses. This was one piece of the overall 'jigsaw', which would later be interpreted in the context of the theory, the research processes and the wider results.

9.4 Results

9.4.1 End of study feedback

In total, 21 (of the 38 posted) end of study questionnaires were returned. This overall sample included 7 RCT participants (intervention arm) and 14 sub-study participants.

9.4.1.1 Ease of use

Consensus as to the ease of use and comprehensibility of the LIBERATE website appeared widespread (Figures 9.1 and 9.2). The vast majority of participants found it easy or very easy to learn how to use the website (100%), access the various sections (90.5%) and find the necessary information (81%, though one RCT participant did report difficulty locating the information they needed, whilst three reported it to be neither easy nor difficult). Furthermore, 100% of the participants questioned found it easy to understand the information provided on the LIBERATE website.

Figure 9.1 Reported ease of use of the LIBERATE website (RCT, n=7)

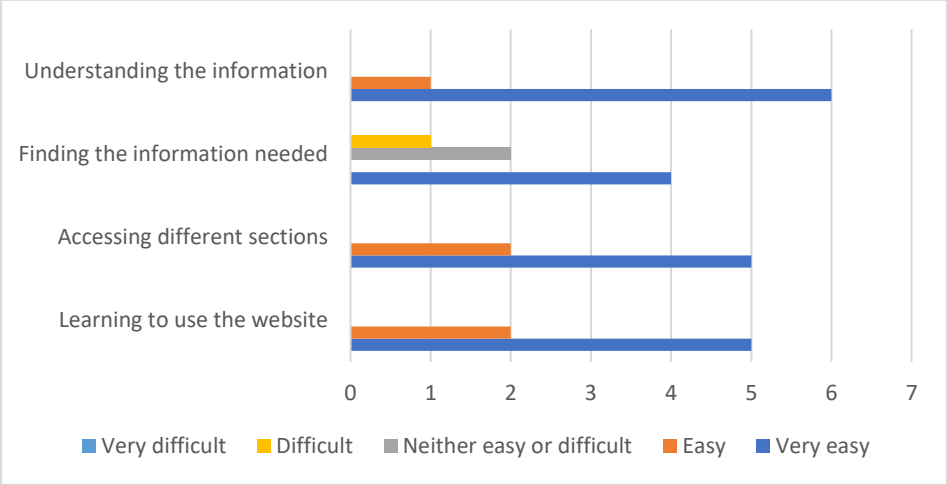
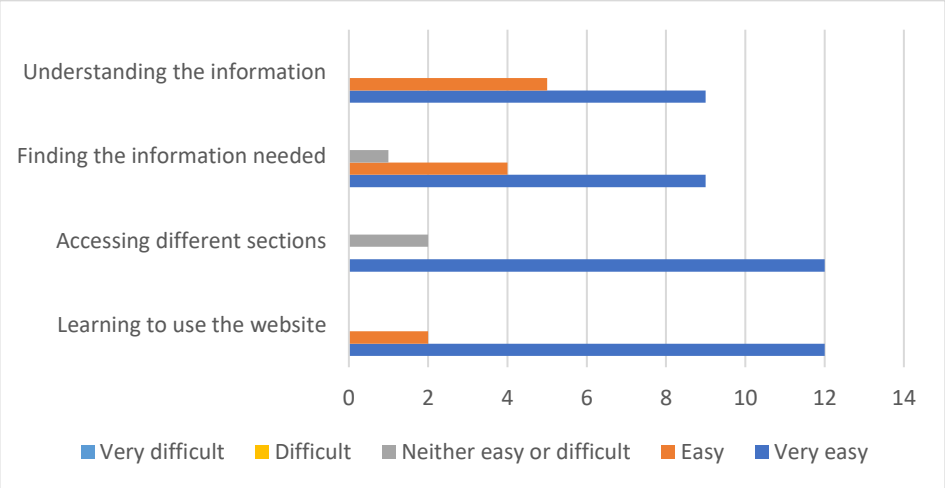


Figure 9.2 Reported ease of use of the LIBERATE website (sub-study, n=14)



9.4.1.2 Frequency of use & overall content

As displayed in Figure 9.3, the vast majority of participants across both studies reported frequent (weekly) use of the LIBERATE website (81%), whilst a smaller proportion used it every few weeks (23.8%). A minority of participants reported infrequent use, whether monthly (14.3%) or every few months (4.8%). Opinion was divided between those who felt the amount of information was 'about right' (71.4% for the RCT and 64.3% for the sub-study) and those who felt it was too little (28.6% and 35.7% respectively). When questioned as to whether anything important was missing from the website (Figure 9.4), a significant proportion of RCT participants (42.9%) and sub-study participants (50%) felt that there was. Generally, this related to a desire for greater detail in the information provided and an increased level of tailoring and specificity to SBC. Features supporting interactivity (e.g. forums) and improved signposting towards grass roots level organisations were also cited.

Figure 9.3 Frequency of use (RCT and sub-study)

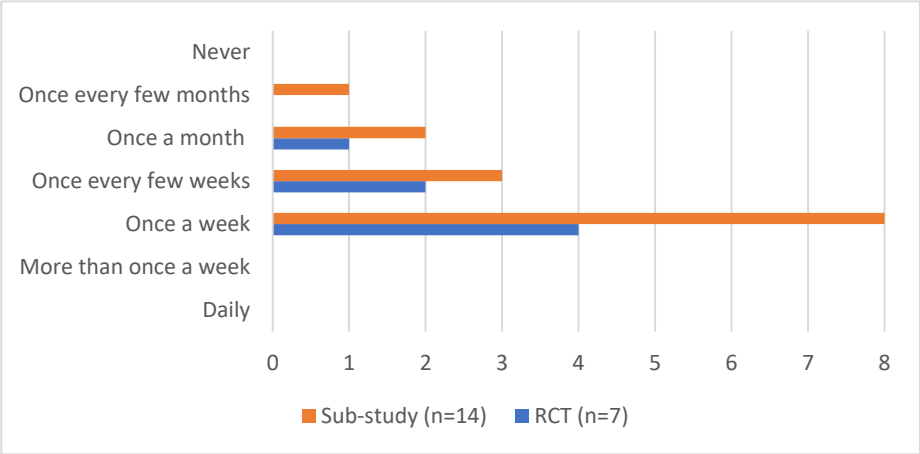
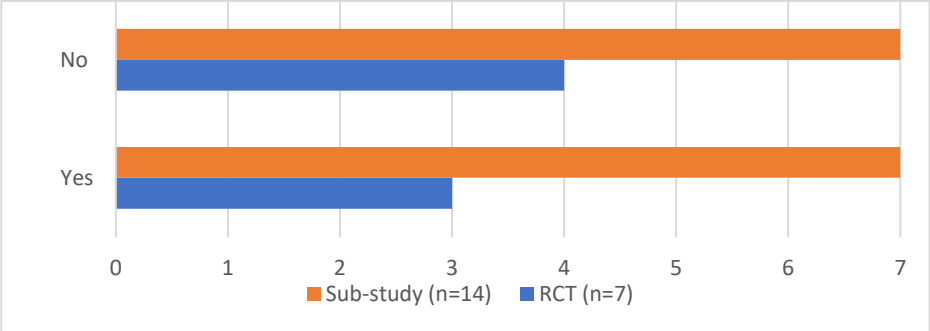


Figure 9.4 Content missing from LIBERATE website (RCT and sub-study)



Overall, opinion was mixed as to the usefulness of each of the core website components (Figures 9.5 and 9.6). The holistic health information was either very useful or a little useful for most participants; just one of the RCT participants found this not at all useful. The value of the case studies section varied, though this appeared to be more useful for those in the sub-study (85.7%) than the RCT (57.2%). Notably, 28.6% of RCT participants (n=2) found these not very or not at all useful. There was a level of uncertainty (38.1%) as to the value of the 'support for others' section, which may have been related to its wider intended audience. However, overall, 52% of participants reported it to be either very or a little useful. Thoughts on the signposting section were similarly divided, more so for the RCT participants. Whilst 57.2% found it very or a little useful, the remaining participants (n=3) were unsure, did not answer or did not find it at all useful. Its value appeared greater for those in the sub-study, with 92.9% finding the signposting very or a little useful (n=1 was unsure). Consensus as to the usefulness of the symptom monitoring component was less divided; in both studies, 57.1% of participants reported finding this very useful whilst 42.9% found it useful.

Figure 9.5 Reported usefulness of website components (RCT, n=7)

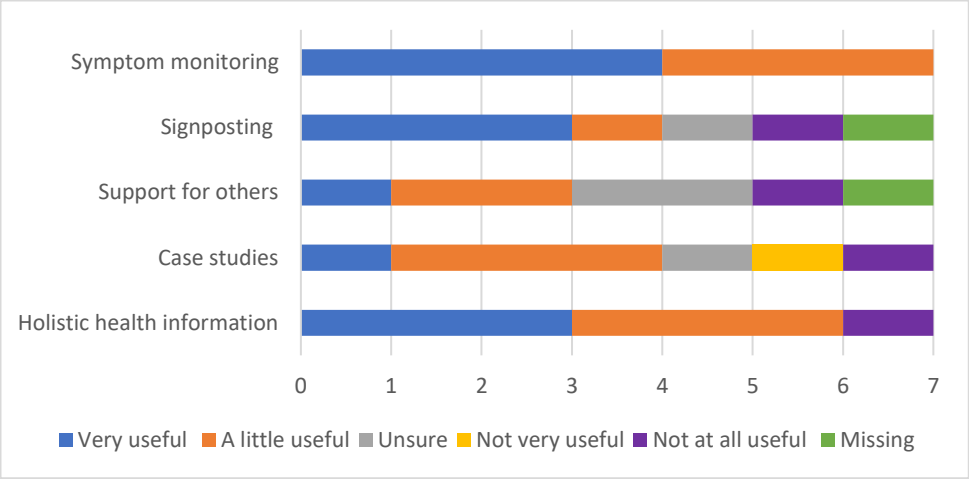
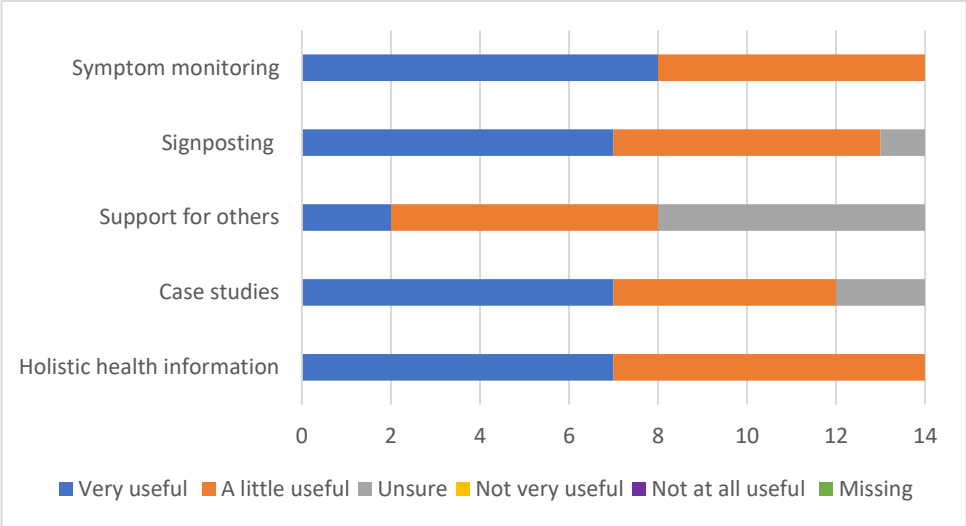


Figure 9.6 Reported usefulness of website components (sub-study, n=14)



9.4.1.3 Symptom monitoring: process & value

Overall, completion of the symptom monitoring questionnaires was both acceptable and feasible for most participants (Figures 9.7 and 9.8).

Most RCT participants were happy with weekly completions, with just one feeling this was a little too often. Acceptability of the requirement to monitor symptoms at least once a week was less clear-cut in the sub-study (Figure 9.7). Whilst 50% (n=7) found weekly completion definitely or a little too often, 42.3% felt this was the right frequency, with one participant stating that she would have been happy to complete more. As displayed in Figure 9.8, 95% of all participants felt that the amount of time it took to complete the questionnaires was 'about right' (one sub-study participant felt that the process was too long).

Figure 9.7 Frequency of symptom monitoring (RCT and sub-study)

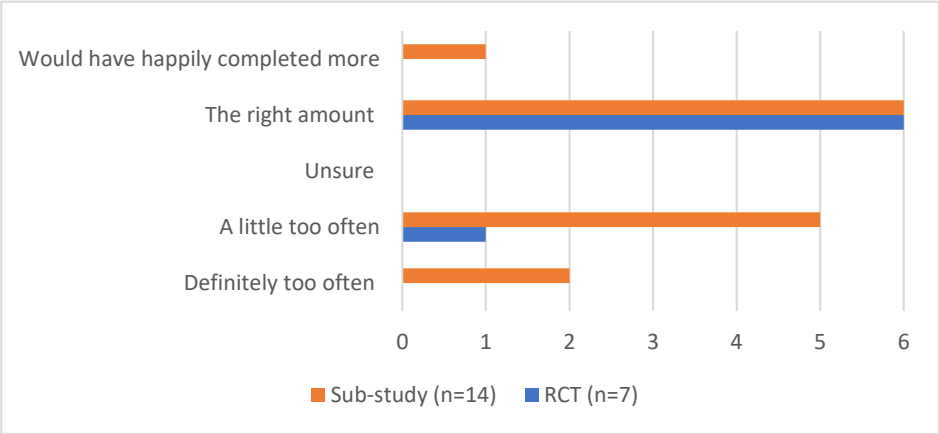
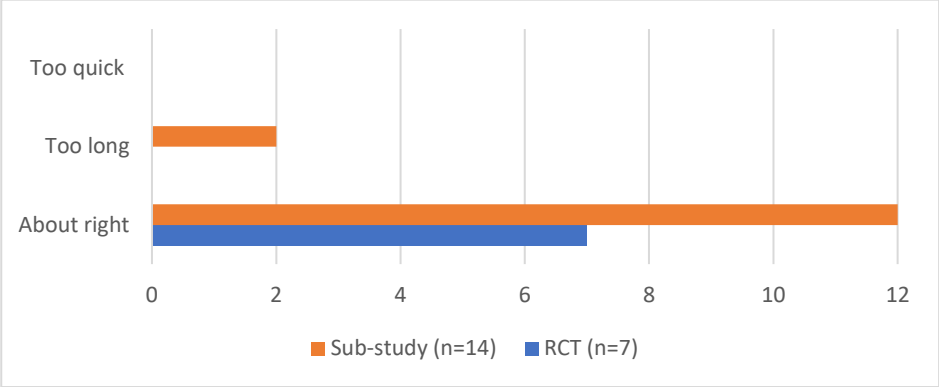


Figure 9.8 Time taken to complete questionnaires



Across both studies, 95% of participants found it very easy or easy to both access and complete the questionnaires (Figures 9.9 and 9.10), with just one RCT participant finding these aspects neither easy nor difficult. Within the RCT, 57.1% of participants found the symptom questions very relevant to them (the remaining participants finding them 'quite relevant'). Conversely, in the sub-study, just one participant found the questions very relevant to them, the vast majority reporting them to be 'quite relevant'. Overall, 100% of RCT participants and 85% of sub-study participants found the self-management advice generated by their responses to be very or a little useful. Those remaining (n=2, sub-study) felt that this was not very useful (Figures 9.9 and 9.10).

Figure 9.9 Ease, relevance & usefulness of symptom monitoring (RCT, n=7)

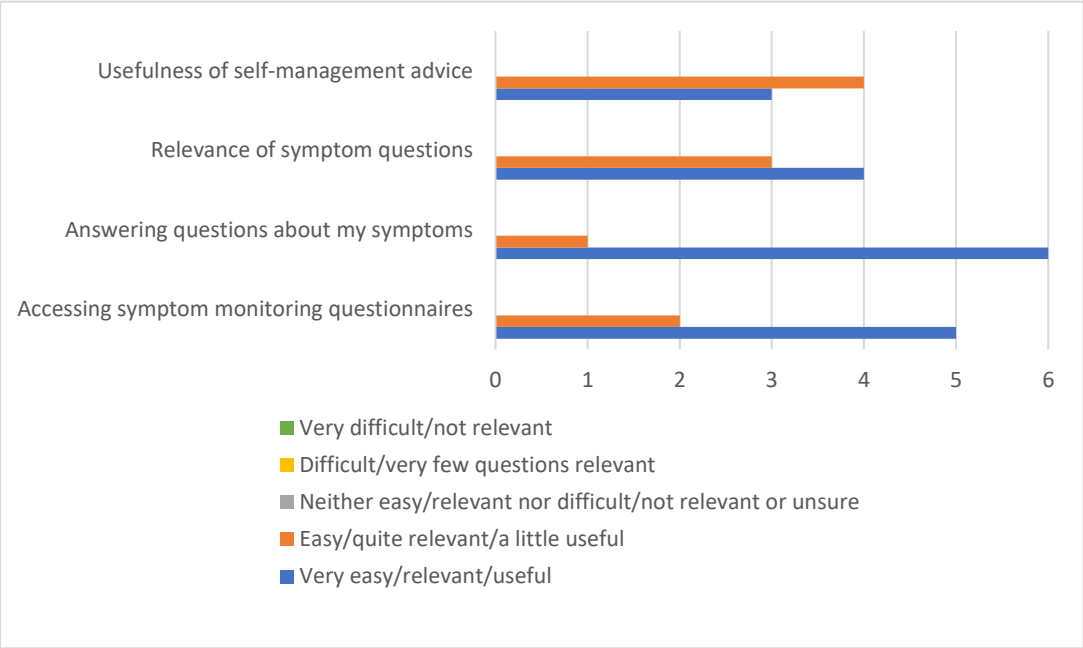
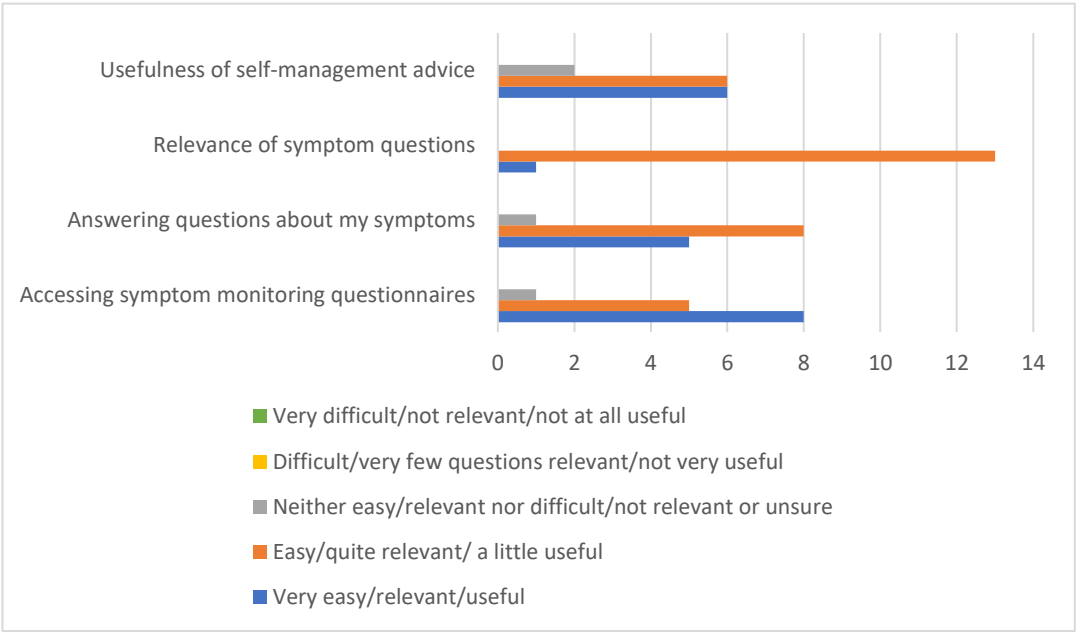


Figure 9.10 Ease, relevance & usefulness of symptom monitoring (sub-study, n=14)



Participants' experiences and thoughts on the value of symptom monitoring results within the clinical consultation varied (Figures 9.11-9.13). When asked if their clinicians had discussed their results with them, 42.9% (n=3) of those in the RCT reported that they had quite a bit, whilst 28.6% (n=2) experienced this sometimes and those remaining (n=2) hadn't at all. Participants in the sub-study were asked whether they themselves had raised their symptom monitoring results during interactions with their health professionals. Whilst one participant had done so 'quite a bit' and one 'sometimes', the overwhelming majority (85.7%) had not. Of the 5 RCT participants who had experienced this clinical integration, most (n=3) felt that this had improved their consultations 'quite a bit' and all agreed that these results were useful for

their health professionals to see. The 2 sub-study participants were divided in their opinions. One felt that the results had improved their consultations sometimes and were unsure of how useful they were for their health professionals. In contrast, the other felt that integration of their results had improved their consultations quite a bit and were very useful for their health professionals to see.

Figure 9.11 Reported use of symptom results in the consultation setting (RCT, n=7)

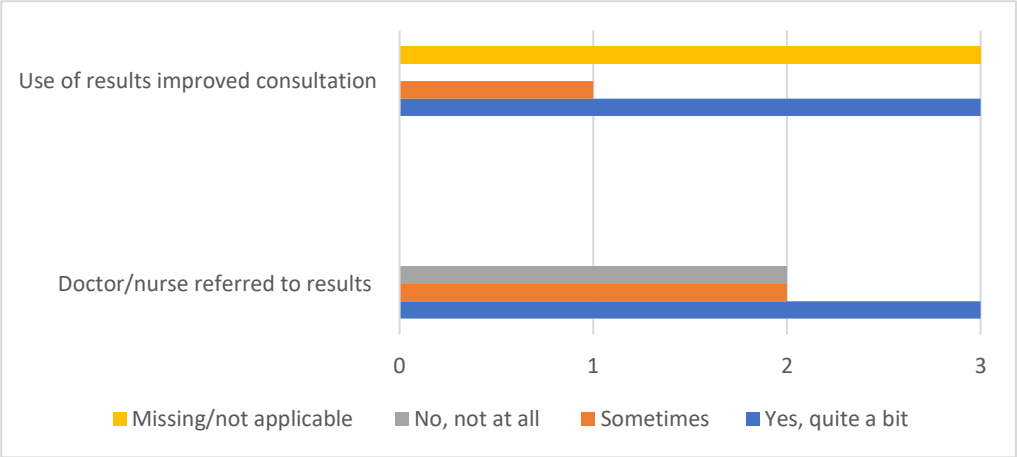


Figure 9.12 Reported use of symptom results in the consultation setting (sub-study, n=14)

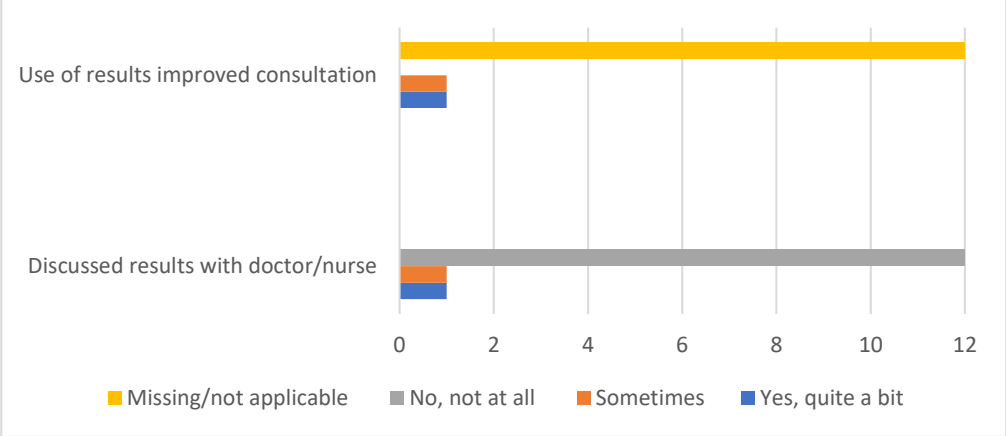
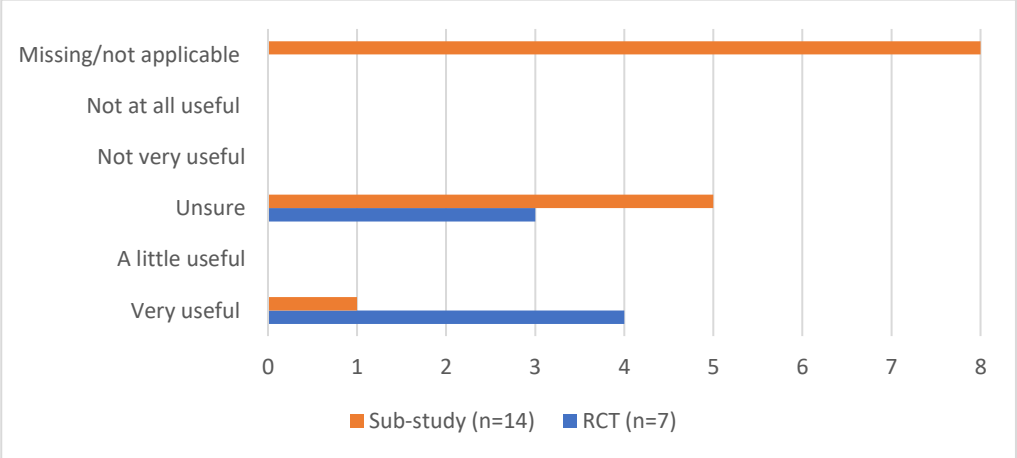


Figure 9.13 Perceived value of clinicians reviewing symptom results (RCT and sub-study)



9.4.1.4 Study involvement

Opinions as to the feasibility and acceptability of wider study requirements were largely positive (Figures 9.14-9.16). All participants were happy to complete the paper outcome questionnaires at baseline and 12 weeks, 95.2% feeling that the amount of time taken to do so was about right (the remaining participant felt that this was too long). Similarly, the overwhelming majority (95.2%) found the questions included in the outcome questionnaires to be very relevant or quite relevant for them (n=1 found them neither relevant nor irrelevant).

