

**Female Breast Cancer Late Presentation in Saudi Arabia: A
Mixed Methods Study**

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I was responsible for the work in term of literature searching, data analysis and writing. The contribution of the other authors was advisory. Lim, J.N.W. Supervised the review including data analysis and contributed to the preparation of the manuscript.

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Dedication

This thesis is lovingly dedicated to my parents, Abdulaziz and Haya, who inspired me with their passion in seeking knowledge. Their encouragement, words, and endless love have supported me through my PhD studies and my life.

I also dedicate this work to my sons, Rashed and Mohammed. Seeking knowledge has many forms, and a research postgraduate study is one of them. I am sure that it was not always easy for you to watch your mother as she worked on this thesis, but maybe this is all you need to know: no thesis could ever take the place in my heart that you two hold. Working hard and seeking knowledge, these are also ways of honouring loved ones.

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Abstract

Breast cancer is one of the most common cancers in the developed world, and it is rapidly increasing in developing countries, such as Saudi Arabia. Early stage diagnosis of breast cancer is an aim that would enable better outcomes, especially survival. The impact of early presentation of breast cancer on prognosis is so profound that the investigation into factors influencing late presentation of female breast cancer in Saudi Arabia is vital to attain timely diagnoses.

A mixed methods research design was used to gain insight into the factors associated with late presentation and the reasons for their association; quantitative and qualitative data were collection, analysed, and integrated from various data sets and perspectives.

Phase I of this thesis comprised a review of Middle East studies in the published literature about factors associated with late-presentation breast cancer. The review confirmed the need to conduct this research and the originality of such research.

Phase II comprised collection of breast cancer-related data from the Saudi National Cancer Registry. In total, 10,663 records for female breast cancer were analysed to investigate the relationship between stage at diagnosis and five independent variables: age, year of diagnosis, nationality, place of residence, and marital status. Analysis found all variables except marital status to be significant.

The quantitative findings were used for sampling participants in Phase III, which comprised semi-structured interviews with 19 women diagnosed with breast cancer at early and late stages. The analysis found an interaction between factors associated with late presentation, in particular with age. Furthermore, the results provided insight into contextual factors influencing time to seek medical care and diagnosis following symptom recognition.

Phase IV comprised a reanalysis of quantitative data to investigate the interaction between variables and stage at diagnosis, which was prompted by the qualitative findings. The analysis illustrated the characteristics of women who typically receive a late-stage diagnosis. These include living in regions with less oncology care and age older than 58 years or younger than 42 years. In further analysis, inference was then generated by integrating findings: explaining the factors found in the

quantitative results through integration with the qualitative findings and then comparing these results with findings in the literature.

This thesis presents an innovative platform for investigating a complex health problem and offers answers to what factors might associate with late presentation of female breast cancer in Saudi Arabia and why.

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List of Abbreviations

Abbreviation	Meaning
ASIR	Age Standardised Incidence Rate
CASP	Critical Appraisal Skills Programme
CHAID	Chi-Squared Automatic Interaction Detector
Chi-Square	χ^2
GCC	Gulf Cooperation Council
GP	General Practitioner
HRT	Hormone Replacement Therapy
IARC	International Agency for research on Cancer
KFSH&RC	King Faisal Specialist Hospital and Research Centre
NAEDI	National Awareness and Early Diagnosis Initiative
PHC	Primary Healthcare Centre
PhD	Doctor of Philosophy
POM	Proportional Odds Model
POR	Proportional Odds Ratio
SEER	Surveillance, Epidemiology and End Results
SNCR	Saudi National Cancer Registry
SPSS	Statistical Package for Social Science
TNM	TNM Classification of Malignant Tumours
UK	United kingdom
US	United States

Chapter 1: Introduction

Worldwide, breast cancer is the most common cancer for females, accounting for 25% of all female cancer cases. An estimated 1.68 million new cases of female breast cancer were diagnosed in 2012. Among men and women, breast cancer accounts for 12% of all cancer diagnoses worldwide and is the most common type of cancer after lung cancer (13%) Cancer Research UK (2014). The incidence of female breast cancer is highest in developed countries, with more than 80 cases per 100,000, and lowest in developing countries, with fewer than 40 cases per 100,000 (Ferlay et al., 2010). The incidence of breast cancer, however, is rising in developing as well as developed countries; in developing countries, the upward trend is thought to be due to population aging, population growth, and life-style changes. An estimated 60% of breast cancer deaths now occur in developing countries (Jemal et al., 2011).

Early-stage diagnosis of cancer yields better female breast cancer outcomes; treatment is more effective and survival higher than with later-stage diagnoses (De Angelis et al., 2014). Best outcomes are achieved when patients start treatment before the onset of breast cancer symptoms, such as when the female patient is diagnosed in a mammography screening, or as soon as possible after the first appearance of symptoms (Richards, 2009a). Upon diagnosis, those who begin treatment as soon as possible have a better prognosis than those who delay (Smith et al., 2013); but breast cancer in women in Saudi Arabia is not always diagnosed in the early stages. The following sections of this chapter introduce the research problem and the aim and objectives of this thesis.

1.1 Cancer in the Gulf Countries

As elsewhere in the world, the most common type of cancer among women in Arab countries is breast cancer, and its incidence is expected to rise (Salim et al., 2010). A ministry decree in Gulf Cooperation Council (GCC) countries (Saudi Arabia, the United Arab Emirates, Oman, Kuwait, Qatar and Bahrain) requires that hospitals and laboratories report all cancer cases to the Gulf Centre for Cancer Registration (Brown et al., 2012). The most common types of cancer in the GCC are breast and thyroid cancers in female patients, and lung and prostate cancers in males (Al-Madouj and Al-Zahrani, 2009). Whilst early detection of cancer in the GCC is

improving with advancements in healthcare provision (Brown et al., 2012), late presentation is a critical issue for the treatment of cancer (Silbermann, 2012) as treatment success is lower for women who present at advanced stages (Salim et al., 2010). Breast cancer screening varies among GCC countries, ranging from the routine screening done in the United Arab Emirates to an absence of standard national screening in Saudi Arabia (Brown et al., 2012). Brown et al. (2012) have emphasised the need to expand and integrate current research on barriers to early detection of breast cancer into the domain of cancer care delivery in the GCC countries. Currently, there is a dearth of research on the role of international and local contexts in cancer care delivery, and consequently, on potential differences arising from variations in needs, social factors, culture and biology. Such research is important because breast cancer outcome has multifactorial influences, some of which are non-modifiable, such as biology, and others which are modifiable, such as patient behaviour, the healthcare system, and interactions between patients and the healthcare system (Wheeler et al., 2013). Accordingly, research addressing these differences could improve the early detection of cancer and cancer control.

This thesis seeks to address this gap in the literature, looking into the much-neglected reasons for late-presentation breast cancer among females in Saudi Arabia. It adopts innovative mixed methods research to do so, employing quantitative and qualitative approaches that take into consideration the perspective of Saudi female breast cancer patients—an approach that has not been systematically undertaken in previous research in this area.

1.2 Breast cancer in Saudi Arabia

The reasons for studying late presentation of female breast cancer in Saudi Arabia: (i) breast cancer is the most common type of cancer in Saudi nationals (males and females), and highest among women, (ii) the incidence of female breast cancer is estimated to increase , and (iii) stage at presentation is later in Saudi Arabia than in developed countries.

In 2009, breast cancer was the most common type of cancer and comprised 14.5% of all cancer diagnoses among adult Saudi nationals (males and females); among Saudi females alone, incidence rose to 26.5%. Breast cancer thus affects males and females more than other cancers: colorectal cancer (12%), thyroid cancer (7.4%), non-

Hodgkin’s lymphoma (7.2%), and liver (4.6%). Table 1 illustrates the significant differences between the most commonly occurring cancers in male and female adult Saudis (Al-Eid and Garcia, 2012).

Breast cancer incidence varies among the Kingdom’s administrative regions, with the Eastern region reporting the highest number of cancer cases, followed by the Riyadh and Makkah regions (Al-Eid and Garcia, 2012). The variation in breast cancer incidence among the regions may indicate variation in stage at diagnosis, and more importantly, variation in the availability of advanced oncology care (see Chapter 2). Thus, this thesis will examine place of residence by region in relation to stage at diagnosis and the impact of late-stage presentation.

Table 1: Distribution of cancer type by gender during 2009

Cancer type	Female		Cancer type	Male	
	Frequency	%		Frequency	%
Breast	1308	26.5	Colorectal	616	14.4
Thyroid	537	10.9	Non-Hodgkin’s lymphoma	386	9
Colorectal	492	10	Prostate	294	6.9
Non-Hodgkin’s lymphoma	277	5.6	Liver	290	6.8
Uterine cancer	253	5.1	Lung	274	6.4
Total	4927		Total	4269	

Source: (Al-Eid and Garcia, 2012)

The Age Standardised Incidence Rate (ASIR) for breast cancer among females in Saudi Arabia was 22.7/100,000 in 2009 (Al-Eid and Garcia, 2012) compared to 125.9/100,000 in the United Kingdom (UK) (Cancer Research UK, 2012) and 123.8/100,000 in the United States (US) (Howlader et al., 2012).

Another reason for choosing to study female breast cancer is that the incidence in Saudi Arabia, among the lowest in the world, is estimated to increase 350% by 2025 due to aging of the population (Ibrahim et al., 2008), with future reproductive and

socioeconomic changes (Babay, 2004) highlight the urgent need to address this problem.

Anderson et al. (2011) have cautioned that developing countries must prepare for the expected increase in breast cancer rates by designing and implementing appropriate breast cancer programmes.

The third reason for choosing to study female breast cancer concerns its generally late presentation in Saudi Arabia compared with developed countries. Although the incidence of breast cancer is currently lower in Saudi Arabia than in the US, for example, most diagnoses were made at an advanced stage, in contrast to at an early stage in the US (See Table 2). A worldwide comparison of breast cancer stages at diagnosis shows the magnitude of late presentation in Saudi Arabia. The Saudi National Cancer Registry (SNCR) categorises cancer stages based on disease progression – localised, regional and distant – as defined in the Surveillance, Epidemiology, and End Results (SEER) Summary Staging Manual – 2000 (Al-Eid and Garcia, 2012). Methods of categorising the stages of cancer vary across the world (Walters et al., 2013a), but comparisons with countries that use a staging system similar to the one used in Saudi Arabia show that although the proportion of late-stage breast cancer diagnoses in Saudi Arabia is similar to in other Gulf states and the Middle East, it varies substantially from in developed countries such as the US,¹ where the percentage of cases diagnosed at the early, localised stage is significantly higher, and the percentage of those diagnosed at later stages is thus considerably lower (Table 2).

Early-stage cancer is localised, while advanced stages are regional and distant. When the cancer is limited to a specific organ and has not spread to other parts of the body, it is diagnosed as localised (Young et al., 2001). The regional stage occurs when cancer cells have spread to nearby lymph nodes, organs or tissues; the distant stage, when cancer cells have spread to distant organs or lymph nodes (Young et al., 2001).

¹ The US was selected for breast cancer comparisons because the tumour-staging system used there is similar to that used in Saudi Arabia.

Table 2: Stage of breast cancer development at diagnosis

Stage at diagnosis	Gulf Countries		Middle East	Developed countries
	Saudi Arabia (2009) ¹	Gulf Countries (1998-2005) ²	Egypt (2000-2002) ³	US (2003-2009) ⁴
Localised	31%	20.9%	25.5%	61%
Regional	42.2%	47%	58%	32%
Distant	18.4%	11.4%	16.5%	5%
Unknown	8.4%	20.9%		2%

¹ (Al-Eid and Garcia, 2012), ² (Al-Madouj and Al-Zahrani, 2009), ³ (World Health Organization, 2009) and ⁴ (Howlader et al., 2012).

Figure 1, constructed from data in Table 2, clearly illustrates the problem of late-stage breast cancer diagnoses in Saudi Arabia. The higher discovery of cancer in the localised stages in the US than in Saudi Arabia may be due to the higher prevalence of mammography screening, which also detects breast cancers that are asymptomatic. The percentage of breast cancer in the distant, metastatic stage, however, is 3.3 times higher in Saudi Arabia than in the US, and this cannot be attributed solely to better screening methods and technologies.

Evidence on late-stage at diagnosis of breast cancer has been reported previously (Al-Eid and Arteh, 2009, Al-Eid and Manalo, 2011), however, trends over time since the SNCR began its registration of cancer are unclear. Thus, this thesis will report year of diagnosis to investigate its association with late-stage at diagnosis.

The fourth reason for choosing this research problem is to reduce the proportion of late-stage diagnoses by helping guide the effective implementation of current healthcare services and inform future policy on screening services (see Chapter 2) to reduce treatment delays and increase the proportion of women who survive more than five years.

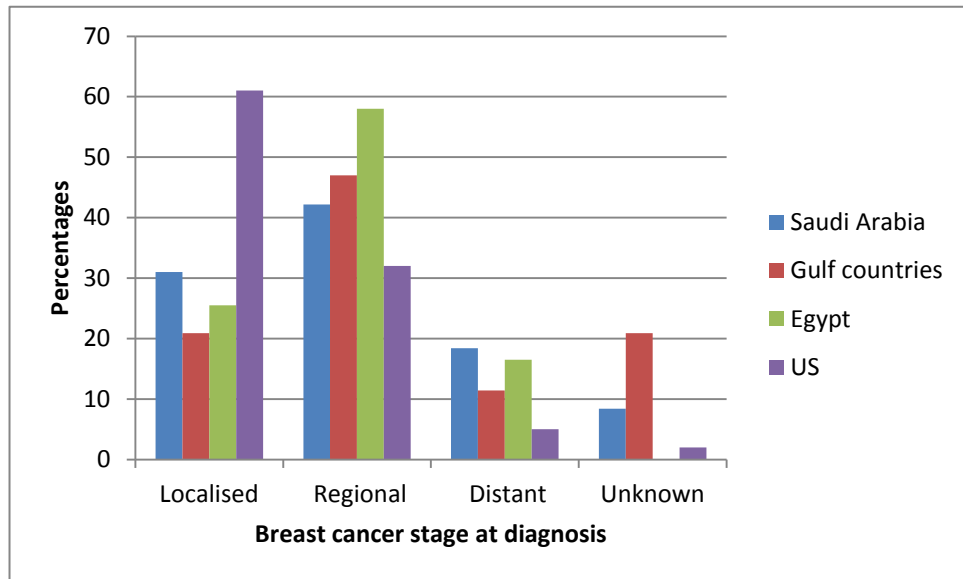


Figure 1: Stages of breast cancer at diagnosis

Source: (Al-Eid and Garcia, 2012, Al-Madouj and Al-Zahrani, 2009, Howlader et al., 2012, World Health Organization, 2009).

One explanation for the higher incidence of breast cancer in regional and distant stages among Saudi Arabian women compared with patients in the US may be biological. Increasing evidence suggests that differences in breast cancer incidences and outcomes are related to ethnicity (Januszewski et al., 2014), with disparities being noted within specific countries, such as the UK and the US (Januszewski et al., 2014). Although differences in tumour biology are recognised, this alone does not describe where and why differences exist in breast cancer outcomes (Januszewski et al., 2014).

A consecutive breast cancer series analysis of 204 Saudi Arabian breast cancer cases and 2,197 Swiss cases found a notable biological difference between Saudi and Swiss patients (Al-Kuraya et al., 2005). Saudi patients had a higher percentage of grade III tumours (65%) compared to Swiss patients (32%). In addition, lower grade tumours (Grade I) were seen in 6% of Saudi patients compared to 27% of Swiss patients (Al-Kuraya et al., 2005). The authors concluded that Saudi women have a greater tendency to develop high-grade tumours than do Swiss women. However, Saudi women had a 14-fold lower risk of developing grade I tumours than Swiss women. The authors suggested that the higher-grade tumours among Saudi breast cancer patients might be explained in two ways: either Saudi women have a higher tendency to develop higher-grade tumours, or they have a lower risk of developing

lower-grade tumours, and genetic and/or lifestyle differences might explain the molecular differences between Saudi and Swiss breast cancer patterns (Al-Kuraya et al., 2005).

Al-Kuraya et al. (2005) study thus provides supporting evidence for ethnic variability in the disease progression of breast cancer (Januszewski et al., 2014). Although this thesis will not examine ethnicity as the study population comprises Saudi nationals, the quantitative study will examine potential differences in stage at diagnosis between Saudi and non-Saudi nationals.

The research literature shows that the risk of developing breast cancer increases as women age (Irminger-Finger, 2010), with the risk of breast cancer increasing substantially for women over age 50 in Western nations (Howlander et al., 2012). Breast cancer patients, however, tend to be younger in Arab nations² than in Western ones, with an average age at diagnosis of 45.4 years; 66% of Arab cases of female breast cancer are under 50 (Najjar and Easson, 2010). In Saudi Arabia, the mean age at diagnosis of patients with female breast cancer is 48; 65% of the cases at diagnosis are under 50 (Al-Eid and Garcia, 2012), and these patterns are similar in all Arab nations (Najjar and Easson, 2010).

Other research examining the characteristics of breast cancer patients in Saudi Arabia provides evidence of a younger average age at diagnosis of breast cancer in Saudi Arabia than that seen in Western nations. A review of 867 breast cancer records for patients diagnosed in the King Faisal Specialist Hospital and Research Centre (KFSH&RC) between 1986 and 2002 showed that patients age 40 and under represented 33.2% of all breast cancer diagnoses (Elkum et al., 2007). This age range, 40 and younger, is a critical prognostic factor for disease-free survival among women in Saudi Arabia (Elkum et al., 2007).

A study conducted in Saudi Arabia's Eastern province compared age at breast cancer diagnosis in Saudi Arabia and the US (Rudat et al., 2012). The retrospective study compared 262 breast cancer diagnoses made between 2004 and 2011 in Saudi Arabia with the published US data from the SEER program. The results confirmed both a younger average age at diagnosis and a higher prevalence of advanced stages at diagnosis among Saudi Arabian patients compared to US patients, with 57.5% of

² Saudi Arabia, Bahrain, Qatar, Kuwait, Emirates, Oman, Yemen, Iraq, Syria, Jordan, Lebanon, Egypt, Libya, Algeria, Tunis, Morocco, and Sudan.

patients diagnosed at under age 50 in Saudi Arabia compared to 12.5% in the US (Rudat et al., 2012).

The younger age at diagnosis and the low incidence of breast cancer in Saudi Arabia raises questions about whether the menopause is a factor associated with breast cancer outcomes. A review of 130 breast cancer patients diagnosed between 1981 and 1991 by a health institution in the Eastern province examined the association between age, menopause and survival (Al-Idrissi et al., 1992). Of these patients, 82 were pre-menopausal and 48 post-menopausal. However, neither unadjusted nor adjusted analyses could identify any significant differences in survival attributable to either age or menopause (Al-Idrissi et al., 1992).

The differences in breast cancer diagnoses between the Arab states and the West in general, and in age at diagnosis between Saudi Arabia and the West, have caught the attention of breast cancer experts, and are the reason that a regional committee, the Middle East and North Africa Breast Cancer Regional Guidelines Committee has proposed modifying the clinical practice guidelines for breast cancer to meet the unique needs of breast cancer patients in the Gulf States and the Middle East (Abulhair et al., 2010a). Thus, this thesis examines the association between age at diagnosis and late-stage diagnosis for female breast cancer; the thesis also includes a literature review since the literature, in particular, shows a strong association between age and delayed presentation of breast cancer (Ramirez et al., 1999).