Figure 9.14 Time taken to complete study outcome questionnaires (RCT and sub-study)

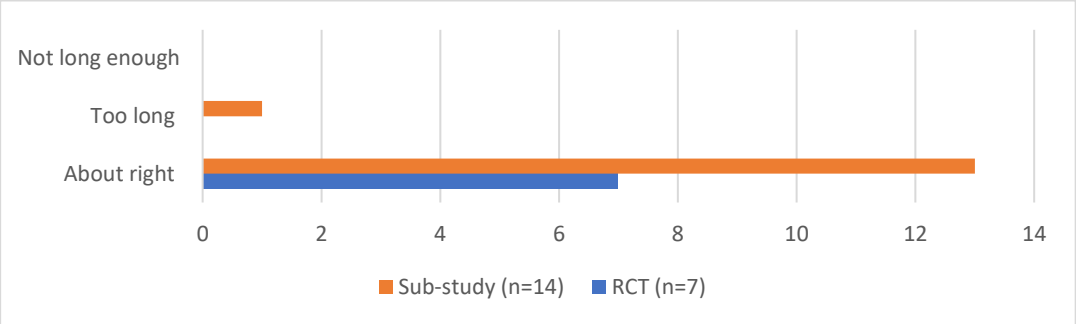
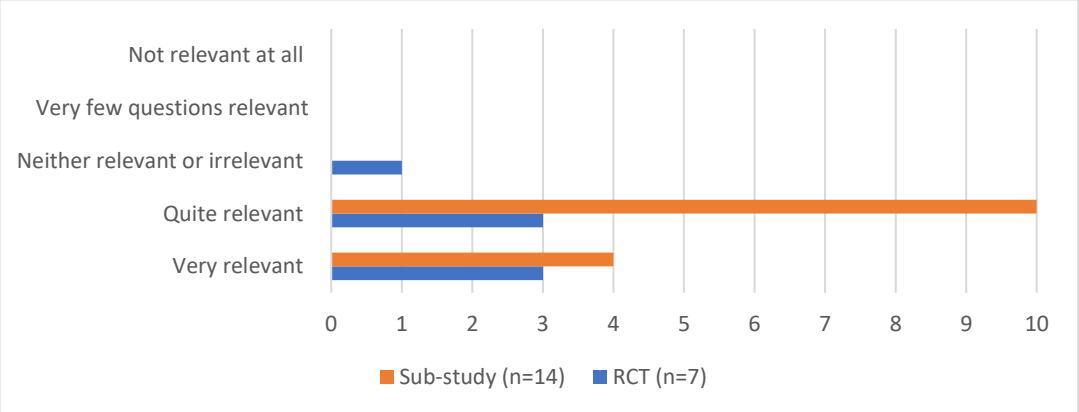
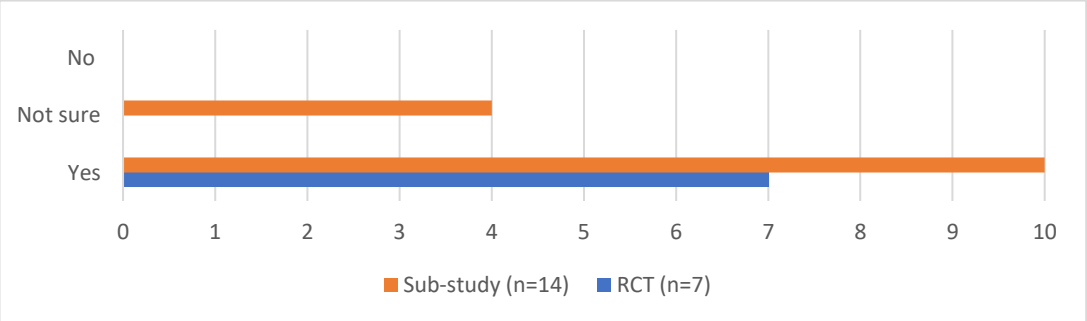


Figure 9.15 Relevance of outcome questionnaires (RCT and sub-study)



Overall, 100% of RCT participants questioned would recommend the LIBERATE website to other women. For sub-study participants, this was true in 71.4% of cases, whilst the remaining 28.6% (n=4) were unsure.

Figure 9.16 Recommendation of website (RCT and sub-study)



9.4.2 End of study qualitative interviews

9.4.2.1. Sample

Overall, 3 RCT participants (intervention arm) and 7 sub-study participants were interviewed. Despite a high rate of completion of 12 week outcome questionnaires, none of the waiting list control participants responded to the interview invitation.

Health professionals who had been involved with recruitment, or had engaged with the clinically integrated intervention, were also asked to provide some feedback. Overall, 3 health professionals were interviewed (2 Consultant Oncologists and 1 Lead Pharmacist).

9.4.2.2 Results of thematic analysis

From a diverse data set, drawing across varying contexts (clinical integration, independent monitoring and health professional-patient consultation) 4 core themes were generated. These were reflected within a breadth of discussions surrounding the LIBERATE intervention overall, the symptom monitoring feature as a pivotal component, contextual factors influencing intervention value and engagement, and considerations relating to research participation and evolution of both the intervention and SBC care.

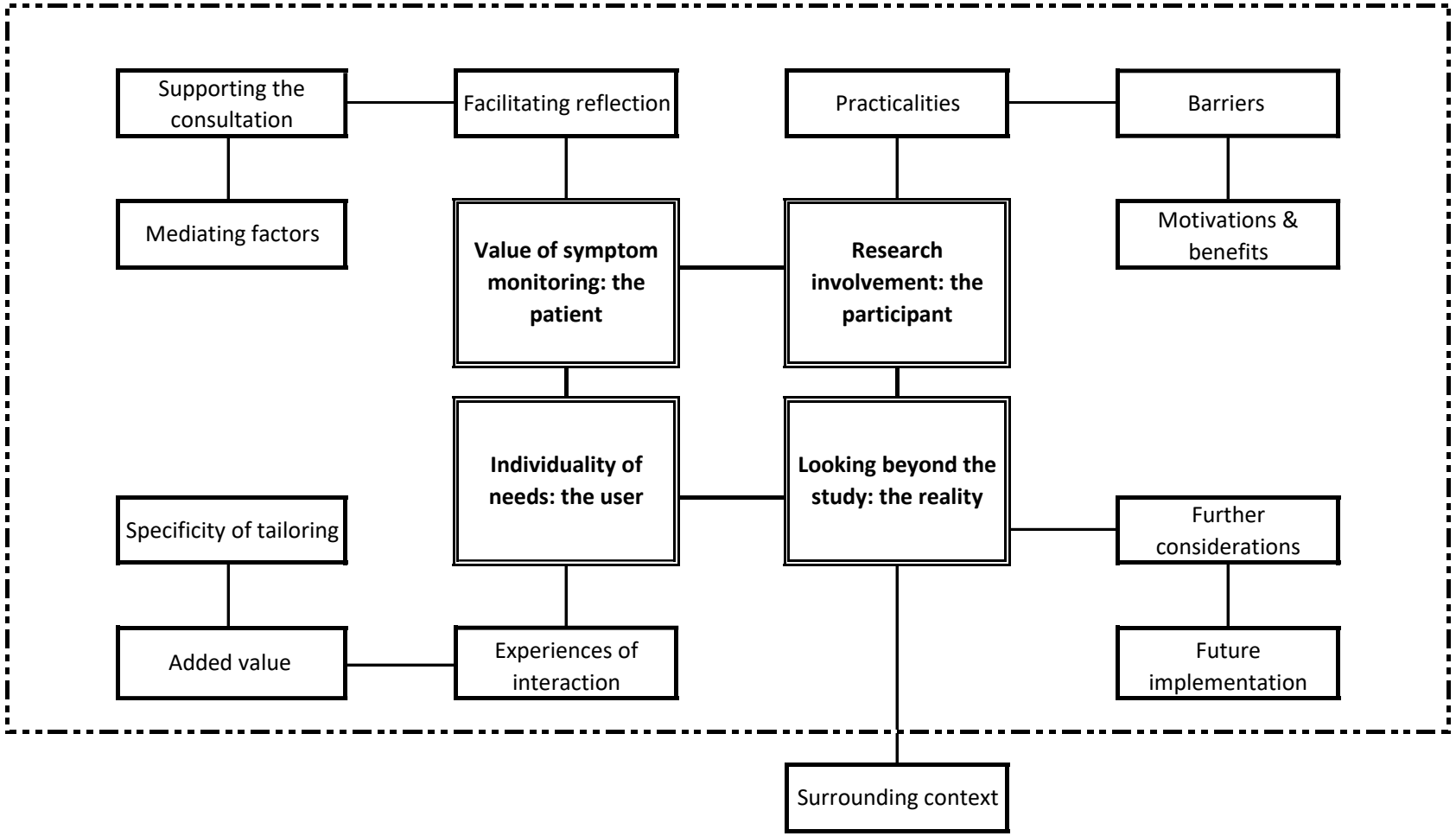
Each of the core themes centred around the range of roles women embraced, both inside and outside the study context. From these themes, a number of sub-themes were also identified. As part of the process of generating, reviewing and refining these themes, a thematic map was developed (Figure 9.17).

(i) Value of symptom monitoring: the patient

The symptom monitoring component was discussed as a pivotal feature of the overall intervention. For some women, this appeared to guide their interaction with the wider intervention; the LIBERATE website was not necessarily used independently of the symptom monitoring component.

The value of the process and outcomes of symptom monitoring was discussed widely, largely relating to the reflections prompted across both sides of the patient-health professional consultation. In this way, discussions surrounding symptom monitoring were embedded in women's role as the SBC 'patient'.

Figure 9.17 Thematic map: core themes and surrounding sub-themes



Facilitating reflection

Women across both the independent monitoring and the clinically integrated settings discussed feeling more supported to, and experiencing the benefits of, reflecting on their symptoms week to week. In facilitating reflection, this component of the intervention prompted participants to recognise patterns in the onset and timespan of their symptoms and to identify where self-management or further support was needed or, indeed, had resulted in a notable difference.

> *"…they took me off letrozole…as soon as that happened and I was pain free, I think you can see from my charts that it was a total turn around and my emotions were much more positive…and I charted that and I thought if nothing, if this questionnaire did nothing else, it pinpointed me at my worst but it also showed me that it's the pain that was doing everything. So, it was a positive reminder to stay on top of the pain…" (SS012)*

For some women, graphical display of results and the diary feature supported their reflections and broader interactions.

> *"… and the little graphs that you get at the end, I'm quite visual, so I quite liked those… and I mean I guess mine didn't move that much, but it was interesting to see some stuff moving up and down a bit… and I started to think oh actually if I look back… I think part of it is the simplicity of it isn't it?" (SS009)*

Increased recognition of the importance, as well as the presence, of symptoms also emerged.

> *"Sometimes you put a lot of things to the back of your mind because you're focusing on the 'big C' and the treatments and all that, and maybe you don't necessarily think about the other things unless somebody raises them with you and you think, oh actually I do have dry eyes! (laughs) You know, it doesn't seem an awful lot compared to everything else but yeah, so I suppose that, that's really good." (SS021)*

Women also discussed being able to reflect on their capacity to self-manage, with the tailored advice improving their ability to do so. Participants generally appeared to regard the self-management advice as useful and relevant, with examples of guidance and practical tips being of benefit.

> *"I found the like, you know, not sexual health but like the intimate questions … I think that questions like that, sometimes you don't feel comfortable broaching things like that with your consultant, especially if you're seeing males… so it was good that that kind of thing is there. Obviously, I've suffered with symptoms like that for ages but this actually suggested things for you to try and for you to use, which obviously you don't know about necessarily unless you research it yourself, so it was very helpful." (RCT017)*

Participants had divergent thoughts on the timing and frequency of reporting. For some, the regularity of weekly reporting supported them to reflect on their symptoms.

> *"…yeah, I think that's probably right because if you're doing it once a month, then monthly you kind of forget a lot of the stuff don't you? And on a week by week basis, it's interesting to look back… especially like when I had headaches and stuff, you don't actually, I'd have forgotten, once they get better you kind of then forget that you actually had them for as long as you'd had them, so yeah it was really good." (RCT017)*

For others, weekly reporting was too frequent for the level and extent of symptoms they were currently experiencing, resulting in minimal observable change. However, there was generally an appreciation of where this could be of value for themselves or others.

> *"…it was probably too regular for me, but I suppose if someone was having a lot of, ticking a lot of those back end boxes of having a lot of issues, then maybe they do need a weekly reflection… if I used it, I think it would be a monthly thing, but then all you need is a change in a symptom or a change in a scan result or something like that and suddenly… you know, things can change very quickly… so I think it's a personal thing, you could choose your regularity couldn't you?" (SS021)*

Supporting the consultation

Whilst discussion of independent reflection and guided self-management was widespread, few women reported feeling encouraged to discuss the results of their symptom monitoring with health professionals. Interestingly, the process and results of symptom monitoring appeared to be more widely used independently of women's interactions with health professionals; this was the case for participants across both the clinically integrated and independent monitoring settings.

For some women, the value of symptom monitoring results in supporting the consultation was instead discussed more as a potential benefit than a reality which they had experienced.

> *"I can't say whether they've used it as a tool because I don't know whether all of the team have been aware that I've taken part in the study… because you can save your results, you can look at them week on week, so you know, you could look back on them with them in an appointment over a month… there's a lot there that they can use…" (RCT002)*

> *"No, I didn't actually, no, it's not something I thought to do, it's something I perhaps should have done really, say that I'd used it to see what, what they thought…" (SS011)*

Perhaps reflective of varying levels of confidence and engagement in the health professional consultation, some women reported discussing symptoms without needing to refer to their symptom monitoring results. For others, whilst they hadn't discussed their results, they could see the benefit of doing so.

> *"…but you know I think these last couple of weeks I've had nearly everything happen so actually being able to put it all down, probably I think I would have taken it to my medics a bit more actually…" (SS009)*

One participant was pleasantly surprised when her health professionals referred to her results.

> *"… but I thought the symptom thing… because the first time I went to oncology after I'd filled the questionnaire in, I didn't realise, it didn't cross my mind that she was going to, I don't know what 'd thought but I didn't realise that they were going to see it and I thought actually that's quite, that's really good…" (RCT012)*

Interestingly, health professionals discussed the value of symptom monitoring as an aid to more effective and informative consultations, for both themselves and their patients, despite the apparent lack of shared discussion expressed by participants using the clinically integrated intervention. In some cases, this appeared more directly linked to health professionals drawing on their experience of using a similar (eRAPID-based) intervention, which was undergoing service evaluation at the time of interview. However, this allowed their general attitude towards the use of symptom monitoring results in consultations to be explored.

Health professionals reported the benefits (whether realised or anticipated) of being able to look across their patients' reports and patterns of symptoms in the time since their last consultation, leading them to follow up on those which were of clear importance to the patient (and to reflect on where this may have otherwise diverged from what they, as the health professional, would prioritise).

> *"…number one, prepping for that patient to walk into the clinic, I usually know everything before they've walked in the clinic, so it's kind of a personal experience for them, it's less time for them in there with me and so it helps me to plan that consultation and I think there are some issues where I might not think it's important but it's clearly very important for the patient and it brings those into the consultation so… very useful indeed." (HP003)*

The tendency for patients to under-report or forget symptoms was discussed by two health professionals; they found that they were better informed and better prepared to initiate conversations as a result of viewing patients' reported results ahead of the consultation.

> *"… I think it's quite helpful because usually, I'll say, you know, how are you and what problems have you had? And they don't always say all of the things that they've put on there so… either because they forgot or they didn't think it was actually that important, but sometimes if it's lots of little things, then that actually affects them, doesn't it? If you've got lots of little niggly things…" (HP001, experience of using LIBERATE symptom monitoring reports.)*

One health professional was less certain of the value of integrated symptom monitoring results in the 'traditional' oncologist-patient consultation. However, they felt that they could facilitate discussion of symptoms in the 'non-traditional' setting, where patients may not be reviewed face-to-face by their doctor on a regular basis e.g. telephone consultations, nurse led clinics and consultations with pharmacists.

"…maybe if nurse-led or pharmacist-led clinics were being used more widely then I think in that situation, this would be a useful addition, there would be more to gain…and I think in telephone consultations, where you don't have the benefit of, the focus is on the communication, yeah, I think that is an interesting idea." (HP002)

Mediating factors

Several factors appeared to mediate the value of this component and, indeed, the act of symptom monitoring in general.

Women tended to ground their thoughts on the value of symptom monitoring in their own symptom experiences. As alluded to, these varied widely and some women felt that they had few, if any symptoms to report, limiting its value.

"So yeah, so I found the tool fine, I think because my symptoms didn't change that much, I was just like (sighs) you know!" (SS009)

Another significant area of discussion surrounded women's experiences of chronic and other health conditions (physical and psychological) and how this posed a challenge to the symptom monitoring process. With questions very much focused on their cancer, women reported struggling to distinguish the origins of some of their symptoms, or being uncertain of what they should report.

"…that was the one thing that I found, you know, my pain levels can vary according to the weather… if it's cold, wet and damp, my arthritis pain is always worse, so you know, irrespective of anything else, at that week if you say how is your pain level? Well it's not good! But irrespective that I've got SBC, my pain level wouldn't have been good anyway…." (RCT002)

This was also apparent where different questions explored similar symptoms, such as pain of varying origins, with some women again feeling uncertain as to how to characterise what they were experiencing.

"Or whether it's, you know, I've got backache, do I just put backache or do I say you know, how can you tell if something is a muscular or a joints sort of pain? I've no idea!" (RCT012)

Several women also discussed aspects which would have heightened the level of tailoring the questionnaires offered and, in turn, the value and relevance of this component for them. The timing of reporting was highlighted as pertinent in relation to the stage of the treatment cycle and how these influenced symptoms, yet neither the questionnaires nor results were attuned to take account of this. One participant also wanted to be able to document where symptoms were present but currently under control due to treatments.

"…where you've got an ongoing problem but then, so in my case insomnia, but then it went away because I'm taking zopiclone but then there wasn't really a box to tick to pick that up, so I was still having the problem but I was sleeping due to the zopiclone…" (SS005)

The sensitivity and wording of the response options was a repeated area of discussion. Their sensitivity was queried in terms of their ability to accurately detect and draw out the significance of symptoms.

"Some of the options for the answer weren't always quite the answer that I wanted to give… if you know what I mean?" (SS019)

"I just needed a bit more, and from week to week, all I could do was answer in the same box because, although one week I might feel more tired than the next week, or you know vice versa, I couldn't, it all came to the same answer because that's where it's at yeah…" (SS014)

Furthermore, issues surrounding the response option examples used to reflect the different levels of severity were also widely discussed. There was a strong sense that these response options were not reflective of women's experiences or of their day to day life. References to 'housework/chores and shopping' were felt to be outdated and were not necessarily accurate indicators of symptom severity, since such activities were often performed regardless of symptom burden.

"… its sort of, it's a bit I suppose to me it's a bit black and white because just to give you an example, like 'e.g. shopping and chores', well I've done, I've cleaned the bath out and I've cleaned the sink out if I've got moderate pain." (SS021)

"… I did get fed up with the housework option, I don't do housework! Well I do (laughs) but what about heavy stuff like gardening or lifting or I don't know…" (RCT012)

For one intervention participant, their choice of response options also appeared to be driven by concern relating to her health professionals being alerted inappropriately, posing a potential barrier to accurate symptom reporting.

"…yes, they needed to be aware, but it certainly made me think, now do I want to go for that second level, because really, I don't need any help in managing the pain, I can do that myself, and it did make me sort of stop and think… and I was wondering if you'd get people who thought like me and thought I won't put that, you know, because I don't want to alarm anybody." (RCT002)

Conversely, a sub-study participant described the value of on-screen alerts (the independent monitoring equivalent of clinician alerts) and appeared far from deterred to report severe symptoms.

"…you sort of think, oh I'm not too sure, and because it says on there, if it's worse please contact… yeah, yeah so I have done…" (SS011)

Divergent opinions elicited from the health professionals also highlight the influence of their own attitudes, perceived value and willingness to incorporate symptom monitoring results.

> *"…our patients, you know, we have allocated up to half an hour with these patients and we'd all like to think we're quite reasonably good communicators to have good relationships with the patients so, there, there may be less of an unmet need in that situation." (HP002)*

> *"…and they clearly like you looking at it, you know, at least they think oh you've looked at it, because otherwise, if you don't, it's like, well what's the point of them doing it, you know? So I make a point of saying something about it every time because otherwise they, I guess they feel it's a little bit of, you know, a waste of time if you don't." (HP001)*

Women appeared attuned to such attitudes, describing varying approaches of their own health professionals and how this influenced their decision of whether or not to share their symptom monitoring results.

> *"…It's always very brief you know, yeah your scans are stable you know, end of, no one is really interested in my symptoms so…" (SS014)*

> *"I had one last week with him and I said to him that I had been able to track that, and track the pain and everything, because I'd just been having telephone conversations with him, and he was quite interested in it all and he's so supportive…" (SS012)*

(ii) Research involvement: the participant

Both women and health professionals discussed the decision to take on the role of a research participant in relation to a breadth of benefits, motivations and barriers, as well as the practicalities of recruitment and involvement.

Practicalities

Health professionals specifically discussed their role in supporting and informing this decision. All three felt that it was feasible for them, and other members of the clinical team, to support recruitment in the way that they did and they were happy to inform women of the study. One health professional added that the researcher's presence in every clinic ensured that these processes were feasible.

> *"I think the bit where it would cease to be feasible is where, if there wasn't one of you in the clinic. If you want doctors to do something on a reliable basis, you have to get somebody else to do it for them! And that would mean you would really need to get 'buy-in' from the nurses in the clinic to, to step into your role of reminding doctors to provide the information…" (HP002)*

> *"Well I think it's very straightforward for us, you know." (HP003)*

For the women interviewed, elements of research participation such as receiving weekly reminders to monitor their symptoms and the need to complete outcome questionnaires at

baseline and 12 weeks were widely accepted, supporting the feasibility of the study design. Indeed, some women embraced these as part of their role as the participant.

> *"Oh no I didn't think it was a burden at all, no not at all. It kind of just reminds you that you're doing it!" (SS021)*

Barriers

Health professionals' thoughts on potential barriers to participation were explored in the context of the high number of declines encountered during recruitment to the RCT. Whilst professionals were not certain of the underlying reasons, several expressing surprise as to the low level of uptake, a number of potential barriers were discussed. These largely related to the perceived time burden of participation, the potential for lower levels of computer literacy or other sociodemographic barriers, and the overwhelming amount of information women can be faced with in consultations.

> *"Yeah, and you know, some people who were maybe erm… have quite busy lives i.e. they're still working and all those kind of things were thinking, 'oh I don't know if it's going to take time to do it' but… you know so I kind of felt a bit of reluctance from those kind of people… I think it's a burden on them, that's what some people were worried about…" (HP001)*

> *"…so some people, in between their 3 weekly or their monthly visits, they just won't want to hear from us really, they want to go and live their life and some people are, won't be savvy on computers and won't want to admit that and will just… some people will say yes and will have no intention because it's just more information in an already information overloaded scenario, so I think it's not surprising in some ways that people will say no to an intervention like this…and I imagine that your patient cohort are in a younger age group… you'll have less of the younger patients, more of the older patients in those sort of, on tablets in the metastatic clinics…" (HP003)*

> *"…one of the concerns obviously, in any research is that we tend to, we get self-selecting, well-educated predominantly white patients…" (HP002)*

Women's differing supportive needs at varying points along the disease trajectory were also discussed as a potential barrier, as well as the current level of support that they receive.

> *"I think the ones who weren't interested were the ones who'd been on treatment for two years and don't really have any problems… but a few of them did say, I think it would be useful, it would have been useful at the beginning… so I think it is important, you know, when you catch people, and I think, you know, the whole thing about information specifically tailored to them is good. They tend to be kind of a well versed group of patients, don't they?" (HP001)*

> *"You know, you've got a heavily consultant led area, we see these patients at each treatment, so there may be less of an unmet need in that particular style of clinic than there could be in some other form…and I guess patients are maybe less likely to enrol in this if they feel that they, that they are getting the opportunity to unburden themselves of their symptoms…" (HP002)*

Motivations & benefits

From an alternative perspective, women were able to discuss their motivations for deciding to participate. These largely related to enjoyment and interest in taking part in research, as well as strong sense of wanting to contribute towards change and improvement of support for women living with SBC.

> *"It was all, it all felt about right and you know, I'm someone that, you know, I quite enjoy sort of taking part in research anyway because I kind of think hopefully it'll help ladies in the future, so you know, I'm, I've found it quite interesting to take part in really, I've found it all really good." (SS005)*

> *"I just think it's really important to feed into this kind of stuff and get it moving forwards…" (SS009)*

Several participants also discussed encountering benefits related to their participation in the study and use of the intervention. For one woman, this was related to the positive change it inspired.

> *"…it did inspire me to go back to the gym…I was so thrilled, because my husband had already started going back to the gym but I was terrified…and then when I went and I read this physical activity section, it really impressed on me how important it was, and my husband checked it all out, and I went back and swam, and I swam every day for a month…" (SS012)*

For another, participation seemed to support feelings of purpose, belonging and self-awareness.

> *"It was good, it was good… it sounds funny saying it gave me something to do, that's not quite what I mean but it made you feel a part of something and probably made you question some of the things that were happening to you that you were maybe taking for granted, made you, I suppose sometimes depress you and highlight how much can go wrong as well (laughs) but then I, suppose that's facing reality, being aware is better than not being aware…" (SS021)*

(iii) Individuality of needs: the user

The LIBERATE website itself was discussed in the context of a range of factors relating to the user (and information seeker) as an individual. In fact, the perceived value of the LIBERATE website overall appeared to be very much dependent upon the wide-ranging individual needs of the person accessing it, whether related to their information requirements, computer competency, supportive preferences or disease trajectory.

Experiences of interaction

When discussing their interactions with the intervention, positive feedback relating to usability and functionality seemed to traverse the group. All participants appeared to find the website generally easy to use and of a good level of functionality regardless of apparent expertise,

needs or expectations. Experiences of navigation, however, varied across individuals. A basic search function, combined with large sections of information on some pages, were raised as potential issues.

> *"So there's some really long pages aren't there? So I thought the information was really strong, and I thought it's fine that it's all in one page but it could be a bit overwhelming for some people…" (SS009)*

> *"On this other website I typed in the drug and it came up straight away, everything about it, the common side effects, so it was the search function, because I tried to do that on yours and it doesn't come up with what you want, you have to read loads and loads and loads to get to it…" (RCT012)*

Some women found the range of signposting links incorporated throughout the main content (directing them towards resources for further information) to be a positive feature.

> *"Yes, and I liked all the different links to different websites because you can go on to cancer research, you can go onto breast cancer now, but having somewhere where all the different information is pooled together, I thought was really, really good." (SS014)*

For others, this limited the scope of the LIBERATE website itself and several women had challenges navigating between sites.

> *"It was easy to navigate around… the trouble I had, it was, I had difficulty, or it was for me, I did get better in the end, but initially I seemed to go into what I was looking for, which was always about the nutrition and the physical activity, and then I seemed to get myself out and I wanted to be back in, do you know?" (SS012)*

> *"…and then to get from the symptom questionnaires back to the LIBERATE website wasn't always straightforward, I don't know why, but it didn't seem to be always." (RCT012)*

This alluded to different styles of interaction driven by differing supportive needs and, potentially, competency or confidence in navigating online resources.

Others suggested features which they felt would have improved upon or increased the frequency of their interactions with the website. Features supporting interactivity, such as discussion forums and support groups, were highlighted by multiple women and several felt that smaller, grassroots organisations could be better represented and directed towards.

> *"…I've found that out of all of the support and help that I have got since diagnosis, chatting to other ladies is the most helpful thing that I've found, you know, if you have any questions or queries, there's always someone that's been through it or who has got advice or reassurance… I think particularly with SBC that is really useful, so I think sort of a forum function would be really, really beneficial." (SS005)*

Added value

Discussing their thoughts on the intervention, women often referenced their developing expertise as experienced users of supportive resources, having sought out such information earlier on in their disease trajectory. In this way, any 'added value' of the intervention appeared to be limited by women's baseline knowledge and expertise.

> *"I mean I'd already known about a lot of the treatments because you know, I'm a person who sort of researches things to death, do you know what I mean? (laughs)… so your information I think would be really useful to somebody who's not, you know, familiar with a lot of the medical things, which is what you need, you need somebody to explain it to you…" (SS019)*

> *"… I mean, I guess you know, two and half years in, I've kind of done a lot of that sort of searching, but it doesn't mean that you don't then go back to it…" (SS014)*

> *"I'm perhaps not the best patient to do it because I've been with the breast unit for 15 years, so I've got quite a lot of knowledge that a lot of people won't have…" (RCT002)*

This wasn't always the case, however, and some women found the LIBERATE website to be a valuable addition to what was already available. In this sense, thoughts on 'added value' were also shaped by comparisons to some other online resources or alternative sources of support.

> *"No, to be honest, I thought it was one of the best, better websites that I've been on, I thought it was really good, because like the websites that I've been on before, they're good and they're informative but what I've found different about this is, whatever you'd answered, it kind of then led you on to something else, so it like directed you through to something else so yeah, everything was kind of there that you needed…" (RCT017)*

Specificity of tailoring

The importance of tailoring was frequently discussed in relation to the symptom monitoring experience, yet also in the sense of the overall intervention and its relevance to both the individual trajectory and shared experiences of SBC more generally. Participants highlighted this through discussion of their own needs, as well as recognising the varying needs of others.

> *"… I just think as I say, everything I've said is, you know, personal to me but I think, you know, it's a great thing moving forward… for someone else, they may want it every week and you know, they might not want all the detail, they might want it more simple so…" (SS014)*

For some, the level of tailoring didn't meet their individual needs in that the information they required was missing or lacking.

> *"And I think there was some stuff on food and diet… I think it could be more useful, possibly could do with a bit more information…" (RCT012)*

More broadly, some women seemed to find the overall intervention very much tailored to SBC, whilst for others this was less so. Again, this highlighted differing needs and expectations of the individual user, with the specificity and complexity of experiences of SBC seemingly not always catered for.

> *"I think it was like I was saying, you know, a lot of things are, rightly so, tailored towards primary breast cancer but there's not an awful lot tailored towards secondary and it did feel quite exclusive if that's the word, like being part of an exclusive area (laughs) so it was just yours, not blended… not that anyone wants to be in this club, but it does feel better in that way, yeah…" (SS021)*

> *"So it's with the secondary breast cancer, there wasn't anything that I could say was more towards the secondary breast cancer, just general…" (SS012)*

(iv) Looking beyond the study: the reality

Participants' discussions often extended beyond the bounds of the study, highlighting the surrounding context in which their interactions with the intervention were embedded, and looking towards further development and future change.

Surrounding context

The intervention was not discussed as an isolated experience, rather it was grounded within women's wider experience of SBC, past and present, and their day to day life. The ongoing COVID-19 pandemic (and their need to shield throughout this time) was discussed in relation to how this influenced women's supportive needs, their interaction with the intervention and their study engagement.

> *"… I think weeks, weeks come around quickly and, certainly in the current situation, weeks come around quickly because you don't have any sort of great structures to the day…" (SS021)*

> *"The only thing I wanted was like the Facebook sites or organisations that would help you, you know, especially with the COVID when you're on your own. That was my main thing really." (SS019)*

The need for support, and opinions as to the value of the intervention, were also justified in relation to women's experiences of living with SBC.

> *"…it's like living on quicksand because, you know, the couple of days before I go for my CT scan I don't sleep because you're wondering whether it's grown, if you get a cough or you get a pain, and I've had ear infections and chest infections, and you don't think, well it's just that you've got a cough, you always think that it's related, you know." (SS012)*

> *"… you're just floundering with this diagnosis really, you know, it's just so frightening to deal with…" (SS019)*

Access to support and experiences of care, past and present, also appeared to shape how women viewed the value and role of the LIBERATE intervention.

> *"Yeah, I mean, I feel like we have to work really hard to find anything about secondaries anywhere, so it's kind of like the more that's… you know I'm a bit ambivalent about the whole 'one stop shop' thing but actually if it was really good at doing what it was doing and signposting other things too…" (SS009)*

Further considerations

Considerations for extending or improving the intervention were widely discussed, with women reflecting on ways to ensure its use and value beyond the study context. Suggestions included expanding upon existing content, adding to and diversifying the case studies, ensuring that the signposting section was highly tailored and the overall website continually updated and evolving.

> *"…if they do continue to keep funding it and it becomes a really, really updated information, case studies and signposting site, then that would be good because it feels like that is something that doesn't really exist at the moment." (SS009)*

> *"Yes, I mean a lot of it I had read already but that's just because I had read around things but as I say, I'm sure that as it is built, you know and more, newer stuff comes on it'll be more and more useful… because there's nothing worse than old information is there?" (SS014)*

Functionally, women emphasised the need for a more advanced search functionality to allow for more refined and targeted use of the intervention, the ability to set personal reminders (to ensure that this feature could be implemented beyond the study setting), and to set more memorable usernames and passwords for the symptom monitoring component.

Issues relating to computer literacy, as well as limited access to or confidence using the internet, were also highlighted as potential barriers requiring further consideration. For one woman, the value of paper copies of supportive information remained.

> *"But I don't know what you do about people who are not technically literate, I just don't know what you do about those, you know, because I found it useful to inspire and to reflect, but if you can't even press a button or things like that, or it frightens you, I don't know, so there will always be that groups of people that you miss won't there?" (SS012)*

Future implementation

Reflecting on their own future, and the future of others with SBC, women expected, or were keen to discuss, plans for future implementation, with a desire for more urgency to extend support provision. Whether or not the LIBERATE website met their own supportive needs or

came at the right time in their disease trajectory, there was an overwhelming sense of positivity and desire for any research or support specific to SBC.

> *"Secondary patients feel forgotten about so it would be important to make this public asap and be sure that it's kept updated." (SS009)*

> *"…and it certainly needs to be out there, certainly the website side of it needs to be out there for SBC patients because we aren't served as well as primary BC patients." (RCT002)*

> *"I mean I just wish, I hope it carries on, I hope you carry on with it." (RCT012)*

This demonstrated where the intervention fitted in the wider context of available (or lacking) support, with clear gaps to be bridged.

> *"…we need all the help we can get." (SS019)*

> *"I think it's a real positive. I think secondary breast cancer does get left behind a little bit… because I suppose obviously on the more sort of like broad spectrum, everyone discusses breast cancer or different types of cancer but they never discuss the secondaries … but I thought it was good and hopefully you will do the website, you know, it will progress." (SS011)*

Health professionals discussed the future 'ideal' of support and care in SBC, looking beyond the study to the growing number of patients who will be accessing these services in the years ahead and to the limits of available resources. In this way, they mapped out the future of service delivery and outlined how resources such as LIBERATE could support this.

> *"I think we have to think about the future, the future is that the numbers of patients coming though is increasing, cancer is what? 1 in 3 at the moment, moving to 1 in 2 … breast care nurses cannot keep up with the numbers, nobody can really and that makes all these remote interventions really important." (HP003)*

> *"I feel the unmet need is less with the sort of service that we provide. Now I also happen to think that the service we provide is incredibly expensive, that paying ageing consultants to see patients every 3 weeks is simply, you know, is arguably not a sustainable way of delivery. Now if you had a service that was less indulgent in terms of the time that the patients get, then there might be more of a role for collecting information remotely, flagging up patients who need the additional intervention…" (HP002)*

9.5 Integration of findings

Building on the findings of the previous chapter, the outlined qualitative research has provided some important further insights and explanations. This section will now seek to interpret these collectively, integrating quantitative and qualitative data to piece together an overall picture of feasibility, with key results grounded in contextual findings and perspectives.

Collectively, findings are interpreted across the core domains or 'roles' which emerged in relation to women's interaction with the intervention, the study and their wider context.

9.5.1 The participant

Recruitment

The feasibility of the recruitment strategies was the crux of the overall feasibility evaluation. Despite an extended recruitment period, the RCT achieved a recruitment rate of just below 23%. Recruitment figures were unable to account for this low level; those declining without reason represented a significant 'blind spot' in the data. As the health professionals were the first point of approach, the researcher did not have a sense of potential barriers which may have led to such low uptake. This was, however, a focus of end of study interviews conducted with health professionals. They were able to provide context to the figures achieved, accounting for a range of potential sociodemographic, behavioural and clinical influences. These included barriers relating to internet and computer access, confidence and literacy, as well as perceived time burden and the potential for women to feel overwhelmed with information in the consultation or unwilling to encounter such information beyond the clinical context. Such hypotheses were reflected in the feedback of the smaller number of women who provided a reason for declining to participate. Counter intuitively, a higher level of existing support was also seen to be a barrier to recruitment by health professionals, a theory which was very much supported across participants' qualitative interviews and feedback. Encompassed by the notion of 'added value', thematic analysis drew out this limiting factor, with expert, well-informed participants (who, accounting for the suggested barriers, were those most likely to participate) gaining less, and requiring more, from the support provided by the intervention.

Comparing to the sub-study, a significantly higher rate of recruitment (66.7%) was achieved, providing strong evidence in support of online methods of recruitment. Observing the fluctuating rate over time, however, emphasised key learning points in ensuring that the process is dynamic (advertised across a range of interactive platforms and targeting different audiences/styles of use) and responsive to the ongoing level on interest. Despite the inherent self-selectiveness of this form of convenience sampling method, the sub-study had a very similar sociodemographic profile to the RCT (both samples of well-educated, predominantly white, married women with a high level of computer experience). Crucially, however, the mean age for the sub-study was notably younger (51.5 years) than that of the overall RCT sample (59.8 years). Furthermore, qualitative interviews highlighted that sub-study participants were generally highly engaged in research and supportive self-management

outside of the current study, which may have positively biased the results in terms of their level of engagement.

Attrition, withdrawals and missing data

Recruitment success aside, the online sub-study did not escape the high rate of attrition widely observed and anticipated across trials of ehealth interventions. In fact, it had a higher rate of attrition (30%) compared to the RCT (24%). In this sense, barriers to research participation did not appear to be confined to those declining to take part, or to be overcome at the point of recruitment. Whilst retention was clearly an issue, it was difficult to know at what point attrition occurred. Eysenbach distinguishes between attrition from the intervention itself ('non-use') and attrition related to follow-up,[419] yet the usage data across the LIBERATE studies was not sufficiently sensitive to make this distinction. All 3 participants failing to complete 12 week questionnaires in the RCT, for example, also had a symptom monitoring questionnaire compliance score of 0, yet this does not account for whether or not they used the LIBERATE website itself. Looking to the reasons behind attrition (at any stage), these were again difficult to explore. However, the wider literature points to some potential clues evident in the data gathered. A breadth of research into the high level of attrition which so often comes hand in hand with internet-based and ehealth studies suggests that certain participant characteristics can significantly influence drop-out. These include lower educational attainment, unemployment, single (unmarried) status and younger age.[420, 438-440]

Within the RCT, a higher proportion of the 'non-completers' were unmarried (60%). Furthermore, they were all retired or unable to work, whilst the employment status across the 'completers' was much more varied, with a number of participants in work or education. This suggested that those completing may have been in better health or more highly functioning, an assertion potentially supported by their significantly longer cancer trajectory (an average of 8.9 years between primary and secondary diagnoses for completers versus 2.8 years for non-completers). Indeed, sociodemographic factors increasing the risk of attrition may have been further compounded by the advanced stage of disease of all participants. Elsewhere, a review exploring reasons behind high rates of attrition across supportive and palliative care clinical trials highlighted a number of potential parallels to this research. Looking across studies, those conducted in the outpatient clinical setting (as was the case for this RCT) and recruiting participants with a high level of symptom burden at baseline, particularly fatigue (which was amongst the most frequently reported symptom across LIBERATE studies and treatment groups) were more likely to have higher levels of drop-out.[441]

Within the sub-study, non-completers were younger on average (compared to sub-study completers and RCT participants) whilst also predominantly retired or unable to work due to ill health, potential indicators of lower functioning or poorer health, which may have posed challenges to research participation. With both young age and unemployment previously highlighted as potential risk factors for attrition, as well as the use of online recruitment strategies more generally, this could explain the higher rate of drop out for the sub-study overall.

9.5.2 The user

The 'user' of the LIBERATE intervention appeared to fit a fairly distinct profile. Analysed collectively, baseline sociodemographic and computer usage characteristics demonstrated that women across both studies were predominantly white, married, highly educated and with a breadth of experience using, and access to, a range of technology. Whilst there was a general consensus across data sources as to the ease of use and comprehension of the LIBERATE website and content, again, looking to the characteristics of the samples across both studies, it is important to acknowledge that this may not be an accurate portrayal of the wider population. Users with less confidence and experience may have been those more likely to decline to participate, resulting in the recruitment of highly educated and computer literate groups of women who may in fact have had less value to gain from such an intervention. Indeed, outcome data demonstrated a high level of baseline self-efficacy across the board. This was further supported within interviews, with women frequently referring to information already encountered earlier on in their disease trajectory.

Varying levels and patterns of intervention engagement were evident both within and across studies, as highlighted across a range of different data sources. Though limited in its scope, website analytics data provided an overview of pages and components most frequently visited. The highest number of unique page views recorded was for the main homepage, suggesting that this was accessed more regularly in order to follow the link to the externally hosted symptom monitoring questionnaires (QTool). Users may not necessarily have returned to the LIBERATE website. This was supported within end of study interviews, with some participants describing use of the LIBERATE website largely guided by the links provided within self-management advice at the end of their online questionnaire completions, as opposed to the website being used in its own right.

Overall, opinion was mixed as to the value and usefulness of each of the core website components, reflecting the individuality of supportive needs. However, the symptom monitoring component stood out as being highly valued, regardless of context and despite the

fact that the clinical integration element was not necessarily harnessed. In this sense, it appeared that the LIBERATE intervention was most often used in its independent monitoring form. Digging a little deeper, caveats to the overall value of this component were evident. With an average compliance score of 0.6, engagement with regular symptom monitoring was generally lower in the RCT and slightly below the proposed frequency of once weekly (which would give a compliance score of 1.0). Again, looking to baseline characteristics, this may in part be explained by computer usage behaviour, with 30% of the RCT's intervention participants (n=3) reporting weekly-monthly use (as opposed to daily use for 100% of sub-study participants). Despite this, 85.7% of RCT participants providing end of study feedback agreed with the suggested frequency of completion. In contrast, qualitative feedback highlighted that sub-study participants were less happy to complete symptom monitoring regularly, despite a higher average compliance with weekly monitoring (0.73) and a much higher average number of symptoms per participant reported. This may be related to a high level of confidence and self-efficacy in self-managing, making such regular monitoring less beneficial. Ongoing compliance with weekly completion may therefore have been more related to interest and engagement in research for this self-selected group, as opposed to being a reflection of supportive need or perceived value.

Participants provided more detailed critique and suggestions for improvement within end of study questionnaires than they did in interviews. This highlighted the importance of incorporating an anonymous means of feeding back within any future study design. The content of this feedback further validated the suggestion that baseline level of expertise, and the extent to which supportive needs are being met at entry to the study, may influence individuals' expectations and perceived efficacy of the intervention. The level of tailoring did not appear to be specific enough to the individual experience of SBC; whilst some women described finding information very relevant to their trajectory, others did not recognise their own experience of SBC across what they felt was more general information. This may have explained the much lower use of wider aspects of the LIBERATE website, as evident in website analytics data. Some women suggested the addition of information which was already available on the website, supporting feedback relating to the need for a greater level of detail, improved navigation and a more advanced search functionality.

9.5.3 The patient

An array of data provided insight into women's interaction with the intervention as the 'patient', allowing its feasibility, acceptability and relevance to be explored in relation to both processes of care and the experience of disease.

Looking to clinical process measures across the RCT, surface level descriptive data indicated minimal additional burden on services in terms of additional contacts outside of the consultation and the number of alerts to clinicians generated. This was further supported by health professionals' interview feedback, in which the feasibility and value of remote symptom monitoring was widely acknowledged. The results of the symptom monitoring questionnaires themselves evidenced the appropriateness of this model of support, with the vast majority of symptoms reported across studies being mild in severity and therefore amenable to self-management advice and minimal clinical contact. Looking more closely, across both studies and treatment groups, there appeared to be a pattern of more chronic, regularly reported symptoms, against a background of transient, less frequently reported symptoms. This was reflected in the experiences of some women, who felt that they did not have enough change in ongoing symptoms to warrant such regular monitoring. Indeed, a number of women across the sub-study described having few symptoms to report, yet the average number of symptoms reported in this group was much higher than in the RCT. It may be that, when reporting milder symptoms, they did not consider these significant enough to constitute 'symptoms' or a 'symptom burden'. This was evidenced in the wider experiences of health professionals, who described a tendency for their patients to under-report symptoms.

Furthermore, the inability of the questions themselves (specifically the response options) to detect the subtleties of change across this chronic trajectory was widely expressed. In this way, though the symptoms covered were widely accepted and reported, it appeared that the questionnaires lacked the sensitivity and level of tailoring needed to both reflect and to guide the management of women's symptom experiences. Despite this, there was wide consensus as to the usefulness of the self-management advice, which may have been related to its relevance across differing experiences (and subtleties in severity) of the symptoms.

Overall, sub-study participants reported a wider breadth of higher level (moderate – severe) symptoms at a greater frequency, when compared to the RCT. This difference in reporting behaviour may have been related to the presence or absence of clinical integration across studies. One RCT participant described under-reporting the severity of some symptoms to prevent what she felt would be an unnecessary alert for her health professionals. The much higher number of both moderate and severe symptoms reported using the independent monitoring version suggests that these participants may have felt more free and able to report honestly, with clinical involvement self-initiated. Interestingly, across both studies, participants treated with hormonal and/or targeted therapies (treatment group B) reported a much higher number of symptoms than those treated with chemotherapy and/or monoclonal antibodies

(treatment group A), suggesting a greater symptom burden (and potentially, a greater need for self-management support) amongst this group of patients.

Supporting the interpretation of these results, more detailed analysis of the RCT participants' clinical picture provided insight into the complexity of the disease trajectory across this short window of time. Descriptive analysis of baseline clinical characteristics, for example, built up a picture of potentially more progressive disease (multi-site and more widespread progression, with later stage primary diagnosis or DCIS which went on to metastasize) for participants in the waiting list control group. This was later supported through more in-depth analysis of disease and treatment related events as the trial progressed and beyond. Whilst the vast majority of RCT participants had multiple clinical events across their 12 week study period, these appeared more concentrated across the waiting list control participants, potentially explaining their lack of engagement with the intervention beyond the waiting list period. Looking to overall survival, the fragility of disease was further evidenced with the death of five participants, all of whom were in the waiting list control group.

Despite this complex clinical picture, participants across both studies scored highly for self-efficacy and QoL at both baseline and 12 weeks, with overall mean scores for all 4 measures demonstrating relatively little change or deterioration in consideration of how much the trajectory was observed to fluctuate for some of these women. Yet the differing disease profiles, evidenced across the varying frequencies and timeframes of disease and treatment related events, provided further context. These helped to distinguish between what the outcome measures portray to be highly functioning individuals. Analysed collectively, it appears that participants were able to maintain a high level of self-care, mobility and usual activities despite clinical complexities. The high proportion of ceiling effects alongside the contrasting picture of well-being raises questions as to the appropriateness of the EQ-5D-5L for this group of patients. Indeed, with such high baseline self-efficacy and QoL, it is unclear whether the amount of 'added value' would be sufficient to be observed in any of the outcome scores. Though their interpretation is limited, estimations of small-moderate effect sizes generally supports this thinking. The SEMCD-6 demonstrated the strongest (moderate) effect size of the four measures. This, alongside a lack of floor or ceiling effects and evident acceptability given the absence of missing data, could suggest that it would be an appropriate measure for future, larger scale evaluation of the intervention.

9.6 Reflections

A strength of this evaluation was its multi-perspective approach, drawing on a breadth of data, from across varying sources, to provide a detailed overview of the intervention, the study methods and the context in which the intervention was evaluated. However, a range of concomitant contextual influences were likely to have been at play during the conduct of this research, with recruitment occurring during the COVID-19 pandemic and varying levels of national lockdown, resulting in disruptions and changes to both healthcare delivery and daily living. This may have influenced (any or all of) recruitment, retention and participants' level of interaction with the intervention and study, though to what extent it is difficult to say. Any conclusions drawn must therefore be done so in appreciation of this dynamic context.

Extending the analysis to provide a more in-depth insight into the disease trajectory of participants (though the use of a swimmer plot and a Kaplan-Meir curve) was invaluable to the overall evaluation. Without this perspective, hypotheses as to how the intervention might work (or indeed, why it might not) and for whom would not be grounded in the contextual realities navigated by women living with SBC.

Contextual insights were crucial to the evaluation of both the intervention and the studies themselves. Interviews with participants highlighted that they had not always been fully aware of the range of features of the intervention (i.e. clinical integration). It may be that the lack of face-to-face explanation and demonstration of the intervention at first approach had a negative impact on recruitment. Some of those who declined may have been more willing to participate if they had the opportunity to see all of the features and appreciate the minimal time burden. Given the restrictions in place in clinic in relation to social distancing and the use of PPE, alongside the evident anxiety and a sense of wanting to limit contact and time in clinic, this was not felt to be possible. Potentially limited awareness of and exposure to symptom monitoring results in the consultation setting (on both sides of the health professional-patient encounter), limited the extent to which clinical integration of the intervention could be evaluated. Indeed, with such small numbers actively using the intervention within the study period, and with increasing numbers of consultations conducted over the telephone (limiting the opportunity for the researcher to prompt clinicians to view results), the integrity of delivery of this feature was compromised.