1.3 Concerns about late-stage diagnosis of breast cancer in Saudi Arabia

From a public health viewpoint, early presentation and diagnosis of breast cancer can both save lives and reduce healthcare costs, because it is more cost effective to treat breast cancer in early stages than in advanced ones. Groot and colleagues (2006) found that treating early stage (stage I) breast cancer and implementing extensive breast cancer programmes³ are the most beneficial interventions for breast cancer control (Groot et al., 2006). Moreover, early diagnosis can also improve a patient's quality of life (Unger-Saldana and Infante-Castaneda, 2009).

³ An extensive breast cancer programme involves the treatment of all stages of the disease, together with breast cancer awareness and early case detection through bi-annual mammographic screening for women age 50–70 years.

In the absence of mammography screening, breast cancer detection relies mainly on patients seeking healthcare for observed abnormalities. The patient thus plays a crucial role in early-stage detection, especially in the absence of routine mammography screening provision.

Studies that investigate the problem of delayed presentation usually consider presentation to be delayed when the time between self-recognition of breast cancer symptoms and seeking medical advice exceeds three months (Ramirez et al., 1999, Richards et al., 1999b). Although the SNCR does not provide estimates of the intervals between symptom recognition and the seeking of healthcare, several studies using institutional data have indicated that there is a problem of late presentation of breast cancer in Saudi Arabia.

Ibrahim (1990) retrospectively reviewed the records of 75 female breast cancer patients in a single healthcare institution and estimated the interval between symptom recognition and treatment seeking to be a median of 5.5 months (range 1–72 months), with 17% of those surveyed having had symptoms for more than a year. There was, however, no significant association between symptom delay and breast cancer prognosis (Ibrahim, 1990).

The birth rate in Saudi Arabia is estimated to be an average of 2.9 children per woman (Ministry of Health, 2012b). Many pregnancies occur in younger women, and this prompted a research group from the KFSH&RC to investigate the association between pregnancy and breast cancer outcome. They reported a mean of 6 months between symptoms discovery and diagnosis among 28 pregnant women compared to a mean of four months among 84 non-pregnant women. They did not find significant difference in term of survival between the two groups (Ezzat et al., 1996). The length of the delay at presentation in breast cancer diagnoses during pregnancy can show whether health professionals play a significant role in speeding up diagnosis, as pregnant women will often be in frequent contact with healthcare providers (Petrek, 1994).

A later study analysed data from 1991 to 1996 on 72 breast cancer patients who had been diagnosed during pregnancy and 216 breast cancer patients who had not been pregnant when diagnosed; all patients had been treated at the same institution, KFSH&RC. The researchers identified a significant difference in average

presentation, with pregnant women being diagnosed in a shorter period (median 5.6 months) than non-pregnant women (median 9.4 months). Although pregnant women have shorter durations of medical-care seeking than non-pregnant women before diagnosis, the cancer stage at the time of diagnosis was similar, with no significant between-group differences in time between definitive diagnoses and treatment. The authors attributed the physiological changes in the breast during pregnancy to the delays in diagnoses (Ibrahim et al., 2000), which means that pregnant women are more likely to be diagnosed by chance.

Abdelhadi (2008) described late presentation and delay in breast cancer management in a single institution in Saudi Arabia. Using 303 breast cancer records of diagnoses made between 1997 and 2007, three instances of delay were identified: patients, Primary Health Centres (PHCs), and hospitals (advanced care). The author attributed the primary factor in delay to patient misconceptions about breast cancer; some patients presented with a tumour of 4–6 centimetres, ulceration, and metastases. The problem of late presentation increased when primary care physicians did not provide support for early detection due to a lack of training and knowledge, and/or when the patient was not seen soon enough by a specialist due to health system referral procedures, and this led to more diagnoses being made at advanced stages (Abdelhadi, 2008).

1.4 Late-presentation breast cancer and survival

The stage of cancer at diagnosis partially explains disparities in breast cancer survival rates in Europe (Sant et al., 2003) and internationally (Sankaranarayanan et al., 2010, Walters et al., 2013b). Cancer stage at diagnosis (its disease extent) is recognised as a prognostic factor in breast cancer survival (Coleman, 1999), with an advanced stage of cancer at diagnosis correlating with decreased survival times in breast cancer patients (Sant et al., 2004, Sant et al., 2003). A collaborative cancer survival study by the International Agency for Research on Cancer (IARC) found that differences in cancer survival correlated with level of healthcare provision and early detection (Sankaranarayanan et al., 2010).

A retrospective review of the causes of death in 427 patients at a teaching hospital in Saudi Arabia during 2008 identified malignancy as the most common cause of death (Ansary et al., 2012). Between 1994 and 1999, the observed survival rate in Saudi

Arabia after five years of breast cancer was 66.4%, and this did not improve in 2000–2004, when the survival rate was 63.1% (Al-Eid and Manalo, 2011). Ravichandran et al. (2005) observed five-year survival rate in the Riyadh region based on stage of cancer at diagnosis for women diagnosed with breast cancer during 1994–1996. They found the rates to be 67.5% for localised cancer, compared to 55.6% for regional, and 57.6% for distant cancer. Although these findings were not statistically significant—based on only 316 cases—the trend of lower survival rates in advanced stages is clear (Ravichandran et al., 2005).

The five-year observed survival rate for female breast cancer patients in Saudi Arabia during 1994–2004 was 64.4% (Al-Eid and Manalo, 2011), which is significantly lower than the relative survival rates of 98% seen in the US during 2002–2008 (Howlader et al., 2012) and 85.1% in the UK during 2005–2009 (Cancer Research UK, 2012). But direct comparison of survival rates for breast cancer in Saudi Arabia with those of other countries can be misleading without considering the difference between observed and relative survival rates. Ries et al. (2003) explain that estimates for relative survival should be higher than those for observed survival because observed survival represents the proportion of cancer patients that survive during a specific time, and therefore includes both deaths due to cancer and to other causes. Relative survival, however, estimates the possibility that cancer patients will die as a result of cancer alone (Ries et al., 2003), and is akin to an observational survival rate adjusted to account for expected mortality (Ederer et al., 1961, Ries et al., 2003).

The SNCR provides data about the incidence of recorded cancer diagnoses, but does not follow up on patients, so it does not routinely collect information on when patients die, for example. In order to estimate survival rates, the SNCR determines whether a cancer patient is alive either by contacting the National Information System (Al-Eid and Manalo, 2011) or by contacting patients directly (Ravichandran et al., 2005). Moreover, its latest information on breast cancer did not examine or estimate the impact of late stage diagnoses on mortality (Al-Eid and Manalo, 2011), which means that the impact of late presentation on breast cancer survival in Saudi Arabia remains unclear. The international literature on breast cancer does however provide data about the impact that late presentation breast cancer has on survival rates (Richards et al., 1999b).

One possible explanation of the differences in breast cancer survival rates is differences in healthcare quality, including presentation time (Coleman, 1999), (Coleman, 1999), and the stage of the cancer at diagnosis and treatment (Sant et al., 2003). Richards et al.'s (1999) systematic review addressed the impact on survival rates of delay before seeking diagnosis and treatment and of the stage of the disease. The authors found a reduction in survival among women who waited 3–6 months to seek treatment compared to those who waited fewer than 3 months. The effect of delay on survival is mediated by stage at diagnosis, with longer delays associating with more advanced stages of cancer (Richards et al., 1999b). One of the main concerns about diagnosing breast cancer relevant to this thesis is that the survival rates for breast cancer have been shown to be better than those for other types of cancer because of the availability of early detection and effective treatments (Parkin et al., 2005).

Al Diab et al.'s (2013) review of published studies on breast cancer in Saudi Arabia included 80 studies examining epidemiology, knowledge and practice of breast self-examination, etiological factors, metastases, and survival. None of the reviewed studies, however, either directly investigated the problem of late presentation or explored the underlying factors contributing to the problem (Al Diab et al., 2013).

Ravichandran et al. (2010) assessed cancer awareness in the Riyadh region of Saudi Arabia. Their study of 1,407 Saudi nationals (688 males and 719 females) indicated that awareness about cancer is poor and is significantly associated with age, with little knowledge about cancer signs and symptoms, or about the benefits of attending PHC and of undergoing screening procedures—the main areas in which knowledge is lacking (Ravichandran et al., 2010). A number of studies have addressed the low level of breast cancer awareness among women in various regions of Saudi Arabia. These studies also found low levels of knowledge about the disease (Alam, 2006, Amin et al., 2009, Dandash and Al-Mohaimed, 2007, Ibrahim et al., 1991b, Jahan et al., 2006, Mahfouz et al., 2013, Sait et al., 2010). Furthermore, Al-Amoudi and Abduljabbar (2012) explored men's knowledge about breast cancer in Jeddah, a coastal city in Western Saudi Arabia. Their study revealed poor levels of awareness among men, with 24% having no knowledge of breast cancer symptoms and 90% unaware of the importance of mammography screening (Al-Amoudi and Abduljabbar, 2012). The lack of awareness about breast cancer raised concerns that

perhaps women may not be aware of the signs of breast cancer, and therefore might not seek medical care for symptoms. This concern impelled the in-depth investigation into the role of breast cancer awareness on late presentation in the qualitative part of this study.