Gaps in the data are reflected in a number of key limitations in the results. A large number of unspecified declines led to uncertainties in relation to the feasibility of the recruitment strategy. This may have been in part related to the context of recruitment; participants may have been reluctant to agree to any additional contact during COVID-19 and health

professionals themselves may have been reluctant to probe for a reason. Reporting the reasons why eligible individuals decline research participation has, however, been highlighted as crucial to overcoming barriers to research and strengthening studies going forwards.[442] Whilst health professionals offered valuable insights into a range of potential reasons, future recruitment strategies must seek to document this information more comprehensively. Though women with varying levels of symptom monitoring compliance were interviewed, the crucial perspective of those who engaged very little, or not at all was missing. Indeed, with none of the waiting list control participants taking up the invite to interview, their perspective and acceptability of this key aspect of study design (i.e. allocation to the waiting list control group) is missing. There were also crucial gaps in the website analytics data. A lack of specificity meant that it was not possible to distinguish between individual users, treatment groups, study arms (RCT) or studies. Furthermore, the data did not fully account for use of the symptom monitoring component, since participants may have been entering directly via the QTool website. On reflection, it would have been more insightful to be able to track individual participants' website activity using their unique username to monitor the types and frequency of webpages visited.

Across both studies, sample sizes were small and below the original targets set. Whilst this limited the interpretation of effect size estimations, this overall recruitment figure is still in the realms of what is considered acceptable in the feasibility setting.[415]

9.7 Summary

This chapter has presented a range of perspectives gathered through qualitative and questionnaire-based methods, building on the quantitative evidence (presented in the previous chapter) by providing wider contextual insights. Through integration of these findings, areas of strength and priorities for improvement have been identified, guided by the needs of women as SBC patients, research participants and intervention users. A need for heightened sensitivity to the individual and to the intricacies of disease was highlighted across several key areas and represents an overarching aspect of learning from the evaluation overall. This was pivotal in shaping the recommendations for future research and development, as will be outlined in the final chapter.

Chapter 10: Discussion & recommendations

10.1 Chapter overview

The call for further research and evidence-based support targeting women living with SBC continues to echo across the field of oncology. The LIBERATE project has sought to respond to this long-recognised need, placing women at the centre of efforts to develop innovative support tailored to their distinct stage of breast cancer, and to consider future steps for much needed implementation and on-going research. This chapter will summarise the key findings gathered across the overall LIBERATE project, highlighting how the identified research aims were achieved. Returning to the overarching critical realist perspective, findings will be discussed in line with the core 'context-mechanism-outcome' line of inquiry, guiding the identification of research implications in consideration of the intervention, the applied methods, and the wider research context.

In looking to take forward the findings of LIBERATE, it is timely to note that an update to the MRC's framework for the development and evaluation of complex interventions has very recently been published (at the time of writing), with greater emphasis now placed on intervention context.[443] This updated guidance very much supports and strengthens LIBERATE's critical realist approach, a summary of which will now be discussed.

10.2 Aims addressed

Overall, this thesis has outlined a multi-phase, multiple and mixed methods approach to the development and evaluation of an online complex intervention. Over the course of the preceding chapters, the following research aims have been addressed:

1. To explore the issues affecting QoL in women living with SBC.
2. To develop an online intervention designed to address the supportive needs and improve the QoL of women living with SBC.
3. To evaluate the feasibility and acceptability of this online intervention across two contexts:
    - Clinically integrated support: self-management activities directly supported through clinician involvement and close ties to the clinical setting.
    - Independent self-monitoring: guided self-management activities conducted independently in the community.

10.3 Overview of findings

10.3.1 Context

Phase I

Chapters 1 and 2 sought to ground the rationale and design of the proposed research within an evidence-based context. Setting the scene, chapter 1 highlighted the breadth of unmet needs of women living with SBC, alongside a paucity of targeted support. Exploring the evolving treatment landscape, the difficult balance between increased survival and the ongoing burden of symptoms and side-effects, which patients and their clinicians must weigh up and manage, was highlighted. The ultimate need for a QoL focus was therefore clear from the outset, as was the crucial yet changing dynamic of the traditional clinical consultation. The growing evidence base for the use of PROMs as part of a tailored approach to the remote monitoring of cancer symptoms and treatment side-effects was explored, supporting their proposed central role in subsequent LIBERATE research. Chapter 2 outlined the methodology planned in line with the MRC's framework for the development and evaluation of complex interventions, grounded in an overarching critical realist perspective.[116, 155] This guided consideration of the intervention context, mechanisms of action and proposed outcomes across both phases of research.

Building on evidence relating to wide-ranging and frequently unmet supportive needs encountered in SBC (discussed in chapter 1), the qualitative interview study outlined in chapter 3 sought to closely examine the lived experience of SBC across a range of contexts and through varying perspectives. Whilst threads of commonality were evident, women's narratives and professionals' experiences also highlighted the diversity and individuality of supportive needs, a breadth of which were identified. Varying levels of adjustment and acceptance were encountered across fluctuating physical and psychological trajectories, reflective of SBC experiences mapped out in the wider literature.[53, 54] Whilst the internet was highly valued and widely used, this did not overcome the need for face-to-face connection and reassurance, particularly in the form of health professional expertise. Again, this resonates with previous studies exploring patient preferences for information and support, in SBC and beyond.[64, 170, 369]

The next step was to explore how and, indeed, whether such multi-faceted support could be effectively delivered via remote and web-based technology. With the early research rationale justifying the intention to harness self-management, supportive information and signposting within a targeted online intervention, a systematic review was conducted (chapter 4) in order to explore the current evidence base for such approaches. The range of technology and intervention features used to address supportive needs in the context of advanced cancer was

narratively synthesised from across a breadth of RCTs. Casting the net wider to focus on all forms of late-stage cancer allowed for a more comprehensive overview in the face of limited SBC-specific interventions. Overall, the review demonstrated widespread efficacy relating to QoL and psychosocial well-being across a range of technology, confirming the potential for an online intervention to support QoL in women living with SBC. Furthermore, a need for interventions focused more specifically on (as opposed to being broadly inclusive of) advanced cancer was identified, further justifying the LIBERATE aims. Across multiple intervention designs and modes of delivery, Interactive Health Communication Applications (IHCAs) emerged as an effective model for addressing diverse supportive needs. Support harnessing varying levels of collaborative input, whether through peers or experts, was also evident across a breath of studies demonstrating efficacy in QoL and psychosocial measures.

Overall, these chapters collectively contributed to the achievement of research aim 1, gathering a breadth of evidence of issues affecting QoL in women living with SBC, and beginning to explore how these might be addressed.

10.3.2 Mechanism

Research aim 2 was met across the following chapters. Chapter 5 explored a range of theory, seeking an appropriate theoretical framework to support the delivery of an intervention which would address the range of issues elicited across the qualitative interviews. Collectively, the Middle Range Theory of Self-Care of Chronic Illness and Bandura's Self-Efficacy Theory were applied in line with programme theory, proposing theoretically driven mechanisms of change and action.[279, 287, 288] Self-efficacy was found to represent a fundamental determinant of QoL in the face of self-care requirements.[290, 313]

Chapter 6 brought together the range of research so far conducted, synthesising this within a target population-centred, evidence and theory-based approach to the design and development of the LIBERATE intervention.[319] Through expert consensus, the early proposed outline for a complex intervention was expanded upon, translating phase I findings into an intervention design comprising 5 core components: holistic health information, symptom monitoring support, case studies (experiences of others), signposting and support for others. Chapter 7 outlined the study designs for a dual approach to feasibility evaluation. Whilst an RCT, conducted in the clinical setting, evaluated the feasibility of a clinically integrated intervention, a single-arm sub-study applied online recruitment methods to allow for remote evaluation of the intervention in its independent monitoring form. Both were conducted using a mixed methods approach, allowing for in-depth consideration of the varying contexts.

Phase II

10.3.3 Outcome

Across phase II, outcomes centred around the feasibility and acceptability of both the intervention and methods for its evaluation, addressing research aim 3. Chapters 8 and 9 outlined the analysis and results of the feasibility RCT and sub-study, from which a number of key findings emerged.

(i) Feasibility of the study methods

Strategies for recruitment were found to be feasible when assessed as a flexible and hybrid approach, combining both face-to-face and online methods. Clinic based recruitment alone did not achieve the specified target and a number of potential barriers to recruitment, and reasons for decline, were identified. Health professionals involved in recruitment highlighted the potential for a range of barriers to recruitment, from the burdens of time and too much information, to a lesser burden of supportive need at certain points along the trajectory.

Despite minimal evidence of added burden on clinical services, the integrity of delivery of the clinically integrated intervention was variable. Poor engagement of health professionals appeared to be a key factor, exacerbated by the small number of intervention arm participants, meaning that the opportunity to review and discuss symptom monitoring results was limited. Furthermore, across both studies, there were further indications that the intervention may not have been delivered as intended; the symptom monitoring component appeared to be used in isolation to the wider intervention by some participants. Even in the clinically-integrated setting, most participants used the intervention in its independent monitoring form, to support self-reflection and self-management.

(ii) Feasibility of the intervention

Sensitivity was a core theme emerging throughout the overall feasibility evaluation, in terms of how capable intervention components (and evaluation outcome measures) were of identifying and addressing individual diversity across the wider SBC experience. Across both studies, participants felt that this was a key area for improvement. Whilst the systematic review (chapter 4) highlighted a need for interventions targeting advanced cancer specifically, the feasibility evaluation demonstrated that tailoring at the level of cancer stage is not targeted enough. The usefulness of the overall intervention appeared largely dependent on participants' level of expertise, experience in accessing support and, in some cases, the length of time since their diagnosis. Whilst the symptom monitoring feature was the most widely valued of the intervention components, users felt that the questionnaire response options lacked sensitivity to the varying degrees of symptom severity they experienced. Interestingly,

different symptom reporting behaviours were observed across study settings, with a wider breadth and higher frequency of moderate and severe symptoms reported by sub-study participants (in the absence of alerts to clinicians). Crucially, for the intervention overall, whilst widely acceptable, participants reported a need for greater detail and heightened tailoring of content.

10.4 Implications

An online self-management resource such as LIBERATE has the potential to bridge significant and ongoing gaps in the provision of SBC specific support. Future, further development must focus on heightening the level of tailoring and specificity in line with the diversity of the SBC experience.

The implications of these findings are two-fold. Overall, they have:

1. Contributed to a greater understanding of the SBC experience.
2. Informed future research conduct and priorities in the context of SBC.

Collectively, these could drive forward more tailored development and targeted evaluation of interventions such as LIBERATE, increasing the potential for successful and timely provision of much needed support.

10.4.1 Understanding the SBC experience

The LIBERATE research has contributed to much needed efforts to further and update our understanding of this evolving disease landscape.

Targeted timepoints

Returning to the programme theory, whilst potential key timepoints for use were identified in the development stages, these were not considered in relation to times at which support may be *less* needed. In other words, where a self-management intervention may provide less added value. For example, during periods of disease stability, low symptom burden or at a point along the trajectory where a level of expertise or self-sufficiency has been achieved. Experiences gathered within the qualitative interview study, alongside wider research in the field, suggested that unmet supportive needs were experienced right across the SBC trajectory.[58, 61] Women with evident expertise still expressed the need for improved and tailored support. However, within the feasibility setting, some women reported finding the intervention less useful, feeling it would have been of more value in different circumstances (e.g. if they were experiencing more symptoms or sooner after their diagnosis). This may have been related to the high baseline self-efficacy scored by participants across both studies. The

research itself may have drawn the interest of those more engaged in support and more capable and confident in meeting their own supportive needs. When asked to report unmet needs in the qualitative interview study, it may have been that participants did this on behalf of the collective (i.e. areas where tailored support in SBC is lacking more generally), rather than in relation to their own, current needs.

Similar findings were observed with the recently developed 'Oncokompas', an online self-management intervention for cancer survivors.[89] Looking to explain why 23% of participants did not use the intervention, researchers found that few or absent symptoms were the most frequently cited reason. Lack of time, interest and relevance to their individual circumstances were also reported.[444] Collectively, these seem to suggest that the intervention did not come at a time where it was needed or could be of value to these cancer survivors, who may have otherwise been going about their lives as 'normal'. Whilst these participants were treated curatively, many parallels can be drawn with the LIBERATE findings.

In the case of LIBERATE, though compliance with symptom monitoring was relatively high, engagement with the wider intervention was less so. Participants didn't always feel it was necessary for them to monitor their symptoms so regularly, though did so in line with the study reminders and in order to fulfil the study requirements. This was evident in the overwhelming majority of symptoms reported being mild to moderate in nature. It could be that those most in need of this intervention (i.e. those experiencing the highest symptom burden and/or the most unmet needs) were in fact those least likely to participate in research. Perhaps related to this, few of the participants recruited to the waiting list control arm went on to use the intervention after receiving access post study. This could well have been related to a high symptom burden or significant instability in their cancer, as was demonstrated when mapping the disease and treatment related events which occurred during their 12 weeks of participation. Furthermore, at baseline, the waiting list control participants had predominantly multi-site metastases, whilst the intervention arm had largely single site disease. This may have indicated more progressed and symptomatic disease for those in the waiting list control arm, with their support needs at that time potentially beyond the scope of what the intervention could offer.

Whilst this may have explained their lack of engagement, research has also demonstrated that poorer physical condition in advanced cancer is related to both greater levels of psychological distress and poorer self-efficacy.[300] Across study settings, those less likely to engage due to higher symptom burden may therefore represent those most likely to benefit. It could be that such interventions must be targeted at a point where the individual is well enough to engage, identifying the opportunity to develop self-efficacy so that a 'reserve' can be built for the times

when it is most needed. For those who did engage with the intervention, and who reported gaining little or no value, this reserve (demonstrated with high baseline self-efficacy) may have already been sufficient. Indeed, it is recognised that patterns of self-management will fluctuate in line with the trajectory of chronic disease; for example, behaviours may be performed episodically in response to changing demands, consistently for more on-going needs or for a shorter, defined period in response to a health crisis.[445] Returning to the SBC context, this may relate to Kida et al's conceptualisation of the acute and chronic phases of SBC, during which differing needs will demand differing levels of self-efficacy.[53] Across this varying trajectory, finding the key timepoints at which women can be most effectively targeted, and will be most able to engage and most likely to benefit, is therefore crucial to addressing their evolving supportive needs.

10.4.2 Future research needs & priorities

Specificity

Though all aspects of the LIBERATE intervention were written and targeted towards SBC, this stage-specific focus may still have been too generalised. Indeed, some participants did not recognise their own experiences or needs within the intervention. It may therefore be that LIBERATE is not sufficiently specific to the diversity of the SBC trajectory or sensitive to the distinct experiences which occur across this, informing a crucial area of future, further research and development. Whilst the symptom monitoring component allowed for self-management advice tailored to participant responses, it appeared that the response options themselves were not sensitive enough to the intricacies of symptoms experienced. Though the question items were SBC focused and developed with patient involvement, responses were guided by the broader cancer experience. Their lack of relevance again highlights the complexities of the advanced cancer trajectory; fatigue experienced during curative treatment may be a completely different entity to fatigue experienced several years into treatment for SBC. Echoing the concerns of earlier research, considering survivorship as an overarching experience may fail to recognise where the needs of those with advanced cancer differ.[17, 18]

Relatively minimal change was noted in outcome measures throughout the study period. However, as discussed, participants across study settings scored highly for both self-efficacy and QoL at baseline, which may in part explain the lack of observable improvement. Whilst efficacy of the intervention itself was not a focus of these feasibility studies, calculation of effect sizes guided the selection of appropriate outcome measures for potential future further evaluation. With the largest effect size (of moderate magnitude) and a total absence of missing data, the SEMCD-6 was found to be the most appropriate of the four outcome measures assessed. This supports, to some degree, the chosen outcome. However, future evaluation

may be strengthened by acknowledging the task-specific nature of self-efficacy as a measurable construct. Foster et al, for example, developed the Cancer Survivors Self-efficacy scale. This modified version of the SEMCD-6 incorporated 5 additional behaviours specific to cancer.[446] Gathering and reporting such measures in relation to individual or cancer-specific domains of functioning (e.g. self-efficacy relating to symptom management, accessing health information, relationships, emotional well-being, diet and exercise etc.), rather than a single, combined score, would allow for more in-depth and accurate assessment as to whether domain-level changes in self-efficacy occurred. As such, this would give a more definitive determination of whether the theory of self-efficacy (and the closely related Middle Range Theory of Self-Care of Chronic Illness) accurately explains the intervention. In a more applied sense, this would also allow for more targeted delivery of support in line with individuals' needs for self-efficacy in task-specific domains.

Supported self-management

Furthermore, looking to the recently evaluated eRAPID complex intervention, the crucial role of health professionals in supporting self-management was definitively evidenced.[108] In fact, the participants who benefited most from eRAPID were not only targeted at a specific timepoint (earlier on in their diagnosis and with a lower symptom burden), they were also actively engaged through discussions with their clinicians. The importance of this collaboration was statistically proven; clinicians' engagement with the intervention was linked to greater patient adherence (p= 0.02). Furthermore, higher adherence resulted in improved physical well-being for participants at 12 weeks (p= 0.01).[108] This supports the qualitative insights across the LIBERATE studies, with participants valuing the involvement and support of health professionals, collectively providing further evidence of the crucial importance of the 'supported' aspect of SSM. In the clinically integrated context, whilst most participants appeared to use the LIBERATE intervention to independently monitor their symptoms, improved engagement of health professionals may have encouraged more effective clinical integration and shared discussions. Though a more independent form of monitoring may be the preferred means of support for some patients, the option for varying degrees of supported self-management through health professional involvement is an element which undoubtedly warrants further development in future research. Indeed, the systematic review (chapter 4) demonstrated that, despite a shift in emphasis towards empowerment of the individual in self-management, the value of features for collaboration (whether with peers or professionals) in supportive interventions remains.

Looking beyond the LIBERATE intervention, there are a plethora of widely available mobile applications supporting more independent forms of symptom monitoring and self-

management in cancer.[447, 448] In the absence of any form of clinical integration, however (whether simple reminders to perform self-monitoring or direct integration of results in medical records, +/- alerts to clinicians) self-motivation of the patient becomes paramount. Returning to LIBERATE's theoretical underpinnings, motivation is a crucial factor influencing self-care behaviours. For these behaviours and skills to be maintained, so too must the patient's motivation.[449] Furthermore, Shannon highlights the role of health professionals in validating information derived through self-management resources, providing patients with both motivation and encouragement. Outside the clinically integrated or SSM context, this can easily be lost.[323, 450]

Timing is again likely to be paramount. For the vast majority of participants across both eRAPID and LIBERATE, their symptoms were mild to moderate. As such, they may have been at a point on their trajectory where independent self-management was sufficient. To provide more targeted support to women encountering fluctuating, ongoing and ultimately progressive disease and symptoms, it is important to recognise the points at which collaboration is key.

10.5 Strengths and limitations

Overall, this research has a number of key strengths. Integrating women's voice at both the design and evaluation stages ensured that the LIBERATE project was guided by the lived experience of SBC, channelling their vital perspective into an area which is significantly under-researched.

From a critical realist standpoint , this was crucial to exploring wide-ranging personal and contextual factors influencing the intervention's causal pathway. This allowed for a 'realistic' assessment of how future supportive interventions can be effectively targeted and successfully implemented in this underserved population. A multiple and mixed methods approach was well suited to the diverse research aims, supporting qualitative exploration of women's QoL, which went on to guide both quantitative and qualitative determination of intervention feasibility and acceptability. Though the research was limited by delays and restrictions imposed by the unfolding COVID-19 pandemic, methods were applied in a way which was both iterative and responsive, not only to the emerging findings but also to the evolving research and clinical context. Placing greater emphasis on online recruitment, for example, allowed the strengths of this remote pathway to be harnessed at a time where patients, clinicians and researchers alike were increasingly reliant upon and familiar with online platforms.

The importance of theory as a driving force in the development of complex interventions is widely acknowledged, yet frequently lacking.[318] The LIBERATE research therefore explored a wide range of relevant theories, integrating these alongside current evidence, frameworks and

guidelines, to determine a theoretically-driven and evidence based intervention design which was ultimately guided by the patient experience.

However, a number of limitations are also evident. On reflection, additional time spent in the development phase may have paid dividends in the evaluation phase. Though the intervention was guided by early qualitative research, as well as patients' collaboration in the expert consensus group and usability testing, greater involvement of women living with SBC during key developmental stages (e.g. collating website content and developing symptom monitoring questionnaires) may have resulted in the higher level of tailoring which appears to be lacking. Greater consideration of the diverse disease trajectory, which may have been incorporated with stronger emphasis on the 'person-based' (target population-centred) approach, may also have resulted in a more dynamic intervention. Frequent disease-related events and treatment changes, for example, were not reflected in the static symptom monitoring questionnaires, which themselves related to participants' baseline treatment. This may have contributed to reduced relevance and value of the intervention as women progressed through the study. Furthermore, had time allowed, the addition of COVID-19 specific information and support may have made the intervention more relevant and appealing to women and their current (potentially even more challenging) circumstances. In relation to this, the fact that routine clinical follow-up was being performed by telephone during this time meant that those who were seen in clinic tended to be in a much poorer state of health. This is clearly reflected in the women sampled, particularly the waiting list control group, with multiple instances of disease progression and deterioration observed in some cases. Women at this point on the disease trajectory (with deteriorating disease and potentially nearing the end of life) may have been less likely to engage with and derive benefit from the intervention. As such, different results may have been seen with a more diverse sample of in terms of participants' state of health.

Given the evident value of health professional collaboration in self-management, the significance of which has been highlighted across multiple areas of the LIBERATE research, their poor engagement was a key limitation. Though practical constraints relating to time and COVID-19 restrictions made it difficult to have discussions and face-to-face demonstrations with health professionals, more concerted efforts to engage them may have led to more successful and informative evaluation of the clinically-integrated intervention.

Looking to the future, there is a need to widen the reach of research in this area. The vast majority of participants identified as white, married or in a civil partnership, and were both highly educated and experienced in the use of computers and the internet. Again, thinking about who the intervention is targeting, it is likely that women falling outside of these sociodemographic categories may be more in need of a supportive intervention. Furthermore,

whilst embracing the increasingly rapid shift towards online and technology-assisted cancer support which has been intensified by the COVID-19 pandemic, there must be concerted efforts to ensure that individuals lacking the confidence, access and digital literacy required are not left behind. The value of the internet and digital health in supporting self-care and self-management must be carefully balanced with the potential for widening disparities in an already underserved group of patients.[451]

10.6 Recommendations

The below recommendations summarise the overall research findings, providing key actions to be taken forwards in order to implement change.

10.6.1 Future research

Future research conducted in the SBC setting should encompass the following considerations:

- Hybrid & responsive recruitment strategies

Recruitment strategies should be sufficiently flexible to evolve in response to emerging rates of consent and decline, incorporating a range of face-to-face and online channels. More inclusive strategies are also needed to ensure that research and support targets women from diverse socioeconomic and ethnic backgrounds.

- Urgency & innovation

More innovative, alternative forms of research should be explored. A service evaluation style of research may be more appropriate to the needs and clinical trajectory of this patient group, and more able to reach implementation with the level of urgency required. Seeing its use in the clinical setting may have made participants more likely to associate the intervention with their care pathway, as well as facilitating greater engagement of health professionals. Involving women more directly in future intervention development, through formal methods of Experience Based Co-Design, would also drive forward more successful targeting and implementation of support.[452]

- Specificity in outcome measures

Self-efficacy was measured (and improved) in evaluations of both the eRAPID and ASyMS symptom monitoring interventions, supporting this as a crucial driver and valuable measure for the evaluation of LIBERATE or other similar interventions going forwards.[106, 108] However, reporting measures in a way which reflects the recognised task-specific nature of this construct, making use of tools such as the Cancer Survivor's Self-efficacy Scale,[446] may highlight more nuanced change and support more targeted delivery of support.

10.6.2 Further and future intervention development

Further development and implementation of supportive interventions such as LIBERATE should also encompass the following:

- Higher level tailoring

A greater degree of tailoring is required to address the diversity and individuality of supportive need in SBC. The recently developed 'Oncokompas' intervention represents a key example of how such higher level tailoring can be achieved (using participatory design to develop an intervention which incorporates responsive, personalised feedback and support) and future interventions would be strengthened by learning from this approach.[89] Whilst LIBERATE achieves some level of responsive tailoring through the symptom monitoring component, this also needs to be reflected across the intervention as a whole. Just as targeted therapies are permitting increasingly personalised treatment, harnessing technological advancements in the application of algorithms and artificial intelligence will support the progression from surface level tailoring to more responsive, personalised cancer support.

- Evolving in line with clinical research

Development and provision of support must keep up with the pace of change in clinical research, as well as the pace of disease progression for women. Continued use of PROMs in the clinical trial setting will guide greater understanding of evolving supportive needs as new treatments continue to emerge. The ongoing development of an EORTC QoL questionnaire specific to SBC will greatly facilitate this.

- Advancing the evidence base for ehealth & self-management in cancer

Though the evidence base for ehealth as a facilitator of self-management across cancer survivorship continues to expand, more targeted research is needed to pinpoint the specifics of who can be most effectively targeted, at which crucial stages and timepoints, and on what particular treatments. This would help to ensure that the value of such interventions is maximised at times of greatest supportive need.

- Continued efforts to support clinical integration

Finally, whilst advances in the management of SBC continue to alter the context and dynamics of the heath professional-patient relationship, the value of a 'supported' element to self-management remains clear. The development of innovative technological infrastructure to support integration between the home and clinical settings (such as that developed within eRAPID) can only be realised through the engagement of both the health professional and the patient in this collaboration. For clinical integration to be most effectively harnessed, it may be that it needs to be viewed as very much a part of the patient pathway for both the patient and

professional. This sort of resource could be more valuable when directly embedded in the care pathway, as health professionals' experiences of an ongoing service evaluation demonstrated. As mentioned, this may remove some of the barriers to uptake and engagement (of both participants and health professionals) which were encountered in the LIBERATE study. However, evaluations conducted within individual services and trusts will not ensure the equity of access to support provision which is needed for all women to benefit.

10.7 Conclusion

Following a target population-centred, theory and evidence-based approach, the LIBERATE research has led to the development of a tailored, online intervention to support self-management in SBC, across clinically integrated and independent monitoring contexts. Whilst evaluation has demonstrated mixed findings in relation to the feasibility and acceptability of the LIBERATE intervention, this should be considered as the first stage of an iterative cycle of design and re-evaluation. A return to the development stage is clearly warranted, in order to build on elements of success and to incorporate a greater level of tailoring and specificity. Aspects of both the intervention and the study methods demonstrated clear feasibility, however, and should be taken forwards alongside the outlined recommendations to advance both support provision and research conduct in the context of SBC.

Overall, this research has contributed to the growing evidence base supporting the use of the internet and innovative technology to facilitate self-management across the spectrum of cancer survivorship. However, it still falls one step short of tangible action for the many women living with and dying from SBC. In order to harness and maximise the potential of technology supporting symptom monitoring and self-management, we must now narrow our focus and determine the patient characteristics and key timepoints on the trajectory which can be most effectively targeted.[453] Whilst this research has made an important contribution to better understanding the survivorship experience in advanced cancer, it is only through the translation and implementation of these findings that disparities in support provision will be addressed. Going forwards, support provision must be dynamic and responsive to this continually evolving disease and treatment landscape; the new treatments of today will shape the disease trajectories and supportive needs of future patients.

Research findings so often call for further research, yet patients' calls ring resolutely for urgent change. As scientists and clinicians continue to advance treatments and prolong survival for these women, there is an obligation to ensure that they are supported to live well, for however long their trajectory extends. This urgency of need must be reflected in urgent funding, conduct and, crucially, implementation of research findings and services to support

the needs of women living with SBC today. NHS England's upcoming national Metastatic Breast Cancer Audit, a landmark achievement of Breast Cancer Now's campaigning efforts, will support and encourage further research efforts, which I hope will further the findings of the LIBERATE project and shine a spotlight on the needs of these women.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer Journal for Clinicians. 2021;71(3):209-49.
2. Maddams J, Utley M, Møller HJBjoc. Projections of cancer prevalence in the United Kingdom, 2010–2040. British Journal of Cancer. 2012;107(7):1195-202.
3. Truant TL, Fitch MI, O'Leary C, Stewart J. Global perspectives on cancer survivorship: From lost in transition to leading into the future. Canadian Oncology Nursing Journal. 2017;27(3):287.
4. Rowland JH, Mariotto AB and Elena JW. Epidemiology. In: Feuerstein M and Nekhlyudov L, editors. The Handbook of Cancer Survivorship. Second edition. Cham: Springer International Publishing; 2018. p. 7-28
5. Marzorati C, Riva S, Pravettoni G. Who is a cancer survivor? A systematic review of published definitions. Journal of Cancer Education. 2017;32(2):228.
6. National Institute of Cancer. Dictionary of Cancer Terms: Survivorship [Internet]; 2020 [cited 2020 March 24]. Available from: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/survivorship
7. Twombly R. What's in a name: who is a cancer survivor? Journal of the National Cancer Institute. 2004;96(19):1414-5.
8. Rowland JH, Hewitt M, Ganz PA. Cancer survivorship: a new challenge in delivering quality cancer care. Journal of Clinical Oncology. 2006;24(32):5101-4.
9. American Cancer Society. Understanding Advanced Cancer, Metastatic Cancer and Bone Metastasis [Internet]; 2020 [Cited 2020 March 28]. Available from: https://www.cancer.org/treatment/understanding-your-diagnosis/advanced-cancer/what-is.html
10. Haylock PJ. Advanced cancer: Emergence of a new survivor population. Seminars in Oncology Nursing. 2010;26(3):144-50.
11. Maher J, Velikova G, Betteley A. Incurable, but treatable: how to address challenges for an emerging group. BMJ Supportive & Palliative Care. 2015;5:322-24.
12. Peppercorn JM, Smith TJ, Helft PR, DeBono DJ, Berry SR, Wollins DS et al. American society of clinical oncology statement: toward individualized care for patients with advanced cancer. 2011;29(6):755-60.
13. Harley C, Pini S, Bartlett YK, Velikova G. Defining chronic cancer: patient experiences and self-management needs. BMJ Supportive and Palliative Care. 2012;2(3):248-55.
14. Rainbird K, Perkins J, Sanson-Fisher R, Rolfe I, Anseline P. The needs of patients with advanced, incurable cancer. British Journal of Cancer. 2009;101(5):759-64.
15. National Research Council. From cancer patient to cancer survivor: lost in transition. Washington (DC): National Academies Press; 2005.
16. Richards M, Corner J, Maher J. The National Cancer Survivorship Initiative: new and emerging evidence on the ongoing needs of cancer survivors. British Journal of Cancer. 2011;105(1):S1-S4.
17. Mayer D, Green M, Check D, Gerstel A, Chen R, Asher G et al. Is there a role for survivorship care plans in advanced cancer? Supportive Care in Cancer. 2015;23(8):2225-30.
18. Park EM, Rosenstein DL. Living with advanced cancer: unmet survivorship needs. North Carolina Medical Journal. 2014;75(4):279-82.
19. Di Lascio S, Pagani. Is it time to address survivorship in advanced breast cancer? A review article. The Breast. 2017;31:167-72.

20. Moghaddam N, Coxon H, Nabarro S, Hardy B, Cox K. Unmet care needs in people living with advanced cancer: a systematic review. Supportive Care in Cancer. 2016;24(8):3609-22.
21. Sambi M, Qorri B, Harless W, Szewczuk MR. Therapeutic options for metastatic breast cancer. Breast Cancer Metastasis and Drug Resistance. 2019:131-72.
22. O'Shaughnessy J. Extending survival with chemotherapy in metastatic breast cancer. The Oncologist. 2005;10:20-9.
23. Cancer Research UK. Breast Cancer Stages, Types & Grades: Stage 4 [Internet]; 2020 [Cited 2020 Aug 18]. Available from: https://www.cancerresearchuk.org/about-cancer/breast-cancer/stages-types-grades/number-stages/stage-4
24. Cardoso F, Spence D, Mertz S, Corneliussen-James D, Sabelko K, Gralow J et al. Global analysis of advanced/metastatic breast cancer: decade report (2005–2015). The Breast. 2018;39:131-8.
25. Irvin Jr W, Muss HB, Mayer DK. Symptom management in metastatic breast cancer. The Oncologist. 2011;16(9):1203.
26. Breast Cancer Now. The Unsurvivors [Internet] Breast Cancer Now; 2019 [cited 2020 Aug 18]. Available from: https://breastcancernow.org/sites/default/files/bcn_theunsurvivors_campaignreport_oct2019.pdf
27. Vrdoljak E, Gligorov J, Wierinck L, Conte P, De Grève J, Meunier F et al. Addressing disparities and challenges in underserved patient populations with metastatic breast cancer in Europe. The Breast 2020;55:79-90.
28. Lu P, Santa-Maria CA, Ballinger TJ, Sheng J. Landmark trials in the medical oncology management of metastatic breast cancer. Seminars in Oncology [Internet] 2021 Jul 16 [Cited 2021 Sep 10]. doi.org/10.1053/j.seminoncol.2021.06.003
29. Santa-Maria CA, Gradishar WJ. Changing treatment paradigms in metastatic breast cancer: lessons learned. JAMA Oncology. 2015;1(4):528-34.
30. Sundquist M, Brudin L, Tejler GJ. Improved survival in metastatic breast cancer 1985–2016. The Breast. 2017;31:46-50.
31. Tevaarwerk AJ, Gray RJ, Schneider BP, Smith ML, Wagner LI, Fetting JH et al. Survival in patients with metastatic recurrent breast cancer after adjuvant chemotherapy: little evidence of improvement over the past 30 years. Cancer. 2013;119(6):1140-8.
32. National Institute of Cancer. Cancer Stat Facts: Female Breast Cancer [Internet] 2021 [Cited 2021 Sep 10]. Available from: https://seer.cancer.gov/statfacts/html/breast.html
33. Breast Cancer Now. Secondary breast cancer treatment [Internet] 2021 May [Cited 2021 Sep 10] Available from: https://breastcancernow.org/information-support/facing-breast-cancer/secondary-metastatic-breast-cancer/secondary-breast-cancer-treatment
34. Yersal O, Barutca SJ. Biological subtypes of breast cancer: Prognostic and therapeutic implications. World Journal of Clinical Oncology. 2014;5(3):412.
35. Figueroa-Magalhães MC, Jelovac D, Connolly RM, Wolff AC. Treatment of HER2-positive breast cancer. The Breast. 2014;23(2):128-36.
36. American Cancer Society. Breast Cancer Hormone Receptor Status [Internet] 2019 Sep 20 [Cited 2021 May 11]. Available from: https://www.cancer.org/cancer/breast-cancer/understanding-a-breast-cancer-diagnosis/breast-cancer-hormone-receptor-status.html
37. Louie MC, Sevigny MB. Steroid hormone receptors as prognostic markers in breast cancer. American Journal of Clinical Oncology. 2017;7(8):1617.
38. Cleator S, Heller W, Coombes RC. Triple-negative breast cancer: therapeutic options. The Lancet Oncology. 2007;8(3):235-44.

39. Breast Cancer Now. Chemotherapy side-effects [Internet]; 2021 [Cited 2021 May 11]. Available from: https://breastcancernow.org/information-support/facing-breast-cancer/going-through-breast-cancer-treatment/side-effects/side-effects-chemotherapy
40. Hassan M, Ansari J, Spooner D, Hussain SA. Chemotherapy for breast cancer. Oncology Reports. 2010;24(5):1121-31.
41. Osborne CK, Yochmowitz MG, Knight III WA, McGuire WL. The value of estrogen and progesterone receptors in the treatment of breast cancer. Cancer. 1980;46(S12):2884-8.
42. Brito C, Portela MC, de Vasconcellos MT. Adherence to hormone therapy among women with breast cancer. BMC Cancer. 2014;14(1):1-8.
43. Masoud V, Pagès G. Targeted therapies in breast cancer: New challenges to fight against resistance. World Journal of Clinical Oncology. 2017;8(2):120.
44. Cancer Research UK. Monoclonal Antibodies (MABs) [Internet]; 2021 [Cited 2021 May 11]. Available from: https://www.cancerresearchuk.org/about-cancer/cancer-in-general/treatment/targeted-cancer-drugs/types/monoclonal-antibodies
45. Zhong L, Li Y, Xiong L, Wang W, Wu M, Yuan T et al. Small molecules in targeted cancer therapy: advances, challenges, and future perspectives. Signal Transduction and Targeted Therapy. 2021;6(1):1-48.
46. Bedard PL, Hyman DM, Davids MS, Siu LL. Small molecules, big impact: 20 years of targeted therapy in oncology. The Lancet. 2020;395(10229):1078-88.
47. American Cancer Society. Immunotherapy for Breast Cancer [Internet]; 2021 Aug 30 [Cited 2021 Sept 10] Available from: https://www.cancer.org/cancer/breastcancer/treatment/immunotherapy.html
48. American Cancer Society. Targeted Drug Therapy for Breast Cancer [Internet]; 2021 Apr 8 [Cited 2021 Sept 10]. Available from: https://www.cancer.org/cancer/breast-cancer/treatment/targeted-therapy-for-breast-cancer.html
49. Tai P, Yu E, Vinh-Hung V, Cserni G, Vlastos G. Survival of patients with metastatic breast cancer: twenty-year data from two SEER registries. BMC Cancer. 2004;4(1):1-8.
50. Weide R, Feiten S, Friesenhahn V, Heymanns J, Kleboth K, Thomalla J et al. Metastatic breast cancer: prolongation of survival in routine care is restricted to hormone-receptor-and Her2-positive tumors. Springer Plus. 2014;3(1):1-8.
51. Gobbini E, Ezzalfani M, Dieras V, Bachelot T, Brain E, Debled M et al. Time trends of overall survival among metastatic breast cancer patients in the real-life ESME cohort. European Journal of Cancer. 2018;96:17-24.
52. Ren Z, Li Y, Hameed O, Siegal GP, Wei S. Prognostic factors in patients with metastatic breast cancer at the time of diagnosis. Pathology-Research and Practice. 2014;210(5):301-6.
53. Kida K, Olver I, Yennu S, Tripathy D, Ueno NT. Optimal supportive care for patients with metastatic breast cancer according to their disease progression phase. JCO Oncology Practice. 2021;17(4):177-83.
54. Reed E, Corner J. Defining the illness trajectory of metastatic breast cancer. BMJ Supportive and Palliative Care. 2015;5(4):358-65.
55. Velikova G, Stark D, Selby P. Quality of life instruments in oncology. European Journal of Cancer. 1999;35(11):1571-80.
56. Karimi M, Brazier J. Health, health-related quality of life, and quality of life: what is the difference? Pharmacoeconomics. 2016;34(7):645-9.
57. Reed E, Simmonds P, Haviland J, Corner J. Quality of life and experience of care in women with metastatic breast cancer: a cross-sectional survey. Journal of Pain and Symptom Management. 2012;43(4):747-58.
58. Cardoso F, Harbeck N, Mertz S, Fenech D. Evolving psychosocial, emotional, functional, and support needs of women with advanced breast cancer: results from the Count Us, Know Us, Join Us and Here & Now surveys. The Breast. 2016;28:5-12.

59. Mosher CE, Johnson C, Dickler M, Norton L, Massie MJ, DuHamel KJ. Living with metastatic breast cancer: a qualitative analysis of physical, psychological, and social sequelae. The Breast. 2013;19(3):285-92.
60. Stevanovic A, Lee P, Wilcken N. Metastatic breast cancer. Australian family physician. 2006;35(5):309.
61. Aranda S, Schofield P, Weih L, Yates P, Milne D, Faulkner R et al. Mapping the quality of life and unmet needs of urban women with metastatic breast cancer. European Journal of Cancer Care. 2005;14(3):211-22.
62. Mayer M. Lessons learned from the metastatic breast cancer community. Seminars in oncology nursing . 2010;26(3):195-202.
63. Cardoso F, Cardoso M, Beishon M. Global status of advanced/metastatic breast cancer: 2005-2015 decade report [Internet]; 2016 [Cited 2021 Aug 14]. Available from: https://www.abcglobalalliance.org/pdf/Decade-Report_Full-Report_Final.pdf
64. Harding V, Afshar M, Krell J, Ramaswami R, Twelves C, Stebbing J. 'Being there' for women with metastatic breast cancer: a pan-European patient survey. British Journal of Cancer. 2013;109(6):1543-8.
65. Caplan ES, Mayer M, Grober SE. Silent Voices: accessing and meeting the information, support and practical services needs for women living with metastatic breast cancer. The Breast. 2011;20:S52-S3.
66. Novartis Oncology. Here and Now Survey [Internet]; 2013 [Cited 2021 Aug 22]. Available from: https://www.novartis.co.uk/sites/www.novartis.co.uk/files/here-now-patient-survey.pdf
67. Snyder CF, Blackford AL, Aaronson NK, Detmar SB, Carducci MA, Brundage MD et al. Can patient-reported outcome measures identify cancer patients' most bothersome issues? Journal of Clinical Oncology. 2011;29(9):1216-20.
68. Food and Drug Administration. Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labelling Claims – Guidance for industry [Internet]; 2009 [Cited 2021 Aug 14]. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-reported-outcome-measures-use-medical-product-development-support-labeling-claims
69. van Egdom LS, Oemrawsingh A, Verweij LM, Lingsma HF, Koppert LB, Verhoef C et al. Implementing patient-reported outcome measures in clinical breast cancer care: a systematic review. Value in Health. 2019;22(10):1197-226.
70. Lipscomb J, Reeve BB, Clauser SB, Abrams JS, Watkins Bruner D, Burke LB et al. Patient-reported outcomes assessment in cancer trials: taking stock, moving forward. Journal of Clinical Oncology. 2007;25(32):5133-40.
71. Cardoso F, Wilking N, Bernardini R, Biganzoli L, Espin J, Miikkulainen K et al. A multi-stakeholder approach in optimising patients' needs in the benefit assessment process of new metastatic breast cancer treatments. The Breast. 2020;52:78-87.
72. Valderas J, Kotzeva A, Espallargues M, Guyatt G, Ferrans C, Halyard M et al. The impact of measuring patient-reported outcomes in clinical practice: a systematic review of the literature. Quality of Life Research. 2008;17(2):179-93.
73. Velikova G, Booth L, Smith AB, Brown PM, Lynch P, Brown JM et al. Measuring quality of life in routine oncology practice improves communication and patient well-being: a randomized controlled trial. Journal of Clinical Oncology. 2004;22(4):714-24.
74. Howell D, Mayer DK, Fielding R, Eicher M, Verdonck-de Leeuw IM, Johansen C et al. Management of cancer and health after the clinic visit: A call to action for self-management in cancer care. Journal of the National Cancer Institute. 2020;113(5):523-31.

75. Anvik T, Holtedahl KA, Mikalsen H. "When patients have cancer, they stop seeing me"–the role of the general practitioner in early follow-up of patients with cancer–a qualitative study. BMC Family Practice. 2006;7(1):19.
76. Weller DP, Harris MF. Cancer care: what role for the general practitioner? Medical Journal of Australia. 2008;189(2):59.
77. Breast Cancer Now. Secondary. Not second rate [Internet]; 2018 March [Cited 2021 Aug 17]. Available from: https://breastcancernow.org/sites/default/files/the_case_for_change_summary_report.pdf
78. Górnaś M, Szczylik C. Oral treatment of metastatic breast cancer with capecitabine: What influences the decision-making process? European Journal of Cancer Care. 2010;19(1):131-6.
79. Brady TJ, Murphy L, O'Colmain BJ, Beauchesne D, Daniels B, Greenberg M et al. A meta-analysis of health status, health behaviors, and health care utilization outcomes of the chronic disease self-management program. Preventing Chronic Disease [Internet] 2013 Jan 17 [Cited 2021 Aug 17];10.Available from: https://www.cdc.gov/pcd/issues/2013/12_0112.htm
80. Taylor SJ, Pinnock H, Epiphaniou E, Pearce G, Parke HL, Schwappach A et al. A rapid synthesis of the evidence on interventions supporting self-management for people with long-term conditions: PRISMS–Practical systematic Review of Self-Management Support for long-term conditions. Southampton: NIHR Journals Library;2015. PMID: 25642548.
81. Institute of Medicine (US) Committee on the Crossing the Quality Chasm. Patient Self-Management Support In: Adams KG, AC; Corrigan JM, editors. The 1st Annual Crossing the Quality Chasm Summit: A Focus on Communities. Washington (DC): National Academies Press (US); 2004.
82. Howell DD. Supported self-management for cancer survivors to address long-term biopsychosocial consequences of cancer and treatment to optimize living well. Current Opinion in Supportive and Palliative Care. 2018;12(1):92-9.
83. Howell D, Harth T, Brown J, Bennett C, Boyko S. Self-management education interventions for patients with cancer: a systematic review. Supportive Care in Cancer. 2017;25(4):1323-55.
84. Hammer MJ, Ercolano EA, Wright F, Dickson VV, Chyun D, Melkus GD. Self-management for adult patients with cancer: an integrative review. Cancer Nursing. 2015;38(2):E10-E26.
85. Boland L, Bennett K, Connolly D. Self-management interventions for cancer survivors: a systematic review. Supportive Care in Cancer. 2018;26(5):1585-95.
86. Budhwani S, Wodchis WP, Zimmermann C, Moineddin R, Howell D. Self-management, self-management support needs and interventions in advanced cancer: a scoping review. BMJ Supportive and Palliative Care. 2019;9(1):12-25.
87. Dickinson R, Hall S, Sinclair JE, Bond C, Murchie P. Using technology to deliver cancer follow-up: a systematic review. BMC Cancer. 2014;14(1):1-16.
88. Smith AB, Bamgboje-Ayodele A, Butow P, Klein B, Turner J, Sharpe L et al. Development and usability evaluation of an online self-management intervention for fear of cancer recurrence (iConquerFear). Psycho-oncology. 2020;29(1):98-106.
89. Van Der Hout A, van Uden-Kraan CF, Holtmaat K, Jansen F, Lissenberg-Witte BI, Nieuwenhuijzen GA et al. Role of eHealth application Oncokompas in supporting self-management of symptoms and health-related quality of life in cancer survivors: a randomised, controlled trial. 2020;21(1):80-94.
90. Krusche A, Bradbury K, Corbett T, Barnett J, Stuart B, Yao GL et al. Renewed: Protocol for a randomised controlled trial of a digital intervention to support quality of life in cancer survivors. BMJ Open [Internet] 2019 Mar 01 [Cited 2021 Sep 10];9(3):e024862. doi: 10.1136/bmjopen-2018-024862

91. Office for National Statistics (ONS)Internet users, UK: 2020 [Internet] 2020 Aug 7 [Cited 2021 Sep 10]. Available from: https://www.ons.gov.uk/businessindustryandtrade/itandinternetindustry/bulletins/internetusers/2020
92. Lee K, Hoti K, Hughes JD, Emmerton L. Dr Google and the consumer: a qualitative study exploring the navigational needs and online health information-seeking behaviors of consumers with chronic health conditions. Journal of Medical Internet Research [Internet] 2014 Dec 2 [Cited 2021 Sep 10];16(12):e262. doi:10.2196/jmir.3706
93. Eysenbach G. The impact of the Internet on cancer outcomes. CA: A Cancer Journal for Clinicians. 2003;53(6):356-71.
94. Jansen F, van Uden-Kraan CF, van Zwieten V, Witte BI, Verdonck-de Leeuw IM. Cancer survivors' perceived need for supportive care and their attitude towards self-management and eHealth. Supportive Care in Health. 2015;23(6):1679-88.
95. Chou WYS, Liu B, Post S, Hesse B. Health-related Internet use among cancer survivors: data from the Health Information National Trends Survey, 2003–2008. Journal of Cancer Survivorship. 2011;5(3):263-70.
96. Foster C. An exploration of the internet as a self-management resource. Journal of Research in Nursing. 2009;14(1):13-24.
97. Saltman DC. COVID-19 in 2021: Is it the major disrupter that eHealth needs? Australian Journal of General Practice [Internet] 2021 Feb 15 [Cited 2021 Sep 12]; 50(47). doi: 10.31128/AJGP-COVID-47
98. Luther A, Agrawal A. A practical approach to the management of breast cancer in the COVID-19 era and beyond. E-cancer medical science [Internet] 2020 Jun 17 [Cited 2020 Sep 12];14. doi 10.3332/ecancer.2020.1059
99. Mayor S. COVID-19: impact on cancer workforce and delivery of care. The Lancet Oncology. 2020;21(5):633.
100. Leykin Y, Thekdi SM, Shumay DM, Muñoz RF, Riba M, Dunn LB. Internet interventions for improving psychological well-being in psycho-oncology: review and recommendations. Psycho-oncology. 2012;21(9):1016-25.
101. Kim A, Park HA. Web-based Self-management Support Interventions for Cancer Survivors: A Systematic Review and Meta-analyses. Studies in Health Technology and Health Informatics. 2015;216:142-7.
102. Fridriksdottir N, Gunnarsdottir S, Zoëga S, Ingadottir B, Hafsteinsdottir EJ. Effects of web-based interventions on cancer patients' symptoms: review of randomized trials. Supportive Care in Cancer. 2018;26(2):337-51.
103. MBC Advocacy Working Group. Bridging gaps, expanding outreach: metastatic breast cancer advocacy working group consensus report. The Breast. 2009;18(5):273-5.
104. Loiselle CG, Ahmed S. Is connected health contributing to a healthier population? Journal of Medical Internet Research. 2017;19(11):e386.
105. Basch E, Deal AM, Kris MG, Scher HI, Hudis CA, Sabbatini P et al. Symptom monitoring with patient-reported outcomes during routine cancer treatment: A randomized controlled trial. Journal of Clinical Oncology. 2016;34(6):557-65.
106. Maguire R, McCann L, Kotronoulas G, Kearney N, Ream E, Armes J et al. Real time remote symptom monitoring during chemotherapy for cancer: European multicentre randomised controlled trial (eSMART). British Medical Journal. 2021;374:n1647.
107. Denis F, Basch E, Septans AL, Bennouna J, Urban T, Dueck AC et al. Two-year survival comparing web-based symptom monitoring vs routine surveillance following treatment for lung cancer. JAMA. 2019;321(3):306-7.