Al-Alaboud and Kurashi (2006) evaluated barriers to the early detection of breast cancer by surveying 79 female General Practitioners (GPs) in PHCs from three cities in the Eastern Province. The main barrier that these GPs cited was the lack of a national screening programme. A charitable breast cancer screening service was launched in Riyadh in September 2007, and the prevalence of breast cancer has been assessed using the 1,215 women that utilised the service over one year period (between September 2007 and September 2008 (Abulkhair et al., 2010b)). Only 16 women were diagnosed with breast cancer; 39% of the 1,215 women were symptomatic, their most common symptom being breast pain (Abulkhair et al., 2010b). That women are using this service shows encouraging signs that early presentation could increase. However, the limited availability of cancer screening services across Saudi Arabia makes it unlikely that the majority of breast cancer patients will be diagnosed at earlier stages. To achieve this will require tackling late presentation for female breast cancer by improving breast cancer awareness.

In developed countries such as the US, travel time for mammography screening is not a determinant of stage diagnosis of breast cancer, as shown by an analysis of 161,619 women with breast cancer from 10 states' cancer population-based registries in the US; but ethnicity, poverty, and insurance status are all associated with late-stage diagnosis (Henry et al., 2013). In the UK, despite a free universal health system providing national screening, late presentation still occurs due to low awareness about breast cancer in ethnic minority groups (Forbes et al., 2011), much like the population examined in this study (see Chapter 2 for further details about healthcare in Saudi Arabia).

In 2008, the National Awareness and Early Diagnosis Initiative (NAEDI) was launched in the UK as a part of the Cancer Reform Strategy to promote early diagnosis (Richards, 2009b). The NAEDI works on the hypothesis that delays in seeking medical care result in more advanced stages of breast cancer being recorded at diagnosis and that this negatively influences survival rates (Richards, 2009b). It has adopted a pathway approach for examining different hypotheses about late

diagnosis. The first component of this pathway concerns how low awareness among the public (or specific groups of the public) about cancer signs and symptoms and the presence of negative beliefs about cancer can lead to late presentation to primary care and a low uptake of screening. The second component concerns the role that primary care has in avoiding delays in diagnosis by considering patients' symptoms as being potentially cancer-related and facilitating their access to diagnostic tests. The third component concerns the delays that can follow referrals to specialists. Thus, efforts in the UK have been made to achieve defined time-targets (Richards, 2009b).

The approach adopted by the NAEDI could be studied and aspects of it implemented in Saudi Arabia to improve the early detection of cancer there. For example, the Cancer Awareness Measure – a validated tool for assessing public awareness about cancer (Stubbings et al., 2009) – could be used to evaluate cancer awareness at a national level in order to promote awareness and early detection, as well as to assess the effectiveness of breast cancer promotion campaigns. It would be valuable to produce estimates on how many avoidable deaths are likely to be related to the late diagnosis of breast cancer in Saudi Arabia.

1.5 The concept of late presentation

Late presentation is synonymous with delay in cancer treatment. This goes back to Pack and Gallo (1938) work “The culpability for delay in the treatment of cancer”. Their work emphasises avoiding delay, a responsibility shared between patients and healthcare professionals. Patient delay refers to the time between self-recognition of symptoms and first contact with the physician (Pack and Gallo, 1938). The threshold for delay is assessed differently in various breast cancer studies, however, less than three months is the common rule. The length of patient delay is usually assessed by asking the patient directly. Though this raises some concern about validity due to recall bias, researchers noticed that women were careful to record the time when they first noticed breast cancer symptoms (Facione, 1993).

The point when a patient seeks medical attention is when the healthcare provider role begins. Provider delay reflects the time from diagnosis to the start of treatment. Pack and Gallo (1938) consider 1 month between physician contact and subsequent action to be an acceptable timeframe. The length of the provider delay is not only patient

related due to misdiagnosis leading to diagnosis at advanced 'non-survivable' stages (Facione, 1993).

Various methods have been applied in breast cancer delay studies. Quantitative methods have assessed the prevalence of delay and factors associated with it, pointing out the importance of symptom recognition to overcoming delay (Ramirez et al., 1999). Qualitative methods have also been used to understand delay. Smith et al. (2005) systematically synthesised concepts and themes in 32 qualitative studies that investigated help-seeking experiences in cancer. They found that symptom recognition and interpretation, fears related to the consultation, and gender are important factors affecting whether patients seek help promptly.

Facione (1993) argued that researchers tend to describe breast cancer delay without judging its appropriateness. This is because assessing delay is complex and seeking medical care is not a straightforward process. The great attention given to delay in cancer emphasizes the methodological challenges in addressing delay in breast cancer and improving our understanding of this problem (Andersen et al., 2009).

A review of the relevant literature shows that no firm consensus on a definition of late presentation has been reached, and that several definitions of late and delayed presentation and terms describing factors related to delay are being used. The following sections discuss four terms used in the literature to categorise delay or late presentation: delay avoidance, time delay, sources of delay, and tumour stages.

1.5.1 Delay avoidance

One way to analyse late presentation is by whether the delay was preventable or not. According to Kutner (1958), there are two phases in the late presentation of breast cancer. First, there is 'unavoidable delay', which describes the interval between the biological start of the disease and the recognition of the symptom(s). This is the silent phase of the disease, in which patients are not aware of any symptoms. If late presentation occurs in this period, it is not related to patient knowledge, as patients are unaware of any symptoms or changes in their body. The second phase is that of 'avoidable delay', in which patients recognise symptoms but do not seek medical care. A synonym for avoidable delay is procrastination (Kutner et al., 1958).

1.5.2 Time delay

Late presentation by breast cancer patients is also assessed in terms of the intervals of delay. Qualitative studies may refer to this period of delay as the ‘patient help-seeking’ period (Smith et al., 2005). In 1938, Pack and Gallo distinguished between two periods of delay. They used the term ‘undue patient delay’ when the delay period—that is, the time it takes from when a patient first notices symptoms to when they actually see a doctor—takes more than three months. They, and others, thus consider a period of fewer than three months to be a reasonable time period from first noticing symptoms to seeking a doctor’s advice or care (Pack and Gallo, 1938, Ramirez et al., 1999, Sharma et al., 2012). Others have argued that one month represents a more realistic cut-off point for undue delay (Harirchi et al., 2005). Delay can also refer to the period from when symptom(s) are first recognised to the patient’s diagnosis, which can obviously vary a great deal between patients depending on their presentation and their GP (Wilkinson et al., 1979). But the majority of the studies that investigate patient-related delay for cancer treatment do so in terms of time delay— that is, the period from first noticing symptoms to seeing a doctor about them.

1.5.3 Sources and phases of delay

Sources (Hansen et al., 2008) and phases (Burgess et al., 1998, Richards et al., 1999b) of delay provide another way of understanding late or delayed presentation. The terms “sources” and “phases” reflect the importance of the process of help-seeking for medical attention, diagnosis, and treatment (Burgess et al., 1998, Hansen et al., 2008, Richards et al., 1999b). Hansen (2008) categorised delays in cancer care in terms of patient, doctor, and health-system delays. “Patient delay” refers to the time from symptom recognition to initial contact with healthcare professionals; “doctor delay” refers to the time from the patient’s first contact with the doctor to the initiation of medical investigations; and “system delay” refers to the time between the commencement of medical investigations and the commencement of treatment. Thus, delays can be related to patients, doctors, the health system, or any combination of them (Hansen et al., 2008).

1.5.4 Tumour stages

The stage of cancer is assessed when a tumour is diagnosed. So, determining what is considered to be ‘late-stage’ cancer is also relevant in studies investigating late and delayed presentation. The existing literature contains no consensus regarding what is considered to be ‘late’ or ‘advanced’ stage cancer. Some studies use the TNM Classification of Malignant Tumours (TNM) (Edge and Compton, 2010) and define Stage II and onwards as the late stages of breast cancer (Cuthbertson et al., 2009), while others define only Stages III and IV as advanced (Downing et al., 2007). Moreover, some studies consider advanced cancer to be indicated by nodal or metastatic spread (Adams et al., 2004), while those that used SEER Staging define advanced cancer as the distant stage of the disease (Clegg et al., 2009, Merkin et al., 2002). The term “advanced stage” has also been used to discuss and represent late presentation of breast cancer and in estimations of breast cancer survival (Allemani et al., 2013, Sant et al., 2003).

1.5.5 Late presentation: definitions used in this thesis

Examining the various definitions of late or delayed presentation shows that scholars have different ways of evaluating the problem. The lack of a standard definition affects analyses of how different variables impact late presentation and how these variables will be examined. This raises a methodological issue related to the validity of measures of late presentation, not only in the context of this thesis but in the wider literature as well. Thus, it is important to select a valid and appropriate definition of late presentation for this study before deciding which factors most require examination.

The notions of delay and late presentation are thus used to refer to a variety of factors, such as the time delay in seeking healthcare or presentation at a late stage of the cancer’s development, with “late” being conceived differently in different studies. Thus, researchers are increasingly avoiding use of the term “delay” (Macleod et al., 2009) because of the confusion it causes regarding whether delay is related to time factors or presentation at an advanced stage of cancer. Furthermore, the term “delay” may unduly emphasise the patient’s actions and attitudes toward healthcare, and imply a lack of motivation or action on the part of the patient (Macleod et al., 2009). Thus, generally using “delay” to describe cases in which diagnosis was slow or simply made at an advanced stage of cancer is considered

inappropriate, as there may be no conscious delay on the patient's part in seeking help (Corner et al., 2006).

In addition, focusing on delay places more emphasis on the patient and neglects the role of the tumour's characteristics and aggressiveness in determining the stage of cancer at diagnosis (Al-Kuraya et al., 2005). Bloom (1965) highlighted the importance of considering tumour histology when studying the effect of patient delay and found that the histology of the tumour influenced survival, with the duration of breast cancer symptoms and survival after hospital admission being greater (more than double) for Grade I than for Grade III tumours. But although the histology of the tumour is an important determinant of survival, most studies of breast cancer delay do not properly investigate it (Bloom, 1965). This thesis does not investigate tumour aggressiveness, though it does consider aggressiveness as another reason for the inappropriateness of using the term 'delay', especially in Saudi Arabia.