108. Absolom K, Warrington L, Hudson E, Hewison J, Morris C, Holch P, et al. Phase III Randomized Controlled Trial of eRAPID: eHealth Intervention During Chemotherapy. Journal of Clinical Oncology [Internet] 2021 Jan 8 [Cited 2021 Mar 28].doi. org/10.1200/JCO.20.02015 1
109. Berry DL, Hong F, Halpenny B, Partridge AH, Fann JR, Wolpin S et al. Electronic self-report assessment for cancer and self-care support: results of a multi-center randomized trial. Journal of Clinical Oncology. 2014;32(3):199.
110. Holch P, Warrington L, Bamforth L, Keding A, Ziegler L, Absolom K et al. Development of an integrated electronic platform for patient self-report and management of adverse events during cancer treatment. Annals of Oncology. 2017;28(9):2305-11.
111. Stefanovic S, Wallwiener M, Karic U, Domschke C, Katic L, Taran F-A, et al. Patient-reported outcomes (PRO) focused on adverse events (PRO-AEs) in adjuvant and metastatic breast cancer: clinical and translational implications. Supportive Care in Cancer. 2017;25(2):549-58.
112. Berry DL, Blumenstein BA, Halpenny B, Wolpin S, Fann JR, Austin-Seymour M, et al. Enhancing patient-provider communication with the electronic self-report assessment for cancer: a randomized trial. Journal of Clinical Oncology. 2011;29(8):1029.
113. Velikova G, Brown J, Smith A, Selby PJ. Computer-based quality of life questionnaires may contribute to doctor–patient interactions in oncology. British Journal of Cancer. 2002;86(1):51-9.
114. Lorig KR, Ritter PL, Laurent DD, Plant K. Internet-based chronic disease self-management: a randomized trial. Medical Care. 2006;964-71.
115. Lorig KR, Ritter PL, Dost A, Plant K, Laurent DD, McNeil I. The Expert Patients Programme online, a 1-year study of an Internet-based self-management programme for people with long-term conditions. Chronic Illness. 2008;4(4):247-56.
116. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M. Medical Research Council Guidance. Developing and evaluating complex interventions: the new Medical Research Council guidance. BMJ. 2008;337:a1655. doi:10.1136/bmj.a1655.
117. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M. Developing and evaluating complex interventions: new guidance. [Internet] Medical Research Council; 2006 [Cited 2020 Mar 23]. Available from: https://mrc.ukri.org/documents/pdf/complex-interventions-guidance/
118. Anguera MT, Blanco-Villaseñor A, Losada JL, Sánchez-Algarra P, Onwuegbuzie AJ. Revisiting the difference between mixed methods and multi-methods: Is it all in the name? Quality & Quantity. 2018;52(6):2757-70.
119. Strudsholm T, Meadows LM, Robinson Vollman A, Thurston WE, Henderson R. Using mixed methods to facilitate complex, multi-phased health research. International Journal of Qualitative Methods. 2016;15(1). doi:1609406915624579.
120. Morgan DL. Paradigms lost and pragmatism regained: Methodological implications of combining qualitative and quantitative methods. Journal of Mixed Methods Research. 2007;1(1):48-76.
121. Johnson RB, Onwuegbuzie AJ, Turner LA. Toward a definition of mixed methods research. Journal of Mixed Methods Research. 2007;1(2):112-33.
122. Creswell JW, Plano Clark, VL. Designing and Conducting Mixed Methods Research. Thousand Oaks, California: SAGE Publications; 2007.
123. Bazeley P. Integrating data analyses in mixed methods research. Thousand Oaks, California: SAGE Publications; 2009.
124. Tashakkori A, Teddlie C. Handbook of Mixed Methods in Social & Behavioral Research. Thousand Oaks, California: SAGE Publications; 2010.
125. Hesse-Biber SN, Johnson RB. The Oxford Handbook of Multimethod and Mixed Methods Research Inquiry. Oxford: Oxford University Press; 2015.

126. Johnson RB, Onwuegbuzie AJ. Mixed methods research: A research paradigm whose time has come. Educational Researcher. 2004;33(7):14-26.
127. Saks M, Allsop J, editors. Researching Health: Qualitative, Quantitative and Mixed Methods. Thousand Oaks, California: SAGE Publications; 2012
128. Johnson RB, Christensen L. Educational Research: Quantitative, Qualitative and Mixed Approaches. 6th ed. Thousand Oaks, California: SAGE Publications; 2017.
129. Tariq S, Woodman J. Using Mixed Methods in Health Research. JRSM Short Reports [Internet] 2013 May 31 [Cited 2020 Apr 04];4(6). doi.org/10.1177/2042533313479197
130. Greene JC, Caracelli VJ, Graham WF. Toward a conceptual framework for mixed-method evaluation designs. Educational Evaluation and Policy Analysis. 1989;11(3):255-74.
131. Busetto L, Luijkx K, Calciolari S, González-Ortiz LG, Vrijhoef HJ. The development, description and appraisal of an emergent multimethod research design to study workforce changes in integrated care interventions. International Journal of Integrated Care. 2017;17(1):1-11.
132. Scotland J. Exploring the philosophical underpinnings of research: Relating ontology and epistemology to the methodology and methods of the scientific, interpretive, and critical research paradigms. English Language Teaching. 2012;5(9):9-16.
133. Crotty M. The Foundations of Social Research: Meaning and Perspective in the Research Process. Thousand Oaks, California: SAGE Publications; 1998
134. Kuhn TS. The Structure of Scientific Revolutions. 2nd ed. Chicago: University of Chicago Press; 1970.
135. Guba EG, Lincoln YS. Competing Paradigms in Qualitative Research. In: Denzin NK, Lincoln YS, editors. Handbook of Qualitative Research. Thousand Oaks, California: SAGE Publications; 1994.
136. Smith JK, Heshusius L. Closing down the conversation: The end of the quantitative-qualitative debate among educational inquirers. Educational Researcher. 1986;15(1):4-12.
137. Cook, TD. Post-positivist Critical Multiplism. In Shotland RL, & Mark MM. Social Science and Social Policy. Thousand Oaks, California: SAGE Publications; 1985. p. 21-62.
138. Reichardt CS, Cook TD. Beyond qualitative versus quantitative methods. In: Cook TD, Reichardt CS, editors. Qualitative and Quantitative Methods in Evaluation Research. Beverly Hills, California: SAGE Publications; 1979. p. 7-32.
139. Breen LJ, Darlaston-Jones D. Moving beyond the enduring dominance of positivism in psychological research: Implications for psychology in Australia. Australian Psychologist. 2010;45(1):67-76.
140. Noyes J, Booth A, Moore G, Flemming K, Tunçalp Ö, Shakibazadeh E. Synthesising quantitative and qualitative evidence to inform guidelines on complex interventions: clarifying the purposes, designs and outlining some methods. BMJ Global Health [Internet] 2019 [Cited 2021 Sep 04];4(Suppl 1). doi: 10.1136/bmjgh-2018-000893. eCollection 2019.
141. Norgaard RB. The case for methodological pluralism. Ecological Economics. 1989;1(1):37-57.
142. Sayer A. Realism and Social Science. London: SAGE Publications; 2000.
143. Pawson R, Tilley N. Realistic evaluation. London: SAGE Publications; 1997.
144. Maxwell JA. A realist approach for qualitative research. London: SAGE Publications; 2012.
145. Phillips DC. Philosophy, science and social inquiry: Contemporary methodological controversies in social science and related applied fields of research. Oxford: Pergamon Press; 1987.
146. Bhaskar R. A Realist Theory of Science. London and New York: Verso; 2008.
147. Maxwell JA. Causal explanation, qualitative research, and scientific inquiry in education. Educational Researcher. 2004;33(2):3-11.
148. Sayer RA. Method in social science: A realist approach. Hove, UK: Psychology Press; 1992.

149. Bonell C, Fletcher A, Morton M, Lorenc T, Moore L. Realist randomised controlled trials: a new approach to evaluating complex public health interventions. Social Science and Medicine. 2012;75(12):2299-306.
150. Maxwell JA, Mittapalli K. Realism as a stance for mixed methods research In: Handbook of Mixed Methods in Social & Behavioral Research. Thousand Oaks, California: SAGE Publications; 2015.
151. Huberman AM, Miles MB. Assessing local causality in qualitative research. In: Berg DN, Kenwyn KS editors. The Self in Social Inquiry: Researching Methods. Thousand Oaks, California: SAGE Publications; 1985. p. 351-81.
152. Shadish WR, Cook TD, Campbell DT. Experimental and Quasi-experimental Designs for Generalized Causal Inference. Boston: Houghton Mifflin; 2002.
153. Christ TWJQI. Scientific-based research and randomized controlled trials, the "gold" standard? Alternative paradigms and mixed methodologies. Qualitative Inquiry. 2014;20(1):72-80.
154. Fletcher A, Jamal F, Moore G, Evans RE, Murphy S, Bonell CJE. Realist complex intervention science: applying realist principles across all phases of the Medical Research Council framework for developing and evaluating complex interventions. Evaluation. 2016;22(3):286-303.
155. Pawson R. The Science of Evaluation: A Realist Manifesto. London: SAGE Publications; 2013.
156. Blackwood B, O'Halloran P, Porter S. On the problems of mixing RCTs with qualitative research: the case of the MRC framework for the evaluation of complex healthcare interventions. Journal of Research in Nursing. 2010;15(6):511-21.
157. Squires JE, Valentine JC, Grimshaw JM. Systematic reviews of complex interventions: framing the review question. Journal of Clinical Epidemiology. 2013;66(11):1215-22.
158. O'Cathain A, Croot L, Duncan E, Rousseau N, Sworn K, Turner KM et al. Guidance on how to develop complex interventions to improve health and healthcare. BMJ Open [Internet] 2019 Aug 15 [Cited 2020 March 26];9(8):e029954. doi: 10.1136/bmjopen-2019-029954
159. Blackwood B. Methodological issues in evaluating complex healthcare interventions. Journal of Advancer Cancer Nursing. 2006;54(5):612-22.
160. Hawe P. Lessons from complex interventions to improve health. Annual Review of Public Health. 2015;36:307-23.
161. Absolom K, Gibson A, Velikova G. Engaging patients and clinicians in online reporting of adverse effects during chemotherapy for cancer: the eRAPID system (electronic patient self-reporting of adverse events: patient information and aDvice). Medical Care. 2019;57:S59-S65.
162. Campbell M, Fitzpatrick R, Haines A, Kinmouth AL, Sandercock P, Spiegelhalter D et al. Framework for design and evaluation of complex interventions to improve health. BMJ. 2000;321:694-6. doi:10.1136/bmj.321.7262.694.
163. Michie S, Johnston M. Theories and techniques of behaviour change: Developing a cumulative science of behaviour change. Health Psychology Review. 2012; 6(1):1-6.
164. Petticrew M. When are complex interventions 'complex'? When are simple interventions 'simple'? European Journal of Public Health. 2011;21(4):397-8.
165. Thomas J, Petticrew M, Noyes J, Chandler J, Rehfuess E, Tugwell P et al. Intervention Complexity In: Higgins J, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA., editors. Cochrane Handbook for Systematic Reviews of Interventions 6.1 ed. [Internet] London: The Cochrane Collaboration; 2020 [Cited 2020 Apr 12]. Available from: https://training.cochrane.org/handbook
166. Campbell NC, Murray E, Darbyshire J, Emery J, Farmer A, Griffiths F, et al. Designing and evaluating complex interventions to improve health care. BMJ. 2007;334(7591):455-9.
167. Kemp E, Koczwara B, Butow P, Turner J, Girgis A, Schofield P, et al. Online information and support needs of women with advanced breast cancer: a qualitative analysis. Supportive Care in Cancer. 2018;26(10):3489-96.

168. Roesch E, Abraham J. Reflection on Supportive Care Elements During the Metastatic Breast Cancer Journey. JCO Oncology Practice. 2021;17(4):184-5.
169. Alfieri S, Brunelli C, Capri G, Caraceni A, Bianchi GV, Borreani C. A qualitative study on the needs of women with metastatic breast cancer. Journal of Cancer Education [Internet] 2021 Jan 23 [Cited 2020 Dec 15]:1-10. doi.org/10.1007/s13187-020-01954-4
170. Lewis S, Yee J, Kilbreath S, Willis K. A qualitative study of women's experiences of healthcare, treatment and support for metastatic breast cancer. The Breast. 2015;24(3):242-7.
171. Lee Mortensen G, Madsen IB, Krogsgaard R, Ejlertsen BJ. Quality of life and care needs in women with estrogen positive metastatic breast cancer: a qualitative study. Acta Oncologica. 2018;57(1):146-51.
172. Lewis S, Willis K, Yee J, Kilbreath S. Living well? Strategies used by women living with metastatic breast cancer. Acta Oncologica. 2016;26(9):1167-79.
173. Etikan I, Musa SA, Alkassim RS. Comparison of convenience sampling and purposive sampling. American Journal of Theoretical and Applied Statistics. 2016;5(1):1-4.
174. Patton MQ. Qualitative Research and Evaluation Methods. 3rd ed. Thousand Oaks, California: SAGE Publications; 2002.
175. Ritchie J, Lewis J, Nicholls CM, Ormston R. Qualitative Research Practice: A Guide for Social Science Students and Researchers. London: SAGE Publications; 2003.
176. Gill P, Stewart K, Treasure E, Chadwick B. Methods of data collection in qualitative research: interviews and focus groups. British Dental Journal. 2008;204(6):291-5.
177. Braun V, Clarke V. Thematic analysis: a reflexive approach [Internet] 2019 [Cited 2020 Dec 17] Available from: https://www.psych.auckland.ac.nz/en/about/thematic analysis.html#95c4b0bee0b9774eee5f7ba22cb91d53
178. Braun V, Clarke V. Using thematic analysis in psychology. Qualitative Research in Psychology. 2006;3(2):77-101.
179. Nowell LS, Norris JM, White DE, Moules N. Thematic analysis: Striving to meet the trustworthiness criteria. International Journal of Qualitative Methods. 2017;16(1). doi:10.1177/1609406917733847.
180. Fereday J, Muir-Cochrane E. Demonstrating rigor using thematic analysis: A hybrid approach of inductive and deductive coding and theme development. International Journal of Qualitative Methods. 2006;5(1):80-92.
181. Department of Health. Generic choice model for long term conditions. London: Department of Health; 2007.
182. Guest G, Bunce A, Johnson L. How many interviews are enough? An experiment with data saturation and variability. Field Methods. 2006;18(1):59-82.
183. Braun V, Clarke V. Successful Qualitative Research: A Practical Guide for Beginners. London: SAGE Publications; 2013.
184. Murray SA, Kendall M, Boyd K, Sheikh A. Illness trajectories and palliative care. BMJ. 2005;330(7498):1007-11.
185. Warren M. Uncertainty, lack of control and emotional functioning in women with metastatic breast cancer: a review and secondary analysis of the literature using the critical appraisal technique. European Journal of Cancer Care. 2010;19(5):564-74.
186. Rugno FC, Paiva BSR, Nunes JS, Paiva CE. "There won 't'be anything else… it's over": Perceptions of women referred to palliative care only. European Journal of Oncology Nursing. 2014;18(3):261-6.
187. Emery J. Cancer survivorship - The role of the GP. Australian Family Physician. 2014;43(8):521-25.
188. Schütze H, Chin M, Weller D, Harris MF. Patient, general practitioner and oncologist views regarding long-term cancer shared care. Family Practice. 2018;35(3):323-9.

189. Boele F, Harley C, Pini S, Kenyon L, Daffu-O'Reilly A, Velikova G et al. Cancer as a chronic illness: support needs and experiences. BMJ Supportive and Palliative Care [Internet] 2019 Sep 19 [Cited 2020 Feb 12]. doi: 10.1136/bmjspcare-2019-001882.
190. Powell J, Inglis N, Ronnie J, Large S. The characteristics and motivations of online health information seekers: cross-sectional survey and qualitative interview study. Journal of Medical Internet Research [Internet] 2011 Feb 23 [Cited 2020 Feb 12];13(1):e20. doi: 10.2196/jmir.1600
191. Hesse BW, Greenberg AJ, Rutten LJ. The role of Internet resources in clinical oncology: promises and challenges. Nature Reviews Clinical Oncology. 2016;13(12):767-76.
192. Kemp E, Trigg J, Beatty L, Christensen C, Dhillon HM, Maeder A et al. Health literacy, digital health literacy and the implementation of digital health technologies in cancer care: the need for a strategic approach. Health Promotion Journal of Australia. 2021;32(S1):104-114.
193. Klemm P, Bunnell D, Cullen M, Soneji R, Gibbons P, Holecek A. Online cancer support groups: a review of the research literature. CIN: Computers, Informatics, Nursing. 2003;21(3):136-42.
194. Warrington L, Absolom K, Conner M, Kellar I, Clayton B, Ayres M et al. Electronic Systems for Patients to report and manage side effects of Cancer treatment: systematic review. Journal of Medical Internet Research [Internet] 2019 Jan 24 [Cited 2020 Feb 22];21(1):e10875. doi: 10.2196/10875.
195. Marandino L, Necchi A, Aglietta M, Di Maio M. COVID-19 emergency and the need to speed up the adoption of electronic patient-reported outcomes in cancer clinical practice. 2020;16(6):295.
196. Lee MK, Yun YH, Park H-A, Lee ES, Jung KH, Noh D-Y. A Web-based self-management exercise and diet intervention for breast cancer survivors: pilot randomized controlled trial. International Journal of Nursing Studies. 2014;51(12):1557-67.
197. van den Berg SW, Peters EJ, Kraaijeveld JF, Gielissen MF, Prins JB. Usage of a generic web-based self-management intervention for breast cancer survivors: substudy analysis of the BREATH trial. Journal of Medical Internet Research [Internet] 2013 Aug 19 [Cited 2020 Feb 22];15(8):e170. doi10.2196/jmir.2566.
198. Fu MR, Axelrod D, Guth A, Scagliola J, Rampertaap K, El-Shammaa N et al. A web-and mobile-based intervention for women treated for breast cancer to manage chronic pain and symptoms related to lymphedema: randomized clinical trial rationale and protocol. JMIR Research Protocols [Internet] 2016 Jan 21 [Cited 2020 Feb 22];5(1):e5104. doi10.2196/resprot.5104.
199. Winzelberg AJ, Classen C, Alpers GW, Roberts H, Koopman C, Adams RE et al. Evaluation of an internet support group for women with primary breast cancer. Cancer. 2003;97(5):1164-73.
200. Fridriksdottir N, Gunnarsdottir S, Zoëga S, Ingadottir B, Hafsteinsdottir E. Effects of web-based interventions on cancer patients' symptoms: review of randomized trials. Supportive Care in Cancer. 2018;26(2):337-51.
201. Corbett T, Singh K, Payne L, Bradbury K, Foster C, Watson E et al. Understanding acceptability of and engagement with Web-based interventions aiming to improve quality of life in cancer survivors: a synthesis of current research. Psycho-oncology 2018;27(1):22-33.
202. Hong Y, Pena-Purcell NC, Ory MG. Outcomes of online support and resources for cancer survivors: a systematic literature review. Patient Education and Counselling. 2012;86(3):288-96.
203. McAlpine H, Joubert L, Martin-Sanchez F, Merolli M, Drummond KJ. A systematic review of types and efficacy of online interventions for cancer patients. Patient Education and Counselling. 2015;98(3):283-95.

204. Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Medicine [Internet]2009 Jul 21[Cited 2020 Feb 22];151(4):264-69. doi.org/10.1371/journal.pmed.1000097
205. Higgins J, Thomas J, Chandler J, Cumpston M, Tianjing L, Page M, Welch VA, editors. Cochrane Handbook for Systematic Reviews of Interventions. 5.1.0 ed [Internet] London: The Cochrane Collaboration; 2011 [Cited 2020 Feb 22] Available from: https://handbook-5-1.cochrane.org/
206. Amir-Behghadami M, Janati A. Population, Intervention, Comparison, Outcomes and Study (PICOS) design as a framework to formulate eligibility criteria in systematic reviews. Journal of Emergency Medicine. 2020;37(6):387. doi: 10.1136/emermed-2020-209567.
207. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343:d5928.
208. Popay J, Roberts H, Sowden A, Petticrew M, Arai L, Rodgers M et al. Guidance on the Conduct of Narrative Synthesis in Systematic Reviews: A Product from the ESRC Methods Programme. Lancaster: Lancaster University. 2006;1018-4643.
209. Børøsund E, Cvancarova M, Moore SM, Ekstedt M, Ruland CM. Comparing effects in regular practice of e-communication and Web-based self-management support among breast cancer patients: preliminary results from a randomized controlled trial. Journal of Medical Internet Research. 2014;16(12):e295.
210. Gustafson DH, Hawkins R, McTavish F, Pingree S, Chen WC, Volrathongchai K et al. Internet-based interactive support for cancer patients: are integrated systems better? Journal of Communication. 2008;58(2):238-57.
211. Gustafson DH, DuBenske LL, Namkoong K, Hawkins R, Chih MY, Atwood AK et al. An eHealth system supporting palliative care for patients with non-small cell lung cancer: a randomized trial. Cancer. 2013;119(9):1744-51.
212. Huang CC, Kuo HP, Lin YE, Chen SC. Effects of a Web-based Health Education Program on Quality of Life and Symptom Distress of Initially Diagnosed Advanced Non-Small Cell Lung Cancer Patients: A Randomized Controlled Trial. Journal of Cancer Education. 2019;34(1):41-9.
213. Kim HJ, Kim SM, Shin H, Jang JS, Kim YI, Han DH. A Mobile Game for Patients With Breast Cancer for Chemotherapy Self-Management and Quality-of-Life Improvement: Randomized Controlled Trial. Journal of Medical Internet Research. 2018;20(10):e273.
214. O'Carroll Bantum E, Albright CL, White KK, Berenberg JL, Layi G, Ritter PL et al. Surviving and thriving with cancer using a Web-based health behavior change intervention: randomized controlled trial. JMIR. 2014;16(2).
215. Owen JE, Bantum EO, Pagano IS, Stanton A. Randomized Trial of a Social Networking Intervention for Cancer-Related Distress. Annals of Behavioral Medicine. 2017;51(5):661-72.
216. Petzel SV, Isaksson Vogel R, Cragg J, McClellan M, Chan D, Jacko JA et al. Effects of web-based instruction and patient preferences on patient-reported outcomes and learning for women with advanced ovarian cancer: A randomized controlled trial. Journal of Psychosocial Oncology. 2018;36(4):503-19.
217. Ruland CM, Andersen T, Jeneson A, Moore S, Grimsbo GH, Borosund E, et al. Effects of an Internet Support System to Assist Cancer Patients in Reducing Symptom Distress A Randomized Controlled Trial. Cancer Nursing. 2013;36(1):6-17.
218. Steel JL, Geller DA, Kim KH, Butterfield LH, Spring M, Grady J et al. Web-based collaborative care intervention to manage cancer-related symptoms in the palliative care setting. Cancer. 2016;122(8):1270-82.
219. Wise M, Marchand LR, Roberts LJ, Chih MY. Suffering in Advanced Cancer: A Randomized Control Trial of a Narrative Intervention. Journal of Palliative Medicine. 2018;21(2):200-7.