It is very difficult to avoid the term "delay" because it is widely used in the literature (Macleod et al., 2009) Instead of "delay", however, this thesis will use the term "late presentation" when discussing the seeking of healthcare or presentation at an advanced stage of breast cancer. The term "late-stage diagnosis" is often used to indicate that a cancer is in an advanced stage at diagnosis (Lannin et al., 1998). Two factors categorise late presentation: the interval between the patient noticing symptoms and first contact with health professionals, and cancer stage at diagnosis.

The quantitative study in this thesis uses tumour stage as the relevant aspect of late presentation because of its validity in assessing late presentation's impact on breast cancer prognosis, with diagnoses at a later stage increasing the risk of a poor prognosis (Howlader et al., 2012, Sant et al., 2003). Using "stage at diagnosis" will control for the effects of tumour aggressiveness in developing breast cancer at a later stage. The quantitative study analyses data from the cancer registry, the SNCR. The SNCR does not normally record the time between noticing symptoms and the first medical consultation. Thus, this thesis will use tumour stage as a proxy for time to seeking medical care, as those who take longer to seek medical care are at a greater risk of being diagnosed at advanced stages of cancer (Arndt et al., 2001). Thus, late presentation is defined as diagnosis at advanced stages, as understood in terms of the

SEER system of summary staging for cancer, and used by the SNCR (see Chapter 5).

The qualitative study in this thesis seeks to understand the causes of delayed presentation and focuses on patients' experiences around late presentation. The qualitative study examined late presentation through the experiences of women with regard to breast cancer and diagnosis. It is anticipated that those diagnosed at later stages are more likely to have taken longer to seek medical care than those diagnosed at earlier stages. The time to seek medical care after symptoms are noted is known as "patient delay" (Hansen et al., 2008). Late-stage diagnosis is taken to refer to diagnoses that are made at advanced stages (Stage III or IV, according to TNM clinical staging – see Chapters 6 and 7). Although two tumour staging systems are used in this thesis, SEER staging and the TNM staging system for solid tumours, they are comparable and an algorithm can convert between the two systems (Walters et al., 2013a) (although this conversion was not applied in this thesis due to time and resource limitations). To facilitate comparability and consistency, "late stage" is used throughout the thesis to describe late presentation and diagnosis at an advanced stage.

Using breast cancer stage at diagnosis in both the quantitative and qualitative studies provided the opportunity to integrate evidence from two data sets. It minimises validity concerns related to recall bias and overcome the lack of SNCR data on the time to present to healthcare facilities. Moreover, it helps in controlling for the effect of tumour aggressiveness in categorising advanced stages of cancer. As a result, stage at diagnosis is more likely to give an accurate indication of the factors associated with late presentation female breast cancer and to better inform the clinically applied interventions in the study setting.

1.6 Aim and objectives of the thesis

1.6.1 Aim of the thesis

This thesis aims to investigate the factors influencing late presentation of female breast cancer in Saudi Arabia.

1.6.2 Objectives

- 1- To conduct a systematic review of the reasons for late-presentation female breast cancer in the Middle East.
- 2- To analyse registry data from Saudi Arabia to find factors associated with late-stage diagnosis of breast cancer.
- 3- To conduct and analyse interviews with Saudi women recently diagnosed with breast cancer, guided by the literature review and the findings of the registry analysis.
- 4- To integrate findings from the systematic review, the quantitative study, and the qualitative study to build an overview of what factors influence late presentation female breast cancer and their effects.

The mixed methods approach of this thesis uses a sequence of methods (first quantitative, then qualitative, then quantitative) to achieve the thesis objectives. It begins with a systematic review of the literature concerning the late presentation of female breast cancer in the Middle East. This phase highlights the need for future studies and informs the choice of methods.

After this, a quantitative method will be used to explore factors associated with late-stage diagnosis of breast cancer. To better understand what prevents early presentation, the thesis also assesses factors that influence late presentation using qualitative methods. Based on the findings of this qualitative data, the quantitative data is reanalysed to provide a better understanding of the characteristics of women who are at a higher risk of late-stage diagnosis.

Finally, the thesis interprets the quantitative and qualitative data, as well as the findings from the systematic review. This will help to build a better understanding of the problem and bridge the gap in knowledge in this area, as well as suggest future policies and research that should be undertaken to tackle the problem of late-stage diagnosis of breast cancer in Saudi Arabia.

1.7 Thesis structure

This thesis comprises eight chapters. The next chapter provides information on the study setting, Saudi Arabia, while Chapter 3 describes the methods and study design adopted for the thesis. Chapter 4 presents the first phase of the research study—the

systematic review. Chapter 5 explains the second phase, the quantitative study. The third phase of this research—the qualitative study—is split into two chapters, with Chapter 6 outlining the methods used and Chapter 7 presenting the results. Chapter 8 provides interpretation and integration of the quantitative and qualitative aspects of the research and relates the conclusions of the thesis, together with recommendations for future practice and research.

1.8 Summary

The late-stage diagnosis of breast cancer represents a major health problem in Saudi Arabia that is expected to grow in the imminent future and requires in-depth exploration. This thesis examines the reasons for the differences in stage at diagnosis, which may reflect variations in the time it takes for women to seek healthcare for breast cancer symptoms in Saudi Arabia, which has a universal health system in place that, in theory, should be accessible to all citizens. However, the frequency of late-stage breast cancer diagnoses indicates the presence of barriers impeding the early detection of the disease. This thesis intends to examine these barriers and conceptualise them from various perspectives, including the patients' point of view. This represents an original and unique study in this area. The nature of the thesis stresses the need to employ mixed methods because a single research approach could not address all thesis objectives. Thus the use of mixed methods in this thesis (not usually applied in this field) to undertake a comprehensive analysis of late presentation breast cancer is a novel contribution to the literature on late presentation of breast cancer.

Chapter 2: The study setting—The Kingdom of Saudi Arabia

Arabia

2.1 Introduction

This chapter provides information on the study site, and is divided into two main sections. The first section provides general information about the country, such as its population, demography and culture, whilst the second provides an overview of its healthcare system, looking at its strengths and the challenges it faces, together with health indicators relevant to the care of breast cancer patients.

2.2 Overview of Saudi Arabia

Saudi Arabia, officially the Kingdom of Saudi Arabia, is located in Southwest Asia and is the largest country in the Arabian Peninsula (see Figure 2), occupying an estimated area of two million square kilometres (Central Department of Statistics and Information, 2010a). It is the birthplace of Islam, where two of Islam's holiest mosques are found. Saudi Arabia is one of the Middle East's richest countries, and one of the largest oil producers in the World (Almalki et al., 2011), and this helps fund its welfare state. There has been a huge improvement in the country's infrastructure since the government's profit-sharing agreement on oil in 1950 (Long, 2005).



Figure 2: Map of Saudi Arabia⁴

⁴ Source: GIS base maps, modified by Suad Al Manji in GIS software, 2014.

2.2.1 Population demography

The total population of Saudi Arabia at the latest census in 2010 was estimated to be 27,136,977, of whom 18,707,576 (68.9%) were Saudi nationals. The male to female ratio of the population ratio is 50.9% male to 49.1% female, but males constitute 70.4% of the non-Saudi population (Central Department of Statistics and Information, 2010c). The population is rapidly increasing, with an estimated annual growth rate of 2.7% (Central Department of Statistics and Information, 2014). In terms of age demographics, 10.85% of the population are 0–4 years old, 19.52% are 5–14, 66.89% are 15–64, and 2.73% are 65 or over (Ministry of Health, 2012b). 80% of the population are urbanised, with less than 5% remaining semi-settled or nomadic (Al-Yousuf et al., 2002). The government is aiming to reduce the number of illegal immigrants, and 601,753 immigrants have recently been deported from the country (Al Ahmad, 2014).

Saudi Arabia is one of the Arab homogeneous populations; all Saudis are officially Muslims, with the majority being Sunni Muslims (Long, 2005). Arabs constitute 90% of the population, with the rest being “nationals”, mainly comprised of foreign immigrants from Afro-Asian countries (Central Intelligence Agency, 2013). Education is provided free to all citizens, and an estimated 96.5% of Saudi national children in the relevant age group attend primary schools (Central Department of Statistics and Information, 2014), with 17.19% of adults holding bachelor’s degrees or higher, and the illiteracy rate among Saudis standing at 5.6% (Central Department of Statistics and Information, 2013).

2.2.2 Distribution of administrative regions in Saudi Arabia

There are thirteen administrative regions in Saudi Arabia (see Figure 3), and each is assigned a regional governor or Prince. Each administrative region varies in space and population density. The regions, arranged in population density from highest to lowest, are Makkah, Riyadh (Ar Riyadh), Eastern (Ash Sharqiyah), Aseer, Madinah (Al Madinah), Jazan, Qassim (Al Qassim), Tabuk, Ha’il, Najran, Jouf (Al Jouf), Baha (Al Baha), and the Northern region (Al Hudud ash Shamaliyah) (Central Department of Statistics and Information, 2010b).