220. Zhu J, Ebert L, Liu X, Wei D, Chan SW-C. Mobile Breast Cancer e-Support Program for Chinese Women With Breast Cancer Undergoing Chemotherapy (Part 2): Multicenter Randomized Controlled Trial. JMIR mHealth and uHealth. 2018;6(4).
221. Boele FW, Klein M, Verdonck-de Leeuw IM, Cuijpers P, Heimans JJ, Snijders TJ et al. Internet-based guided self-help for glioma patients with depressive symptoms: a randomized controlled trial. Journal of Neuro-Oncology. 2018;137(1):191-203.
222. Carpenter KM, Stoner SA, Schmitz K, McGregor BA, Doorenbos AZ. An online stress management workbook for breast cancer. Journal of Behavioral Medicine. 2014;37(3):458-68.
223. Compen F, Bisseling E, Schellekens M, Donders R, Carlson L, van der Lee M et al. Face-to-face and internet-based mindfulness-based cognitive therapy compared with treatment as usual in reducing psychological distress in patients with cancer: A multicenter randomized controlled trial. Journal of Clinical Oncology. 2018;36(23):2413-21.
224. Galiano-Castillo N, Cantarero-Villanueva I, Fernández-Lao C, Ariza-García A, Díaz-Rodríguez L, Del-Moral-Ávila R et al. Telehealth system: A randomized controlled trial evaluating the impact of an internet-based exercise intervention on quality of life, pain, muscle strength, and fatigue in breast cancer survivors. Cancer. 2016;122(20):3166-74.
225. Greer JA, Jacobs J, Pensak N, MacDonald JJ, Fuh CX, Perez GK et al. Randomized Trial of a Tailored Cognitive-Behavioral Therapy Mobile Application for Anxiety in Patients with Incurable Cancer. Oncologist. 2019;25:25.
226. Knoerl R, Smith EML, Barton DL, Williams DA, Holden JE, Krauss JC et al. Self-Guided Online Cognitive Behavioral Strategies for Chemotherapy-Induced Peripheral Neuropathy: A Multicenter, Pilot, Randomized, Wait-List Controlled Trial. Journal of Pain. 2018;19(4):382-94.
227. Ritterband LM, Bailey ET, Thorndike FP, Lord HR, Farrell-Carnahan L, Baum LD. Initial evaluation of an Internet intervention to improve the sleep of cancer survivors with insomnia. Psycho-Oncology. 2012;21(7):695-705.
228. Rosen KD, Paniagua SM, Kazanis W, Jones S, Potter JS. Quality of life among women diagnosed with breast Cancer: A randomized waitlist controlled trial of commercially available mobile app-delivered mindfulness training. Psycho-Oncology. 2018;27(8):2023-30.
229. Urech C, Grossert A, Alder J, Scherer S, Handschin B, Kasenda B, et al. Web-Based Stress Management for Newly Diagnosed Patients With Cancer (STREAM): A Randomized, Wait-List Controlled Intervention Study. Journal of Clinical Oncology. 2018;36(8):780.
230. Yanez B, McGinty H, Mohr D, Begale M, Dahn J, Flury S, et al. Feasibility, acceptability, and preliminary efficacy of a technology-assisted psychosocial intervention for racially diverse men with advanced prostate cancer. Cancer [Internet]. 2015 [Cited 2020 Feb 22];121(24):4407-15 Available from: http://cochranelibrary-wiley.com/o/cochrane/clcentral/articles/221/CN-01125221/frame.html.
231. Zernicke KA, Campbell TS, Speca M, McCabe-Ruff K, Flowers S, Carlson LE. A Randomized Wait-List Controlled Trial of Feasibility and Efficacy of an Online Mindfulness-Based Cancer Recovery Program: The eTherapy for Cancer Applying Mindfulness Trial. Psychosomatic Medicine. 2014;76(4):257-67.
232. Denis F, Lethrosne C, Pourel N, Molinier O, Pointreau Y, Domont J et al. Randomized Trial Comparing a Web-Mediated Follow-up With Routine Surveillance in Lung Cancer Patients. Journal of the National Cancer Institute. [Internet] 2017 Sep [Cited 2020 Mar 04];109(9)doi: 10.1093/jnci/djx029.
233. Nipp RD, El-Jawahri A, Ruddy M, Fuh C, Temel B, D'Arpino SM et al. Pilot Randomized Trial of an Electronic Symptom Monitoring Intervention for Hospitalized Patients with Cancer. Annals of Oncology. 2018;05:05.
234. Post D, Shapiro C, Cegala D, David P, Katz M, Krok J et al. Improving symptom communication through personal digital assistants: the CHAT (Communicating Health Assisted by

Technology) project. Journal of the National Cancer Institute Monographs [Internet]. 2013 Dec [Cited 2020 Mar 04];(47):153-61. Available from: https://pubmed.ncbi.nlm.nih.gov/24395985/
235. Ruland CM, Holte HH, Røislien J, Heaven C, Hamilton GA, Kristiansen J et al. Effects of a computer-supported interactive tailored patient assessment tool on patient care, symptom distress, and patients' need for symptom management support: a randomized clinical trial. Journal of the American Medical Informatics Association. 2010;17(4):403-10.
236. Strasser F, Blum D, Moos R, Cathomas R, Ribi K, Aebi S et al. The effect of real-time electronic monitoring of patient-reported symptoms and clinical syndromes in outpatient workflow of medical oncologists: e-MOSAIC, a multicenter cluster-randomized phase III study (SAKK 95/06). Annals of oncology [Internet] 2016 Feb 01 [Cited 2020 Mar 04]; 27(2):324-32. Available from: https://www.annalsofoncology.org/article/S0923-7534(19)35568-1/fulltext
237. David N, Schlenker P, Prudlo U, Larbig W. Online counseling via e-mail for breast cancer patients on the German Internet: Preliminary results of a psychoeducational intervention. GMS Psycho-Social-Medicine [Internet] 2011 Sep 1 [Cited 2020 Mar 04];8. doi: 10.3205/psm000074
238. Donovan HS, Ward SE, Sereika SM, Knapp JE, Sherwood PR, Bender CM et al. Web-based symptom management for women with recurrent ovarian cancer: a pilot randomized controlled trial of the WRITE symptoms intervention. Journal of Pain and Symptom Management. 2014;47(2):218-30.
239. Vilhauer RP, McClintock MK, Matthews AK. Online support groups for women with metastatic breast cancer: A feasibility pilot study. Journal of Psychosocial Oncology. 2010;28(5):560-86.
240. Giesler JMP, Keller BMAMPH, Repke TM, Leonhart RP, Weis JP, Muckelbauer RD, et al. Effect of a Website That Presents Patients' Experiences on Self-Efficacy and Patient Competence of Colorectal Cancer Patients: Web-Based Randomized Controlled Trial. JMIR. 2017;19(10).
241. Ryhänen AM, Rankinen S, Siekkinen M, Saarinen M, Korvenranta H, Leino-Kilpi H. The impact of an empowering Internet-based Breast Cancer Patient Pathway program on breast cancer patients' clinical outcomes: a randomised controlled trial. Journal of Clinical Nursing. 2013;22(7-8):1016-25.
242. Stanton AL, Thompson EH, Crespi CM, Link JS, Waisman JR. Project Connect Online: Randomized Trial of an Internet-Based Program to Chronicle the Cancer Experience and Facilitate Communication. Journal of Clinical Oncology. 2013;31(27):3411-7.
243. Ritterband LM, Gonder-Frederick LA, Cox DJ, Clifton AD, West RW, Borowitz SMJPPR, et al. Internet interventions: In review, in use, and into the future. Professional Psychology: Research and Practice. 2003;34(5):527.
244. Davis K, Yount S, Del Ciello K, Whalen M, Khan S, Bass M et al. An innovative symptom monitoring tool for people with advanced lung cancer: a pilot demonstration. Journal of Supportive Oncology. 2007;5(8):381-7.
245. Eng TR, Gustafson DH, Henderson J, Jimison H, Patrick K. Introduction to evaluation of interactive health communication applications: Science Panel on Interactive Communication and Health. American Journal of Preventative Medicine. 1999;16(1):10-5.
246. Murray E, Burns J, Tai SS, Lai R, Nazareth I. Interactive Health Communication Applications for people with chronic disease. Cochrane Database of Systematic Reviews. [Internet] 2005 Oct 19 [Cited 2020 Mar 04](4):CD004274.doi: 10.1002/14651858.CD004274.pub4
247. Krane A, Terhorst L, Bovbjerg DH, Scheier MF, Kucinski B, Geller DA et al. Putting the life in lifestyle: Lifestyle choices after a diagnosis of cancer predicts overall survival. Cancer. 2018;124(16):3417-26.

248. Wang R, Zhu Y, Liu X, Liao X, He J, Niu L. The Clinicopathological features and survival outcomes of patients with different metastatic sites in stage IV breast cancer. BMC Cancer. 2019;19(1):1-12.
249. Greer JA, Jackson VA, Meier DE, Temel JSJCacjfc. Early integration of palliative care services with standard oncology care for patients with advanced cancer. Cancer. 2013;63(5):349-63.
250. Gustafson DH, Hawkins R, Boberg E, Pingree S, Serlin RE, Graziano F, et al. Impact of a patient-centered, computer-based health information/support system. American Journal of Preventitive Medicine. 1999;16(1):1-9.
251. Velikova G. Use of electronic quality of life applications in cancer research and clinical practice. Expert Review of Pharmacoeconomics and Outcomes Research. 2004;4(4):403-11.
252. Page AE, Adler NE. Cancer care for the whole patient: Meeting psychosocial health needs. Washington (DC): National Academies Press; 2008.
253. Holland J, Weiss T. The new standard of quality cancer care: integrating the psychosocial aspects in routine cancer from diagnosis through survivorship. Cancer Journal. 2008;14(6):425-8.
254. Sanson-Fisher R, Girgis A, Boyes A, Bonevski B, Burton L, Cook P et al. The unmet supportive care needs of patients with cancer. Cancer. 2000;88(1):226-37.
255. Clauser SB, Wagner EH, Bowles EJA, Tuzzio L, Greene SM. Improving modern cancer care through information technology. American Journal of Preventitive Medicine. 2011;40(5):S198-S207.
256. Cella DF, Tulsky DS. Quality of life in cancer: definition, purpose, and method of measurement. Cancer Investigation. 1993;11(3):327-36.
257. Kennedy A, Rogers A, Bower PJB. Support for self care for patients with chronic disease. BMJ. 2007;335(7627):968-70.
258. Corbett T, Singh K, Payne L, Bradbury K, Foster C, Watson E, et al. Understanding acceptability of and engagement with Web-based interventions aiming to improve quality of life in cancer survivors: a synthesis of current research. Psychooncology. 2018;27(1):22-33.
259. Rimer BK, Glanz K. Theory at a Glance: A Guide of Health Promotion Practice. 2nd ed. USA: National Cancer Institute; 2005.
260. Lorig KR, Holman HR. Self-management education: history, definition, outcomes, and mechanisms. Annals of Behavioural Medicine. 2003;26(1):1-7.
261. Girgis A. The role of self-management in cancer survivorship care. The Lancet Oncology. 2020;21(1):8-9.
262. Cuthbert CA, Farragher JF, Hemmelgarn BR, Ding Q, McKinnon GP, Cheung WY. Self-management interventions for cancer survivors: A systematic review and evaluation of intervention content and theories. Psychooncology. 2019;28(11):2119-40.
263. Foster C, Fenlon D. Recovery and self-management support following primary cancer treatment. British Journal of Cancer. [Internet] 2011 Nov 3 [Cited 2020 Feb 08];105(1):S21-S8.
264. Howell D, Richardson A, May C, Calman L, Fazelzad R, Moradian S et al. Implementation of self-management support in cancer care and normalization into routine practice: a systematic scoping literature review protocol. Systematic Reviews. 2019;8(1):37.
265. Corbin JM, Strauss AL. Unending work and care: Managing chronic illness at home. San Francisco: Jossey-Bass; 1988
266. Paterson BL. The shifting perspectives model of chronic illness. Journal of Nursing Scholarship. 2001;33(1):21-6.
267. Barlow J, Wright C, Sheasby J, Turner A, Hainsworth J. Self-management approaches for people with chronic conditions: a review. Patient Education and Counselling. 2002;48(2):177-87.

268. McCorkle R, Ercolano E, Lazenby M, Schulman-Green D, Schilling LS, Lorig K, et al. Self-management: Enabling and empowering patients living with cancer as a chronic illness. Cancer. 2011;61(1):50-62.
269. Self-Care Forum. What do we mean by self care and why is it good for people? [Internet]; 2020 [Cited 2020 Jun 02] Available from: https://www.selfcareforum.org/about-us/what-do-we-mean-by-self-care-and-why-is-good-for-people/
270. Adams K, Corrigan JM, editors. Institute of Medicine (US) Committee on Identifying Priority Areas for Quality Improvement. Priority Areas for National Action: Transforming Healthcare Quality. Washington (DC): National Academies Press (US); 2003.
271. Prouse J, Phillips J, editors. Care of older people living with cancer: The role of the specialist nurse and allied health. 2013. Cancer Forum;37(3):226-29.
272. Koch T, Jenkin P, Kralik DJJoan. Chronic illness self-management: locating the 'self'. Journal of Advanced Nursing. 2004;48(5):484-92.
273. Ajzen I. From intentions to actions: A theory of planned behavior. In Kuhl J, Beckmann J, editors. In: Action Control Berlin, Heidelberg: Springer Series in Social Psychology;1985. p.11-39.
274. Fishbein M, Ajzen I. Belief, attitude, intention, and behavior: An introduction to theory and research. Philosophy and Rhetoric. 1977;10(2).
275. Glanz K, Rimer BK, Viswanath K. Health behavior and health education: theory, research, and practice. New Jersey:John Wiley & Sons; 2008.
276. Boston University School of Public Health. Behavioral Change Models [Internet] 2019 [Cited 2020 Jun 02]. Available from: https://sphweb.bumc.bu.edu/otlt/mph-modules/sb/behavioralchangetheories/
277. Sniehotta FF, Presseau J, Araújo-Soares V. Time to retire the theory of planned behaviour. Health Psychology Review. 2014;8(1):1-7.
278. Richard AA, Shea K. Delineation of self-care and associated concepts. Journal of Nursing Scholarship. 2011;43(3):255-64.
279. Riegel B, Jaarsma T, Strömberg A. A middle-range theory of self-care of chronic illness. Advances in Nursing Science. 2012;35(3):194-204.
280. Riegel B, Jaarsma T, Lee CS, Strömberg A. Integrating symptoms into the middle-range theory of self-care of chronic illness. Advances in Nursing Science 2019;42(3):206.
281. Smith MJ, Liehr PR. Understanding middle range theory by moving up and down the ladder of abstraction. In: Smith MJ, Liehr PR, editors. Middle Range Theory for Nursing. 3rd ed. New York: Springer Publishing Company; 2008. p.13-31.
282. Merton RK. On sociological theories of the middle range. In: Social Theory and Social Structure. New York: The Free Press; 1968. p.39-72.
283. Orem DE. Nursing: Concepts of practice. 4th ed. St Louis, MO: Mosby; 1991.
284. Riegel B, Carlson B, Moser DK, Sebern M, Hicks FD, Roland V. Psychometric testing of the self-care of heart failure index. Journal of Cardiac Failure. 2004;10(4):350-60.
285. Sethares KA, Asselin ME, Lung. The effect of guided reflection on heart failure self-care maintenance and management: a mixed methods study. Heart & Lung. 2017;46(3):192-8.
286. Whitaker K, Scott S, Wardle J. Applying symptom appraisal models to understand sociodemographic differences in responses to possible cancer symptoms: a research agenda. British Journal of Cancer. 2015;112(1):S27-S34.
287. Bandura A. Self-efficacy: The exercise of control. New York: W.H. Freeman; 1997.
288. Bandura A. Social Foundations of Thought and Action: A Social Cognitive Theory. Englewood Cliffs, New Jersey: Prentice Hall; 1986.
289. Bandura A. Social Learning Theory. New York: General Learning Press; 1977.

290. Lev EL, Daley KM, Conner NE, Reith M, Fernandez C, Owen SV. An intervention to increase quality of life and self-care self-efficacy and decrease symptoms in breast cancer patients. Scholarly Inquiry for Nursing Practice. 2001;15(3):277-94.
291. Bandura A. Health promotion by social cognitive means. 2004;31(2):143-64.
292. Foster C, Breckons M, Cotterell P, Barbosa D, Calman L, Corner J et al. Cancer survivors' self-efficacy to self-manage in the year following primary treatment. Journal of Cancer Survivorship. 2015;9(1):11-9.
293. Baik SH, Oswald LB, Buitrago D, Buscemi J, Iacobelli F, Perez-Tamayo A et al. Cancer-relevant self-efficacy is related to better health-related quality of life and lower cancer-specific distress and symptom burden among Latina breast cancer survivors. International Journal of Behavioural Medicine. 2020;27(4):357-65.
294. Philip EJ, Merluzzi TV, Zhang Z, Heitzmann CA. Depression and cancer survivorship: importance of coping self-efficacy in post-treatment survivors. Psycho-Oncology. 2013;22(5):987-94.
295. Chirico A, Lucidi F, Merluzzi T, Alivernini F, De Laurentiis M, Botti G et al. A meta-analytic review of the relationship of cancer coping self-efficacy with distress and quality of life. Oncotarget. 2017;8(22):36800.
296. Taylor SE. Adjustment to threatening events: A theory of cognitive adaptation. American Psychologist. 1983;38(11):1161.
297. Lev EL, Dodd MJ, Hinds PS. Patients' strategies for adapting to cancer treatment. Western Journal of Nursing Research. 1992;14(5):595-617.
298. Beckham JC, Burker EJ, Burker EJ, Feldman ME, Costakis MJ. Self-efficacy and adjustment in cancer patients: a preliminary report. Behavioural Medicine. 1997;23(3):138-42.
299. Cunningham AJ, Lockwood GA, Cunningham. A relationship between perceived self-efficacy and quality of life in cancer patients. 1991;17(1):71-8.
300. Hirai K, Suzuki Y, Tsuneto S, Ikenaga M, Hosaka T, Kashiwagi T. A structural model of the relationships among self-efficacy, psychological adjustment, and physical condition in Japanese advanced cancer patients. Pyscho-Oncology. 2002;11(3):221-9.
301. White L, Cohen MZ, Berger AM, Kupzyk KA, Bierman PJ. Self-efficacy for management of symptoms and symptom distress in adults with cancer: An integrative review. Oncology Nursing Forum. 2019;46(1):113-28.
302. Giesler JM, Weis J. Patient competence in the context of cancer: its dimensions and their relationships with coping, coping self-efficacy, fear of progression, and depression. Supportive Care in Cancer. 2021;29(4):2133-43.
303. Hofstetter CR, Sallis JF, Hovell MF. Some health dimensions of self-efficacy: Analysis of theoretical specificity. Social Science and Medicine. 1990;31(9):1051-6.
304. Manne SL, Ostroff JS, Norton TR, Fox K, Grana G, Goldstein L. Cancer-specific self-efficacy and psychosocial and functional adaptation to early stage breast cancer. Annals of Behavioural Medicine. 2006;31(2):145-54.
305. Kreitler S, Peleg D, Ehrenfeld M. Stress, self-efficacy and quality of life in cancer patients. Psycho-Oncology. 2007;16(4):329-41.
306. Lev EL. Bandura's theory of self-efficacy: applications to oncology. Scholarly Inquiry for Nursing Practice. 1997;11(1):21-37; discussion 9-43.
307. Auld JP, Mudd JO, Gelow JM, Hiatt SO, Lee CS. Self-care moderates the relationship between symptoms and health-related quality of life in heart failure. Journal of Cardiovascular Nursing. 2018;33(3):217.
308. Buck HG, Lee CS, Moser DK, Albert NM, Lennie T, Bentley B et al. Relationship between self-care and health-related quality of life in older adults with moderate to advanced heart failure. Journal of Cardiovascular Nursing. 2012;27(1):8-15.

309. Lee CS, Mudd JO, Hiatt SO, Gelow JM, Chien C, Riegel B. Trajectories of heart failure self-care management and changes in quality of life. European Journal of Cardiovascular Nursing. 2015;14(6):486-94.
310. Lee CS, Gelow JM, Mudd JO, Green JK, Hiatt SO, Chien C et al. Profiles of self-care management versus consulting behaviors in adults with heart failure. European Journal of Cardiovascular Nursing. 2015;14(1):63-72.
311. Holzapfel N, Löwe B, Wild B, Schellberg D, Zugck C, Remppis A et al. Self-care and depression in patients with chronic heart failure. Heart & Lung. 2009;38(5):392-7.
312. Lee CS, Moser DK, Lennie TA, Tkacs NC, Margulies KB, Riegel B. Biomarkers of myocardial stress and systemic inflammation in patients who engage in heart failure self-care management. Journal of Cardiovascular Nursing. 2011;26(4):321-28.
313. Chin C-H, Tseng L-M, Chao T-C, Wang T-J, Wu S-F, Liang S-Y. Self-care as a mediator between symptom-management self-efficacy and quality of life in women with breast cancer. PLoS One [Internet] 2021 Feb 4 [Cited 2021 Jun 23];16(2):e0246430. doi.org/10.1371/journal.pone.0246430
314. Rogers PJ. Using programme theory to evaluate complicated and complex aspects of interventions. Evaluation. 2008;14(1):29-48.
315. Funnell SC, Rogers PJ. Purposeful program theory: Effective use of theories of change and logic models. New Jersey: John Wiley & Sons; 2011.
316. Shearn K, Allmark P, Piercy H, Hirst J. Building realist program theory for large complex and messy interventions. International Journal of Qualitative Methods. [Internet] 2017 Nov 29 [Cited 2021 Jun 23] 2017;16(1): doi.org/10.1177/1609406917741796
317. Morgan-Trimmer S SJ, Warmoth K and Abraham C. Creating a logic model for an intervention: evaluation in health and wellbeing. [Internet] Public Health England; 2018 [Cited 2021 Jun 23] Available from: https://www.gov.uk/guidance/evaluation-in-health-and-wellbeing-creating-a-logic-model
318. De Silva MJ, Breuer E, Lee L, Asher L, Chowdhary N, Lund C et al. Theory of change: a theory-driven approach to enhance the Medical Research Council's framework for complex interventions. Trials. 2014;15(1):1-13.
319. Bradbury K, Steele M, Corbett T, Geraghty AW, Krusche A, Heber E et al. Developing a digital intervention for cancer survivors: an evidence-, theory-and person-based approach. NPJ Digital Medicine. 2019;2(1):1-13.
320. Lee K, Hoti K, Hughes JD, Emmerton LM. Consumer use of "Dr Google": a survey on health information-seeking behaviors and navigational needs. Journal of Medical Internet Research [Internet] 2015 Dec 29 [Cited 2021 May 08];17(12):e288.doi: 10.2196/jmir.4345.
321. Kerr C, Murray E, Stevenson F, Gore C, Nazareth I. Internet interventions for long-term conditions: patient and caregiver quality criteria. Journal of Medical Internet Research [Internet] 2006 Jul 28 [Cited 2021 May 08];8(3):e13. doi: 10.2196/jmir.8.3.e13.
322. Smits R, Bryant J, Sanson-Fisher R, Tzelepis F, Henskens F, Paul C, et al. Tailored and integrated web-based tools for improving psychosocial outcomes of cancer patients: the DoTTI development framework. Journal of Medical Internet Research [Internet] 2014 [Cited 2021 May 08];16(3):e76. doi: 10.2196/jmir.2849.
323. Davies NJ, Batehup L. Self-management support for cancer survivors: guidance for developing interventions. An update of the evidence. [Internet] National Cancer Survivorship Initiative Supported Self-Management Workstream; 2010 [Cited 2021 May 12] Available from: http://trustedwriter.com/documents/Guidance-for-Developing-Cancer-Specific-Self-Management-Programmes.pdf