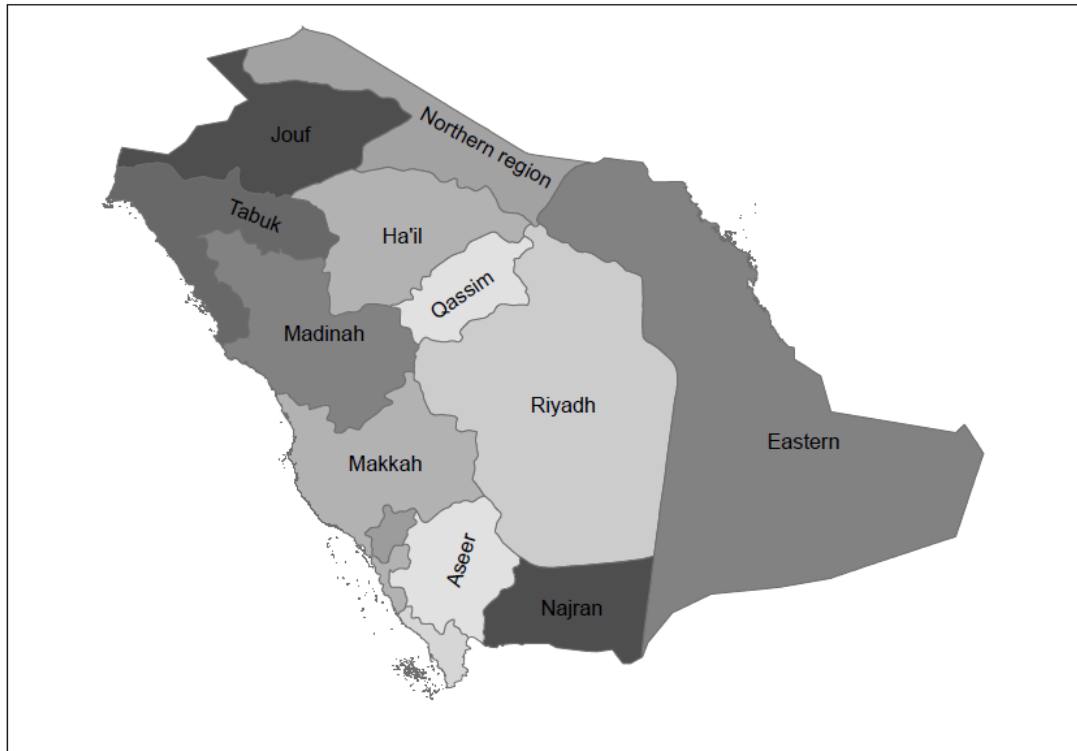


Figure 3: Administrative regions⁵

The study was carried out in Riyadh,⁶ which is located in the centre of the country. Riyadh is both the capital city of Saudi Arabia and the Riyadh region. It developed from a small town to a large modern city, becoming one of the main urban cities in the country. In 2010, its total population was estimated to be 6,777,146, which represents roughly 25% of the total population. Saudi nationals make up 63.4% of Riyadh's population (Central Department of Statistics and Information, 2010).

2.2.3 Cultural aspects

It is important to understand the culture of the Saudi population as this may influence the way in which Saudi behaviour is interpreted. Long (2005), writing about the culture of Saudi Arabia, suggests that “understanding the Saudi behaviour requires understanding not only the substance of a situation, but the context in which it is being viewed” (Long, 2005 p.25). Two main elements are important for understanding Saudi culture: Islam and the family.

⁵ Source: GIS base maps, modified by Suad Al Manji in GIS software, 2014.

⁶ Riyadh is a plural of *rawdah*, it means garden in Arabic

2.2.3.1 Islam

Culture is shaped by different factors, including religion, and Islam is not only the official religion in Saudi Arabia, but also a system that regulates life activities. Islam means peace and submission to the will of God (Allah) and people who follow Islam are Muslims (Long, 2005, Taheri, 2008). Muslims believe that there is no God but Allah and that Muhammad is the Messenger of God. Muslims also believe in Allah's other messengers, such as Moussa and Jesus, with Muhammad being his last prophet, peace be upon them all (Al-Shahri and al-Khanizan, 2005). The Islamic Holy Scripture is Qur'an which advises Muslims in their religious duties. The Prophet Muhammad is considered to be an exemplar by Muslims, and therefore they try to follow his deeds in their own lives through following the Qur'an and his traditions (Taheri, 2008). There is no division between religious and political authority in Islam (Long, 2005). The Islamic law is called Sharia law and the sources of the law are the Qur'an (God's teachings), the Sunna (the prophet Muhammad's teachings) and Muslim scholars' interpretations and reasoned analogies based on the Qur'an and the Sunna (Long, 2005). A distinctive feature of Islamic law that is not present in Western legal systems is the fatwa—legal opinion or learned interpretation. A fatwa can be issued without bringing a case to court. Saudi Arabia applies Islamic or Shari'a law, and the Office of the Grand Mufti, can issue fatwas (Long, 2005).

Islam's influence on the Saudi culture is obvious, and it is very difficult to isolate it from daily activities. People often use phrases such as 'insha Allah', which means 'God willing', and generally understand and explain events in terms of the will of God (Long, 2005). In relation to health, patients generally believe in predestination, attributing illness to the will of God, but not viewing it as God's punishment. The Prophet Muhammad said:

No fatigue, no disease, nor sorrow, nor sadness, nor hurt, nor distress befalls a Muslim, even if it were the prick he receives from a thorn, but Allah expiates some of his sins for that (Al-Shahri and al-Khanizan, 2005 p.432).

This belief does not prevent Saudi people from seeking medical care and treatment for illnesses or from using preventative treatments such as immunisation (al-Shahri, 2002). In fact, Islam encourages taking care of individual health and acting to prevent or treat diseases, with the Prophet Muhammad instructing Muslims to:

Seek treatment, because Allah did not send down a sickness but has sent down a medication for it—known to those who know it and not known to others—except for death (Al-Shahri and al-Khanizan, 2005 p.432).

An important characteristic of Saudi culture is the consultation, which is a norm according to which decisions are made by consensus, and this is rooted in Islam. The consultation and the seeking of consensus are used for decision-making within a variety of structured hierarchical institutions, including the government, businesses and the family (Long, 2005). People might seek consensus from scholars for health-related issues, and also usually seek family members' opinions about life matters, such as whether to seek medical care or not.

The cultural norms relating to the appropriate behaviour for Saudis vary with regard to context and situation, with the behavioural norms towards family members, for instance, being different than those towards non-family members (Long, 2005). Another characteristic that often influences the behaviour of Saudi people is personal trust, and thus establishing a good rapport is a basis for a successful relationship (Long, 2005).

In Saudi Arabia, it is held that healthcare should be practised in accordance with Islam and cultural values (Boyles and Nordhaugen, 1989). Islam generally supports the promotion of health (Rassool, 2000) and the use of scientific medicine to solve human illness (Chamsi-Pasha and Albar, 2013), and this approach towards healthcare is generally adopted within the Saudi healthcare system (Gallagher and Maureen Searle, 1985).

2.2.3.2 The Saudi family

The main unit of the Saudi society is the family. Each family member contributes to the welfare of the family and shares certain family responsibilities, especially with respect to elders. Family members generally retain great respect for elders, both male and female, whose wisdom and power are accepted by young people as a rule (Long, 2005), and both Saudi culture and Islam place a high value on children. Children are not only a part of the Saudi nuclear family, but of the extended family as well. Due to urbanisation, people might move away from their families, but they try to keep as close to other family members as possible. For example, family members may live in compounds, and when it is difficult for families to keep in close proximity, they

sustain a high level of interpersonal communication using phones and the internet (Long, 2005).

Consanguinity is commonly practiced in Saudi Arabia (El-Hazmi et al., 1995). El-Mouzan et al. (2007) estimate the prevalence of inbreeding to be roughly 56% (2004–2005), and it is common in rural and urban areas throughout the country (El-Mouzan et al., 2007). Genetic disorders such as sickle cell anaemia are ubiquitous in the county (El-Hazmi et al., 1995), and the high level of consanguinity may have some impact on the genetic predisposition to breast cancer, but this is not explored further in the present study.

Men's main roles are seen as those of protecting and being responsible for the economy and the family, and it is often frowned upon when women work to earn a living. Women's roles are seen to be those of nurturing and managing homes, although they also participate in family decisions (Long, 2005). However, the percentage of working Saudi women is currently estimated to be 20% of the total Saudi labour force (Central Department of Statistics and Information, 2013). In addition, those Saudi families who can afford to do so use domestic workers to help with household chores. Sex segregation is widely practiced in Saudi Arabia, and is often portrayed as being based on protection rather than restriction. From the Saudi moral point of view, a woman should not associate with a man who is not one of her *mahram*—male relatives, including fathers, husbands, brothers and uncles. Women cannot drive in Saudi Arabia, although they can use public transport or ask male relatives for transportation (Gallagher and Maureen Searle, 1985). Additionally, many families have male drivers, who sometimes live with the family and transport family members, including women.

From the point of view of modesty, women prefer to be seen by female doctors, as Islam forbids unnecessary touching between unrelated adults, including handshakes. The healthcare system is organised to facilitate these cultural needs, providing separate wards and clinics for males and females. The lack of female doctors does not stop women seeking medical advice when necessary, however, even when women feel very bad about being seen by male doctors (al-Shahri, 2002). Sometimes women seek medical advice from well-known doctors regardless of their gender (Al-Yaemni, 2010).

2.2.3.3 Breast cancer and the Saudi Arabian culture

There are a number of positive aspects of the Saudi culture that help women in accepting the diagnosis of breast cancer, especially the strong faith of Saudi people. Many Saudi women with breast cancer report trusting in God, and positively perceiving their diagnosis of breast cancer as a reward from God (Saati, 2013) rather than negatively perceiving having the disease as a punishment (al-Shahri, 2002), because Muslims generally view suffering, including illness and death, as part of life and test from God (Rassool, 2000). Muslims patients consider suffering as a way of atonement for one's sins and Islamic teaching encourages Muslims to relieve suffering (Al-Shahri and al-Khanizan, 2005, Rassool, 2000). Patience and satisfaction is commonly seen among Muslim patients, who ask Allah to reduce their suffering (Rassool, 2000).

Another element that helps Saudi people to accept their illness is the family support they generally receive (Saati, 2013). Special attention will be given to ill persons, particularly if the ill person is a parent or an elder, with family members trying to make life as comfortable as possible for their loved ones. Cancer patients are usually accompanied by relatives when they seek medical care, especially elder patients, and it is uncommon for sick elders to be sent to nursing homes for care as family members will accept responsibility for them unless they require professional medical care (Almuzaini et al., 1998).

Cancer is strongly feared by the Saudi public. Two words are used to denote the presence of a malignancy—the first 'waram' means 'tumour', the second 'saratan' means 'crab or cancer'. The vast majority of Saudi people assume that a tumour is benign when they hear the mention of a 'waram', although it can be used to denote both the benign and malignant behaviour of a tumour (Younge et al., 1997). The word 'saratan', however, invokes a fear of cancer (Younge et al., 1997), and people often use euphemisms such as 'that disease' or 'that bad disease' when they are referring to cancer. Cancer experts have attempted to address the public fear about cancer by increasing awareness about it, particularly about the fact that it is treatable (Bedikian and Saleh, 1985, Ibrahim et al., 1991a). The need to raise awareness about breast cancer is no different than the need to raise awareness about other types of cancer, as such knowledge improves patients' understandings of their conditions and health-seeking behaviours (Ravichandran et al., 2010, Saati, 2013).

2.3 Healthcare in Saudi Arabia

Levels of healthcare have improved in Saudi Arabia, with the average life expectancy rising from 71.4 years in 1998 (Al-Yousuf et al., 2002) to 73.8 years in 2012 (Ministry of Health, 2012b). There has been a reduction in communicable diseases such as measles, which decreased from 3.41/100,000 in 2006 to 1.01/100,000 in 2012, and this accompanies an increase in immunisation coverage, from 95% of the population in 2006 to 98% in 2012. However, the burden of non-communicable diseases has increased with accelerated development. The five leading causes of death in Saudi Arabia in 2012 were from undiagnosed medical conditions (29.8%); injury, poisoning and external diseases (21.2%); diseases of the circulatory system (18.2%); conditions that originated during the perinatal period (6.8%); and neoplasms (4.7%) (Ministry of Health, 2012b). A review of the causes of death listed on death certificates in a single hospital suggested the possibility that a greater percentage of deaths are due to cancer, as the causes of deaths were frequently under-reported (Ansary et al., 2012).

2.3.1 The organization of healthcare services in Saudi Arabia

In 1980, following the Alma Alta conference (1978), the Saudi Ministry of Health adopted the concept of PHC, which is structured to provide universal access to healthcare. The PHC provides the first level of healthcare, including health education; comprehensive maternal and child healthcare; vaccination; the treatment of common diseases and injuries; the provision of essential drugs and the promotion of proper nutrition; the management of chronic diseases, such as diabetes and hypertension; dental healthcare; and the promotion of environmental health. It works as a gateway for sorting health-related issues and organising referrals to advanced or specialised healthcare providers (Al-Yousuf et al., 2002, Almalki et al., 2011). Individuals and families are registered to a PHC in their catchment area, and a group of PHCs in a specific area is in turn attached to a hospital for referrals and coordination. Such hospitals provide secondary care, such as medical, surgical, obstetric, gynaecological, dental, and emergency services. Their countrywide network depends on geographic location and the population density found in that area. The availability of certain services—such as dental clinics, X-ray departments and laboratories—are varied among PHCs, however, depending on the populations they serve (Al-Yousuf et al., 2002). The number of PHCs has shown an increase

over time, with centres serving an average of 13,455 people (Ministry of Health, 2012b).

Healthcare is publically funded by the Ministry of Health, which divides Saudi Arabia into nineteen health regions for administrative purposes, each region having a Regional Director General of Health Services (Al-Yousuf et al., 2002). The Ministry of Health is the main healthcare provider for the country, offering 60% of its total healthcare services (Almalki et al., 2011), and is responsible for the planning and implementation of these services, as well as for monitoring private healthcare and providing advice to health institutions about achieving their goals, although the administrative regions are themselves reasonably autonomous (Al-Yousuf et al., 2002, Almalki et al., 2011). Free healthcare is provided to all Saudi citizens and to non-Saudi public sectors workers (Almalki et al., 2011), whilst expatriates who work in the private sector receive healthcare through their employers' health insurance programmes (Walston et al., 2008).

The Ministry of Health is the main provider of ambulatory and in-patient care (Khaliq, 2012). In 2012, there were 259 hospitals with a total of 35,828 beds (Ministry of Health, 2012b), and some government sectors also offer healthcare, having a total of 11,043 beds. This latter group comprises Armed Forces Hospitals; National Guard Medical services; Ministry of Interior Medical Services; Royal Commission Hospitals; The Saudi Arabian Oil Company (Aramco) Hospitals; the Ministry of Education; School Health Units; Youth Welfare; the Saudi Red Crescent Society; the Institute of Public Administration; and the Saline Water Conversion Corporation. In addition, there are University Hospitals and the KFSH&RC in Riyadh, which has another hospital in Jeddah (Almalki et al., 2011).

2.3.2 Healthcare in Saudi Arabia: strengths and challenges

Access to different levels of healthcare—primary, secondary and tertiary—is a right possessed by all citizens in Saudi Arabia. The quality of healthcare in Saudi Arabia is improving, which can be seen in indicators such as increasing life expectancy and decreasing rates of communicable diseases and infant mortality (Ministry of Health, 2012b).

The practice of the healthcare professional is improving as well. In 1992 (2/6/1413 H), the Saudi Commission Health Specialties was established, with a remit for

improving healthcare practice (Saudi Commission for Health Specialities, 2013), and this institution regulates the training and license of health professionals. Many training programmes and courses are available through it, and an emphasis is placed on increasing the number of Saudi healthcare professionals (Khaliq, 2012). Medical research is increasing, with the most common journals being the Saudi Medical Journal and the Annals of Saudi Medicine, both of which are indexed journals. The majority of research is descriptive and survey-based, however, with only a small amount of clinical randomised trials being undertaken thus far, the goal of many healthcare institutes is to build up biotechnology research through establishing infrastructure for research (Khaliq, 2012).

The Ministry of Health faces many challenges if it is to improve Saudi healthcare. One of these challenges is the current lack of detailed, written, disease-specific national guidelines and, even where guidelines do exist, they are poorly applied in daily practice. Moreover, although there has been an increase in the number of healthcare facilities, less attention has been given to the quality and evidence base of medical provision, which has led to variations in the quality of healthcare services (Ministry of Health, 2012a).

Al-Ahmadi and Roland (2005) assessed the quality of PHCs through a comprehensive literature review of published studies on PHC services in Saudi Arabia. They found these services to be generally accessible and effective in providing immunisation, maternal healthcare, and the control of endemic diseases. However, they found that the quality of clinical care is negatively impacted upon by a lack of evidence-based guidelines, inappropriate prescriptions and the under-referral of patients. Such variations in the quality of healthcare might have a negative effect on the timely seeking of medical care for symptoms of breast cancer, as well as its subsequent diagnosis.

In addition, most health professionals are non-Saudi nationals, with the percentage of Saudi physicians estimated to make up only 22.6% of total physicians. This means that there is a high workforce turnover, and that there are frequent communication barriers between health professionals and Saudi nationals (Almalki et al., 2011). The Government has considered this issue, and efforts have been made to train and teach local healthcare professionals in different health specialities (Almalki et al., 2011).

Healthcare funding is also a challenge, especially given the significant population increase in Saudi Arabia. The Ministry of Health has decentralised healthcare services and offers autonomy to public hospitals, and in order to meet financial and health needs and demands, the Cooperative Health Insurance was established in 1999 to supervise health insurance practises in Saudi Arabia (Almalki et al., 2011). Moreover, an electronic health system has been introduced in several hospitals and organisations, although its uptake by Ministry of Health facilities has been slow. Efforts to improve the current electronic health service are expected to enhance quality of care (Almalki et al., 2011).

Little research in the field of medicine and health has been undertaken with reference to the needs of the Saudi Arabian population, which thus represents a further challenge for health policy and planning. This shortcoming has been recognised, and accredited training programmes are being provided to address it, supported by inter-institutional cooperation to improve research and knowledge in this area. The latest national plan takes these challenges on board in its proposals for improving the quality of care and health indicators (Ministry of Health, 2010).

2.3.3 Options for seeking medical care for breast cancer symptoms

A woman with a self-identified breast cancer symptom might go to the PHC provider she is registered with. However, not all women choose Ministry of Health services as their first option. This might be because they are eligible for healthcare offered by other governmental health services, and so they may seek medical advice from such services. Moreover, some citizens have health insurance provided for them and their families by their employers, and so these people may go to a clinic or hospital that is covered by their insurance. Any woman who has medical insurance might choose this option when she wants to seek medical advice or treatment.

The private sector (personally financed treatment) is another option for medical care, and this option may be chosen because of the convenience of the appointments that it provides and the lack of waiting times, as well as the chance to choose one's own health specialist. Moreover, in some cities, such as Riyadh, a woman can go to a charity-run cancer screening centre, which can refer patients to an oncology unit for further investigations and treatment if they are diagnosed with breast cancer. Finally, the Ministry of Health has also launched a breast cancer line that provides advice

(Ministry of Health, 2012c). Using this phone service may have an impact on the choices that women then make when seeking medical care.

2.3.4 Breast cancer care

Comprehensive government cancer care facilities are located in the Riyadh region (n=4), the Makkah Region (n=3) and the Eastern Region (n=1). A high quality of cancer care is provided in these facilities, with adequate staff, diagnostic equipment and treatment. In addition, each of these cancer care facilities has a hospital-based registry and research centre, although these vary in their functions and sizes (Ibrahim and Ezzat, 2010).

There are an additional five cancer care facilities that are smaller than those above, having fewer oncology staff and facilities. Hospitals in rural and urban areas might have medical oncologists, but will lack oncology specialists, whilst private hospitals offer modest cancer care, but only three private hospitals provide radiation treatment (Ibrahim and Ezzat, 2010).