324. Jonkman NH, Schuurmans MJ, Jaarsma T, Shortridge-Baggett LM, Hoes AW, Trappenburg JC. Self-management interventions: proposal and validation of a new operational definition. Journal of Clinical Epidemiology. 2016;80:34-42.
325. Lorig K. Self-management education: more than a nice extra. Medical Care. 2003;41(6)699-71.
326. Pearce G, Parke HL, Pinnock H, Epiphaniou E, Bourne CL, Sheikh A et al. The PRISMS taxonomy of self-management support: derivation of a novel taxonomy and initial testing of its utility. Journal of Health Services Research. 2016 ;21(2):73-82.
327. O'Cathain A, Croot L, Sworn K, Duncan E, Rousseau N, Turner K et al. Taxonomy of approaches to developing interventions to improve health: a systematic methods overview. Pilot and Feasibility Studies. 2019;5(1):41.
328. Yardley L, Morrison L, Bradbury K, Muller. The person-based approach to intervention development: application to digital health-related behavior change interventions. Journal of Medical Internet Research [Internet] 2015 Jan 30 [Cited 2021 May 08];17(1):e30. doi: 10.2196/jmir.4055
329. Coulter A, Ellins J. Patient-focused interventions: a review of the evidence. Health Foundation London; 2006.
330. Chodosh J, Morton SC, Mojica W, Maglione M, Suttorp MJ, Hilton L, et al. Meta-analysis: chronic disease self-management programs for older adults. Annals of Internal Medicine. 2005;143(6):427-38.
331. Jonkman NH, Schuurmans MJ, Groenwold RH, Hoes AW, Trappenburg JC. Identifying components of self-management interventions that improve health-related quality of life in chronically ill patients: Systematic review and meta-regression analysis. Patient Education and Counselling. 2016;99(7):1087-98.
332. Morrison LG, Yardley L, Powell J, Michie SJT, e-Health. What design features are used in effective e-health interventions? A review using techniques from critical interpretive synthesis. Telemedicine and e-Health. 2012;18(2):137-44.
333. Michie S, Johnston M, Francis J, Hardeman W, Eccles M. From theory to intervention: mapping theoretically derived behavioural determinants to behaviour change techniques. Applied Psychology. 2008;57(4):660-80.
334. Pellegrini CA, Steglitz J, Hoffman SAJ. e-Health intervention development: a synopsis and comment on "what design features are used in effective e-Health interventions? A review using techniques from critical interpretive synthesis". Translational Behavioural Medicine. 2014;4(4):342-5.
335. Fox S. After Dr Google: peer-to-peer health care. Pediatrics. 2013;131(Supplement 4):S224-S5.
336. Lustria MLA, Noar SM, Cortese J, Van Stee SK, Glueckauf RL, Lee J. A meta-analysis of web-delivered tailored health behavior change interventions. Journal of Health Communication. 2013;18(9):1039-69.
337. Baumeister H, Reichler L, Munzinger M, Lin J. The impact of guidance on Internet-based mental health interventions—A systematic review. Internet Interventions. 2014;1(4):205-15.
338. Titov N, Andrews G, Choi I, Schwencke G, Mahoney A. Shyness 3: randomized controlled trial of guided versus unguided Internet-based CBT for social phobia. Australia and New Zealand Journal of Psychiatry. 2008;42(12):1030-40.
339. Titov N, Andrews G, Choi I, Schwencke G, Johnston L. Randomized controlled trial of web-based treatment of social phobia without clinician guidance. Australia and New Zealand Journal of Psychiatry. 2009;43(10):913-9.
340. Raine R, Wallace I, a'Bháird CN, Xanthopoulou P, Lanceley A, Clarke A, et al., editors. Study 2: application of a formal consensus method to develop recommendations to improve the

effectiveness of multidisciplinary team meetings. Improving the effectiveness of multidisciplinary team meetings for patients with chronic diseases: a prospective observational study. Health Services and Delivery Research. 2014;(2)37:1-72.
341. Hohmann E, Brand JC, Rossi MJ, Lubowitz JH. Expert opinion is necessary: Delphi panel methodology facilitates a scientific approach to consensus. Arthroscopy. 2018;34(2):349-51.
342. Jorm AF. Using the Delphi expert consensus method in mental health research. Australia and New Zealand Journal of Psychiatry. 2015;49(10):887-97.
343. Harvey N, Holmes CA. Nominal group technique: an effective method for obtaining group consensus. International Journal of Nursing Practice. 2012;18(2):188-94.
344. Potter M, Gordon S, Hamer P. The nominal group technique: a useful consensus methodology in physiotherapy research. Australia and New Zealand Journal of Psychiatry. 2004;32:126-30.
345. Culyer AJ, Lomas J. Deliberative processes and evidence-informed decision making in healthcare: do they work and how might we know? Evidence and Policy. 2006;2(3):357-71.
346. Breast Cancer Now. Secondary (metastatic) breast cancer [Internet];2021 [Cited 2021 May 06]. Available from: https://breastcancernow.org/information-support/support-you/secondary-metastatic-breast-cancer
347. Macmillan. Macmillan: Cancer Information & Support [Internet];2021 [Cited 2021 May 06]. Available from: https://www.macmillan.org.uk/cancer-information-and-support
348. Cancer Research UK. Secondary breast cancer. [Internet]; 2021 Apr 19 [Cited 2021 May 08]. Available from: https://www.cancerresearchuk.org/about-cancer/breast-cancer/secondary.
349. Hoffman-Goetz L, Clarke JN. Quality of breast cancer sites on the World Wide Web. Canadian Journal of Public Health. 2000;91(4):281-4.
350. Eysenbach G. Infodemiology: The epidemiology of (mis) information. American Journal of Medicine. 2002;113(9):763-5.
351. Meric F, Bernstam EV, Mirza NQ, Hunt KK, Ames FC, Ross MI et al. Breast cancer on the world wide web: cross sectional survey of quality of information and popularity of websites. BMJ. 2002;324(7337):577-81.
352. Silberg WM, Lundberg GD, Musacchio RA. Assessing, controlling, and assuring the quality of medical information on the Internet: Caveant lector et viewor—Let the reader and viewer beware. Generations: Journal of the Medical Society on Aging. 1997;277(15):1244-5.
353. Gibson A, Holch P, Carter R, Clayton B, Dickinson S, Davidson SE et al. Development of online patient advice for the self-management of low-level radiotherapy and chemotherapy related toxicities (eRAPID): involvement of patients and staff. Psycho-Oncology. 2017;26(S2):10-28.
354. Hospice UK. Information & Support [Internet];2021 2021 [Cited 2021 May 06]. Available from: https://www.hospiceuk.org/information-and-support
355. Ashley L, Jones H, Thomas J, Forman D, Newsham A, Morris E et al. Integrating cancer survivors' experiences into UK cancer registries: design and development of the ePOCS system (electronic Patient-reported Outcomes from Cancer Survivors). British Journal of Cancer. 2011;105(1):S74-S81.
356. Ashley L, Jones H, Thomas J, Newsham A, Downing A, Morris E et al. Integrating patient reported outcomes with clinical cancer registry data: a feasibility study of the electronic Patient-Reported Outcomes From Cancer Survivors (ePOCS) system. Journal of Medical Internet Research [Internet] 2013 Oct 15 [Cited 2020 Apr 21];15(10):e230. doi: 10.2196/jmir.2764.
357. Henry A, Holch P, Routledge J, Absolom K, Walker K, Gibson A et al. Pilot Randomized Trial of Online Self-Monitoring of Symptoms During Pelvic Radiotherapy. International Journal of Radiation Oncology, Biology, Physics. 2020;108(3):e211-e2.

358. Lindner OC, Boon IS, Joffe J, Stark DJ. Evaluation of the “Shared Community Follow-up” after a germ cell tumour—A novel initiative for remote cancer follow-up enhanced by online patient-reported outcome measures. European Journal of Cancer Care. 2020;29(5):e13264.
359. Pompili C, Franks KN, Brunelli A, Hussain YS, Holch P, Callister ME, et al. Patient reported outcomes following video assisted thoracoscopic (VATS) resection or stereotactic ablative body radiotherapy (SABR) for treatment of non-small cell lung cancer: protocol for an observational pilot study (LiLAC). Journal of Thoracic Disease. 2017;9(8):2703.
360. Holch P, Warrington L, Potrata B, Ziegler L, Hector C, Keding A et al. Asking the right questions to get the right answers: using cognitive interviews to review the acceptability, comprehension and clinical meaningfulness of patient self-report adverse event items in oncology patients. Acta Oncologica. 2016;55(9-10):1220-6.
361. Absolom K, Holch P, Warrington L, Samy F, Hulme C, Hewison J et al. Electronic patient self-Reporting of Adverse-events: Patient Information and aDvice (eRAPID): a randomised controlled trial in systemic cancer treatment. BMC Cancer. 2017;17(1):1-16.
362. National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0 [Internet] 2017 27 Nov [Cited 2020 Apr 20]. Available from: https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/ctcae_v5_quick_reference_8.5x11.pdf
363. Basch E, Reeve BB, Mitchell SA, Clauser SB, Minasian LM, Dueck AC, et al. Development of the National Cancer Institute’s patient-reported outcomes version of the common terminology criteria for adverse events (PRO-CTCAE). Journal of the National Cancer Institute. 2014;106(9):dju244.
364. Basch E, Artz D, Dulko D, Scher K, Sabbatini P, Hensley M, et al. Patient online self-reporting of toxicity symptoms during chemotherapy. Journal of Clinical Oncology. 2005;23(15):3552-61.
365. United Kingdom Oncology Nursing Society (UKONS). Acute Oncology Initial Management Guidelines (Version 2.0) 2011 [Cited 2020 Apr 20]. Available from: https://www.ukons.org/site/assets/files/1134/acute_oncology_initial_management_guidelines.pdf
366. Kyte D, Draper H, Calvert M. Patient-reported outcome alerts: ethical and logistical considerations in clinical trials. Journal of Medical Association.2013;310(12):1229-30.
367. Miller SM. Monitoring versus blunting styles of coping with cancer influence the information patients want and need about their disease. Implications for cancer screening and management. Cancer. 1995;76(2):167-77.
368. Jiang S, Liu PL. Digital divide and Internet health information seeking among cancer survivors: a trend analysis from 2011 to 2017. Psycho-Oncology. 2020;29(1):61-7.
369. Lee K, Hoti K, Hughes JD, Emmerton L. Dr Google is here to stay but health care professionals are still valued: an analysis of health care consumers’ internet navigation support preferences. Journal of Medical Internet Research [Internet] 2017 Jun 14 [Cited 2020 Apr 08];19(6):e210. doi:10.2196/jmir.7489
370. Kushniruk A, Nohr C, Jensen S, Borycki EM. From usability testing to clinical simulations: Bringing context into the design and evaluation of usable and safe health information technologies. Yearbook of Medical Informatics. 2013;22(01):78-85.
371. Monkman H, Griffith J. A Tale of Two Inspection Methods: Comparing an eHealth Literacy and User Experience Checklist with Heuristic Evaluation. Studies in Health Technology and Informatics. 2021;281:906-10.
372. Monkman H, Kushniruk AW, editors. The Consumer Health Information System Adoption Model. In: Nøhr C., Borycki EM, Kuziemsky CE, Kushniruk AW. Context Sensitive Health

Informatics: Many places, many users, many contexts, many uses. Studies in Health Technology and Informatics. 2015;218. P.26
373. Bleijenberg N, Janneke M, Trappenburg JC, Ettema RG, Sino CG, Heim N et al. Increasing value and reducing waste by optimizing the development of complex interventions: Enriching the development phase of the Medical Research Council (MRC) Framework. International Journal of Nursing Studies. 2018;79:86-93.
374. Hollingsed T, Novick DG, editors. Usability inspection methods after 15 years of research and practice. Proceedings of the 25th annual ACM international conference on Design of communication; 2007. p.249-255
375. Albert W, Tullis T. Measuring the user experience: collecting, analyzing, and presenting usability metrics. 2nd ed. Newnes; 2013.
376. Molich R, Nielsen. Improving a human-computer dialogue. Communications of the Association for Computing Machinery. 1990;33(3):338-48.
377. Jaspers MW. A comparison of usability methods for testing interactive health technologies: methodological aspects and empirical evidence. International Journal of Medical Informatics. 2009;78(5):340-53.
378. Virzi RA. Refining the test phase of usability evaluation: How many subjects is enough? Human Factors. 1992;34(4):457-68.
379. Nielsen J. Usability engineering. MA: Morgan Kaufmann; 1994.
380. Faulkner L. Beyond the five-user assumption: Benefits of increased sample sizes in usability testing. Behavioural Research Methods, Instruments and Computers. 2003;35(3):379-83.
381. Macefield R. How to specify the participant group size for usability studies: a practitioner's guide. Journal of Usability Studies. 2009;5(1):34-45.
382. Schnall R, Cho H, Liu. Health Information Technology Usability Evaluation Scale (Health-ITUES) for usability assessment of mobile health technology: validation study. JMIR mhealth uhealth [Internet] 2018 Jan 5 [Cited 2021 Apr 06];6(1): e4. doi: 10.2196/mhealth.8851.
383. Brewer LC, Hayes SN, Caron AR, Derby DA, Breutzman NS, Wicks A et al. Promoting cardiovascular health and wellness among African-Americans: Community participatory approach to design an innovative mobile-health intervention. PLoS One [Internet] 2019 Aug 20 [Cited 2021 Apr 06];14(8):e0218724.
384. Beller EM, Gebski V, Keech AC. Randomisation in clinical trials. Medical Journal of Australia. 2002;177(10):565-7.
385. Roberts C, Torgerson DJB. Randomisation methods in controlled trials. BMJ. 1998;317(7168):1301-10.
386. Altman DG, Bland JMJB. How to randomise. BMJ. 1999;319(7211):703-4.
387. Altman DG, Bland JMJB. Treatment allocation by minimisation. BMJ. 2005;330(7495):843.
388. Treasure T, MacRae KD. Minimisation: the platinum standard for trials? Randomisation doesn't guarantee similarity of groups; minimisation does. BMJ. 1998;317(7155):362-3.
389. Pocock SJ, Simon R. Sequential treatment assignment with balancing for prognostic factors in the controlled clinical trial. Biometrics. 1975:103-15.
390. Fink A. Research Design, Validity and Best Available Evidence Evidence-Based Public Health Practice. Thousand Oaks, CA: SAGE Publications 2013. p. 107-58.
391. Cunningham JA, Kypri K, McCambridge J. Exploratory randomized controlled trial evaluating the impact of a waiting list control design. BMC Medical Research Methodology. 2013;13(1):1-7.
392. Elliott S, Brown JJBr, therapy. What are we doing to waiting list controls? Behaviour Research and Therapy. 2002;40(9):1047-52.
393. Whitehead WE. Control groups appropriate for behavioral interventions. Gastroenterology. 2004;126(Supp) 1:S159-S63.

394. Hróbjartsson A, Boutron I, Therapeutics. Blinding in randomized clinical trials: imposed impartiality. Clinical Pharmacology and Therapeutics. 2011;90(5):732-6.
395. Stephenson J, Imrie J. Why do we need randomised controlled trials to assess behavioural interventions? BMJ. 1998;316(7131):611-3.
396. Clark L, Fairhurst C, Torgerson DJ. Allocation concealment in randomised controlled trials: are we getting better? BMJ. 2016;355.
397. Baker TB, Gustafson DH, Shaw B, Hawkins R, Pingree S, Roberts L, et al. Relevance of CONSORT reporting criteria for research on eHealth interventions. Patient Education and Counselling. 2010;81:S77-S86.
398. Saghaei M. QMinim Online Minimization [Internet] 2013 [Cited 2021 Apr 06]. Available from: http://rct.mui.ac.ir/q/index.php.
399. Kraska M. Repeated Measures Design. In: Salkind N, editor. Encyclopedia of Research Design 1-0. Thousand Oaks, CA: SAGE Publications; 2010. p. 1244-7.
400. Bell B. Pretest-Posttest Design In: Salkind N, editor. Encyclopedia of Research Design. 1-0. Thousand Oaks, CA: SAGE Publications; 2010. p. 1087-91.
401. Cranmer G. One-Group Pretest–Posttest Design In: Allen M, editor. The SAGE Encyclopedia of Communication Research Methods 1-4. Thousand Oaks, CA: SAGE Publications; 2017. p. 1125-6.
402. Ramadas A, Quek KF, Chan C, Oldenburg B. Web-based interventions for the management of type 2 diabetes mellitus: a systematic review of recent evidence. International Journal of Medical Informatics. 2011;80(6):389-405.
403. Brady MJ, Cella DF, Mo F, Bonomi AE, Tulsky DS, Lloyd SR et al. Reliability and validity of the Functional Assessment of Cancer Therapy-Breast quality-of-life instrument. Journal of Clinical Oncology. 1997;15(3):974-86.
404. Yoo HJ, Ahn SH, Eremenco S, Kim H, Kim WK, Kim SB, et al. Korean translation and validation of the functional assessment of cancer therapy-breast (FACT-B) scale version 4. Quality of Life Research. 2005;14(6):1627-32.
405. Ng R, Lee CF, Wong NS, Luo N, Yap YS, Lo SK, et al. Measurement properties of the English and Chinese versions of the functional Assessment of cancer therapy—breast (FACT-B) in Asian breast cancer patients. Breast Cancer Research and Treatment. 2012;131(2):619-25.
406. FACIT Group. Scoring of the FACIT measures [Internet] 2020 [Cited 2021 Jun 14]. Available from: https://www.facit.org/scoring.
407. Herdman M, Gudex C, Lloyd A, Janssen M, Kind P, Parkin D, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Quality of Life Research. 2011;20(10):1727-36.
408. Janssen M, Pickard AS, Golicki D, Gudex C, Niewada M, Scalone L et al. Measurement properties of the EQ-5D-5L compared to the EQ-5D-3L across eight patient groups: a multi-country study. Quality of Life Research. 2013;22(7):1717-27.
409. Kim SH, Kim HJ, Lee S-i, Jo M-WJQoLR. Comparing the psychometric properties of the EQ-5D-3L and EQ-5D-5L in cancer patients in Korea. Quality of Life Research. 2012;21(6):1065-73.
410. Heitzmann CA, Merluzzi TV, Jean-Pierre P, Roscoe JA, Kirsh KL, Passik SDJPO. Assessing self-efficacy for coping with cancer: Development and psychometric analysis of the brief version of the Cancer Behavior Inventory (CBI-B). Psycho-Oncology. 2011;20(3):302-12.
411. Center for Self-Management Research. Evaluation tools: 6-item Chronic Disease Self-Efficacy [Internet] 2021 [Cited 2021 Apr 16] Available from: https://www.selfmanagementresource.com/index.php/resources/evaluation-tools/english-evaluation-tools.
412. Lorig KR, Sobel DS, Ritter PL, Laurent D, Hobbs M. Effect of a self-management program on patients with chronic disease. Effective Clinical Practice. 2001;4(6):256-62.

413. Wiljer D, Leonard KJ, Urowitz S, Apatu E, Massey C, Quartey NK, et al. The anxious wait: assessing the impact of patient accessible EHRs for breast cancer patients. BMC Medical Informatics and Decision Making. 2010;10(1):1-10.
414. Ritter PL, Lorig KJJoce. The English and Spanish self-efficacy to manage chronic disease scale measures were validated using multiple studies. Journal of Clinical Epidemiology. 2014;67(11):1265-73.
415. Billingham SA, Whitehead AL, Julious SAJBmrm. An audit of sample sizes for pilot and feasibility trials being undertaken in the United Kingdom registered in the United Kingdom Clinical Research Network database. BMC Medical Research Methodology. 2013;13(1):104.
416. Julious SA. Sample size of 12 per group rule of thumb for a pilot study. The Journal of Applied Statistics in the Pharmaceutical Setting. 2005;4(4):287-91.
417. Van Belle G. Statistical rules of thumb. New Jersey: John Wiley & Sons; 2011.
418. Altman DG. Statistics and ethics in medical research: III How large a sample? BMJ. 1980;281(6251):1336. doi:10.2196/jmir.7.1.e11
419. Eysenbach G. The law of attrition. JMIR [Internet] 2005 Mar 32 [Cited 2021 Apr 21];7(1):e11.
420. Geraghty AW, Torres LD, Leykin Y, Pérez-Stable EJ, Muñoz RFJ. Understanding attrition from international internet health interventions: a step towards global eHealth. Health Promotion International. 2013;28(3):442-52.
421. Health Research Authority. GDPR guidance for researchers and study co-ordinators [Internet] 2021 [Cited 2021 Sept 06] Available from: https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/data-protection-and-information-governance/gdpr-guidance/.
422. University of Leeds Verbal informed consent protocol. V1.3 [Internet] 2019 Feb 13 [Cited 2021 Jun 16]. Available from: http://ris.leeds.ac.uk/wpcontent/uploads/2020/07/Verbal_Consent_Protocol.pdf
423. Giangregorio LM, Thabane L. Pilot studies and feasibility studies for complex interventions: an introduction. In: Complex Interventions in Health: an overview of research methods. Richards DA, Rahm Hallberg I; 2015 p.127-35.
424. EuroQol Research Foundation. EQ-5D-5L User Guide [Internet] 2019 [Cited 2021 Apr 06]. Available from: https://euroqol.org/publications/user-guides/
425. Velikova G, Absolom K, Warrington L, Morris C, Hudson E, Carter R et al. Phase III randomized controlled trial of eRAPID (electronic patient self-Reporting of Adverse-events: Patient Information and advice)—An eHealth intervention during chemotherapy. 2020. American Society of Clinical Oncology;39(7).
426. Harris K, Lim CR, Dawson J, Fitzpatrick R, Beard DJ, Price AJ. The Oxford knee score and its subscales do not exhibit a ceiling or a floor effect in knee arthroplasty patients: an analysis of the National Health Service PROMs data set. Knee Surgery, Sports Traumatology, Arthroscopy. 2017;25(9):2736-42.
427. Stucki G, Liang M, Stucki S, Katz J, Lew RA. Application of statistical graphics to facilitate selection of health status measures for clinical practice and evaluative research. Clinical Rheumatology. 1999;18(2):101-5.
428. McHorney CA, Tarlov AR. Individual-patient monitoring in clinical practice: are available health status surveys adequate? Quality of Life Research. 1995;4(4):293-307.
429. Lim CR, Harris K, Dawson J, Beard DJ, Fitzpatrick R, Price A. Floor and ceiling effects in the OHS: an analysis of the NHS PROMs data set. BMJ Open [Internet] 2015 Jul 27 [Cited 2021 Apr 06] 2015;5(7). e007765.doi: 10.1136/bmjopen-2015-007765.
430. Hamilton D, Lane JV, Gaston P, Patton J, Macdonald D, Simpson A, et al. What determines patient satisfaction with surgery? A prospective cohort study of 4709 patients following total joint replacement. BMJ Open. 2013;3(4). doi.org/10.1136/bmjopen-2012-002525.

431. Paulsen A, Odgaard A, Overgaard SJB. Translation, cross-cultural adaptation and validation of the Danish version of the Oxford hip score: assessed against generic and disease-specific questionnaires. Bone and Joint Research. 2012;1(9):225-33.
432. Greene ME, Rader KA, Garellick G, Malchau H, Freiberg AA, Rolfson OJCO, et al. The EQ-5D-5L improves on the EQ-5D-3L for health-related quality-of-life assessment in patients undergoing total hip arthroplasty. Clinical Orthopaedics and Related Research.2015;473(11):3383-90.
433. Berben L, Sereika SM, Engberg S. Effect size estimation: methods and examples. International Journal of Nursing Studies. 2012;49(8):1039-47.
434. Dudley WN, Wickham R, Coombs N. An introduction to survival statistics: Kaplan-Meier analysis. Journal of Advanced 2016;7(1):91.
435. Boslaugh S. Kaplan-Meier method. Encyclopedia of Epidemiology. Thousand Oaks, California: SAGE; 2008.
436. Altman DG, Bland JM. Time to event (survival) data. BMJ. 1998;317(7156):468-9.
437. Cohen J. Statistical power analysis for the behavioral sciences. Academic press; 2013.
438. Salyers Bull S, Lloyd L, Rietmeijer C, McFarlane M. Recruitment and retention of an online sample for an HIV prevention intervention targeting men who have sex with men: the Smart Sex Quest Project. AIDS Care. 2004;16(8):931-43.
439. Couper M, Peytchev A, Strecher V, Rothert K, Anderson. Following up nonrespondents to an online weight management intervention: randomized trial comparing mail versus telephone. JMIR [Internet] 2007 Jun 13 [Cited 2020 Jun 02];9(2):e16.
440. McKay H, Danaher B, Seeley J, Lichtenstein E, Gau. Comparing two web-based smoking cessation programs: randomized controlled trial. JMIR [Internet] 2008 [Cited 2020 Jun 02] ;10(5):e40. doi: 10.2196/jmir.993
441. Hui D, Glitza I, Chisholm G, Yennu S, Bruera E. Attrition rates, reasons, and predictive factors in supportive care and palliative oncology clinical trials. Cancer. 2013;119(5):1098-105.
442. Brintnall-Karabelas J, Sung S, Cadman ME, Squires C, Whorton K, Pao M. Improving recruitment in clinical trials: why eligible participants decline. Journal of Empirical Research in Human Resaerch Ethics. 2011;6(1):69-74.
443. Skivington K, Matthews L, Simpson SA, Craig P, Baird J, Blazeby JM et al. A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. BMJ. 2021;374
444. van der Hout A, van Uden-Kraan C, Holtmaat K, Jansen F, Lissenberg-Witte B, Nieuwenhuijzen G, et al. Reasons for not reaching or using web-based self-management applications, and the use and evaluation of Oncokompas among cancer survivors, in the context of a randomised controlled trial. Internet Interventions. 2021;25:100429.
445. Audulv ÅJ. The over time development of chronic illness self-management patterns: a longitudinal qualitative study. BMC Public Health. 2013;13(1):1-15.
446. Foster C, Breckons M, Hankins M, Fenlon D, Cotterell P. Developing a scale to measure self-efficacy to self-manage problems following cancer treatment. Psycho-Oncology. 2013;22:16.
447. Kapoor A, Nambisan P, Baker. Mobile applications for breast cancer survivorship and self-management: A systematic review. Health Informatics Journal. 2020;26(4):2892-905.
448. Cannon C, editor. Telehealth, mobile applications, and wearable devices are expanding cancer care beyond walls. Seminars in oncology nursing. 2018;34(2):118-25.
449. Shigaki C, Kruse RL, Mehr D, Sheldon KM, Ge B, Moore C et al. Motivation and diabetes self-management. Chronic Illness. 2010;6(3):202-14.
450. Shannon RJ. Motivational interviewing: Enhancing patient motivation for behavior change. International Handbook of Occupational Therapy Interventions. New York: Springer; 2015. p. 885-94.

451. Estacio EV, Whittle R, Protheroe J. The digital divide: examining socio-demographic factors associated with health literacy, access and use of internet to seek health information. Journal of Health Psychology. 2019;24(12):1668-75
452. Tsianakas V, Robert G, Maben J, Richardson A, Dale C, Wiseman T. Implementing patient-centred cancer care: using experience-based co-design to improve patient experience in breast and lung cancer services. Supportive Care in Cancer. 2012;20(11):2639-47.
453. Chan RJ, Howell D, Lustberg MB, Mustian K, Koczwara B, Ng CC et al. Advances and future directions in the use of mobile health in supportive cancer care: proceedings of the 2019 MASCC annual meeting symposium. Supportive Care in Cancer. 2020;28(9):4059-67.

Additional information

Core study related documents for phases I and II (Participant Information Sheets, consent forms, questionnaires and the LIBERATE User Guide) are available to view on the LIBERATE section of the Patient Centred Outcomes Research group's website. (https://pcor.org.uk/liberate-living-better-with-advanced-breast-cancer-symptom-monitoring-self-management-and-sign-posting-support-for-women-living-with-secondary-breast-cancer/)