There are numerous challenges for the provision of cancer care in Saudi Arabia. As comprehensive cancer care facilities are only located in the three main regions listed above, this creates a travel burden or barrier for patients living in other regions to access this care, especially those living in rural areas. The shortage of oncology specialists, especially among Saudi nationals, is also a large hurdle for providing high quality cancer care. Finally, the lack of comprehensive cancer care in some facilities might interfere with proper healthcare and outcomes, and the lack of public awareness might interfere with the timely diagnosis and treatment of cancer (Ibrahim and Ezzat, 2010).

Cancer registration started in the GCC in 1998, with the main branch being located in KFSH&RC, Riyadh, which collect local cancer data from the Gulf countries and follows IARC recommendations on cancer registration and data analysis (Al-Hamdan et al., 2009). Cancer registration in Saudi Arabia is conducted by the SNCR, which has collected cancer-related data since 1994—before cancer registration in the Gulf states—and provides useful epidemiological data that guides the future needs of cancer care (Al-Eid and Garcia, 2012). The quality of cancer registration is high, which allows data related to breast cancer to be included in

international studies comparing cancer survival rates (Sankaranarayanan et al., 2010). Further details about SNCR are provided in Chapter 5.

According to data from the SNCR, the ASIR for female breast cancer ranged from 6–31.8/100,000 women in the different regions of Saudi Arabia in 2008 (Alghamdi et al., 2013). Figure 4 shows the substantial variations that exist in breast cancer rates across the country, with the regions that have the highest incidence of breast cancer being the Eastern, Makkah and Riyadh regions, and those that have the lowest being Aseer, Najran and the Northern region. The distribution of cancer services described above fits with this variation in the incidence rates of breast cancer. The likelihood of an association between late presentation and place of residence will be examined in Chapter 5.

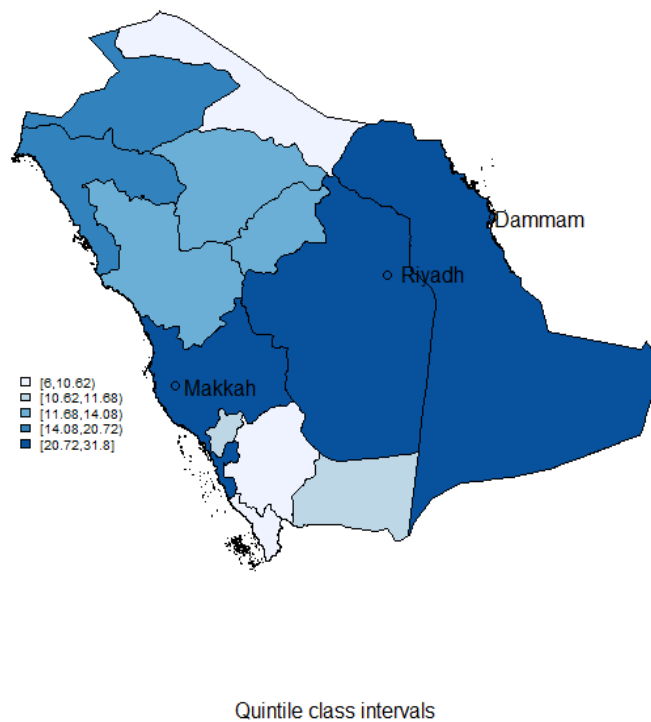


Figure 4: ASIR for breast cancer by region in Saudi Arabia⁷

Source of ASIR : (Alghamdi et al., 2013)

As has been noted, there is no national programme for breast cancer screening in Saudi Arabia, although there have been and continue to be a number of local

⁷ Source: Shape files downloaded from Otlet.sims.berkeley.edu/imls and modified by Robert West using R software with a map tools and maps libraries, 2014

screening initiatives in place that have been designed to provide screening (Ibrahim and Ezzat, 2010). For example, Abdul Lateef Charitable Screening Centre provides mammography screening and forty years is officially recommended that women begin mammography screening in Saudi Arabia (Abulhair et al., 2010b). Implementing a national screening programme in Saudi Arabia might not be a cost-effective strategy for controlling the breast cancer burden because of the lower incidence of breast cancer there compared to that seen in developed countries, together with a low awareness of the importance of screening—as women’s compliance with timely screening is regarded as a parameter of the success of breast cancer screening programmes (Al-Foheidi et al., 2013, Nyström, 2000).

An increase of 350% in breast cancer rates is predicted to occur by 2025—an alarming rise in breast cancer cases (Ibrahim et al., 2008). These changes can be attributed to a number of factors, including population growth, aging, declines in fertility, increases in age at first pregnancy, increases in obesity and physical inactivity, and changes in dietary habits (Al-Foheidi et al., 2013).

The government of Saudi Arabia, like those of other Gulf States, has responded to the needs that will arise from this cancer burden by establishing a National Cancer Care Programme. This initiative is still in its early stages, but is expected to provide greater support for cancer care (Ibrahim and Ezzat, 2010). Meanwhile, the National Cancer Control Programme launched by the Ministry of Health has focused on breast cancer as part of their agenda for cancer prevention and control (Ministry of Health, 2013). In 2012, the Ministry of Health launched a national campaign for breast cancer awareness and early detection in Riyadh. This campaign includes a breast cancer awareness programme, a telephone consultation service, and breast cancer screening clinics and referrals for breast cancer care for women diagnosed with breast cancer (Ministry of Health, 2012c). A non-governmental organisation called the Saudi Cancer Society offers support to cancer patients and public education initiatives regarding cancer and screening services for breast cancer. It also works in partnership with the Ministry of Health and other sectors to support cancer research and care (Saudi Cancer Society, 2012).

Even though advances in cancer care are being made, more focus needs to be given to patient behaviour concerning cancer and other health problems (Ibrahim and Ezzat, 2010). Women’s reasons for early and late presentation for breast cancer

diagnosis and treatment following symptoms discovery will be addressed. This thesis intends to help to address this problem through gaining insights about why late presentation occurs in female patients with breast cancer.

2.4 Summary

This chapter has provided information about the study setting—Saudi Arabia. It has described the country, its population, and the most important aspects of its culture in relation to breast cancer diagnosis and treatment—Islam and the family. In addition, it has described how healthcare in Saudi Arabia is organised; looking at the strengths of the system and the challenges it faces for providing and disseminating information about breast cancer care. This chapter has thus contributed to understanding the study site. The next chapter will now explain the methods used to acquire and analyse the relevant data for the thesis.

Chapter 3: Methodology

3.1 Introduction

This PhD thesis contributes to the understanding of the reasons behind late presentation for breast cancer diagnosis in women, focusing on patient-related factors. The current chapter describes the methodologies used to address the aim and the objectives of the thesis together with the rationale for their use. The methods were carefully selected to comprehensively address the problem of late presentation, with each phase in this PhD being designed to inform the next one, although some flexibility was necessary for examining the problem of late presentation and for enabling the development of research skills.

Exploring the factors that are cited in association with delayed breast cancer diagnoses in the current literature (see Chapter 4) showed that the research problem is multifactorial and complex, and that a single research approach would be insufficient for achieving the thesis objectives. Thus, a study design was designed during the first year of the PhD to meet the thesis objectives, and is described in section 3.4.1. After the data collection and the analysis of the quantitative and qualitative studies had been carried out, the study design required modification to provide a better understanding of the interactions between the relevant factors (see section 3.4.5). These two versions of the study design show the value of employing a mixed methods approach for understanding late presentation and diagnosis of breast cancer in Saudi women.

The current chapter describes the mixed methods and the design utilised in the thesis (section 3.2) together with the rationales for using this design (section 3.3), as well as outlining the study design used to address the PhD objectives (section 3.4).

3.2 Thesis design

This PhD thesis uses a “mixed methods” (Teddlie and Tashakkori, 2009 p.4) research design that combines quantitative and qualitative approaches in order to provide a comprehensive investigation into late presentation of female breast cancer diagnosis in the Middle East and Saudi Arabia in particular. Creswell and Plano Clark (2007) define mixed methods research as:

A research design with philosophical assumptions as well as methods of inquiry. As a methodology, it involves philosophical assumptions that guide the direction of the collection and analysis and mixture of qualitative and quantitative approaches in many phases of the research process. As a method, it focuses on collecting, analysing and mixing both quantitative and qualitative data in a single study or series of studies. Its central premise is that the use of quantitative and qualitative approaches, in combination, provides a better understanding of research problem than either approach alone (Creswell and Plano Clark, 2007 p.5).

There are two main research paradigms: the quantitative and the qualitative. Mixed methods research is increasingly recognised as a third research paradigm involving multiple perspectives, viewpoints and positions (Johnson et al., 2007) which, as Campbell and Fiske (1959) have argued, can be used for validation (Creswell and Plano Clark, 2011, Dellinger and Leech, 2007). There are several terms used for denoting the use of multiple methods, including ‘multi-methods research’ and ‘multiple research’. However, the term ‘mixed methods research’ has recently become the norm for denoting the use of quantitative and qualitative research methods that mix or integrate evidence from both methods with the aim of providing a superior level of results to answer the relevant study questions (Creswell and Plano Clark, 2011, Johnson et al., 2007, Teddlie and Tashakkori, 2009). Quantitative research is deductive and hypothetically driven, while qualitative research is inductive and grounded in narrative data that is systematically collected and analysed. However, the process of evidence-generation in mixed methods research is abductive (inductive-deductive), thus ‘making inference to the best available explanation’ (Rychetnik et al., 2004) by moving beyond the statistical prediction of the inductive model to a generalised mixed methods inference in which both numerical and narrative data are gathered to address research questions (Teddlie and Tashakkori, 2009).

The mixed methods approach thus represents a third research movement that enables dialogue between researchers from the quantitative and qualitative research groups. The proponents of the first research group pursue scientifically-grounded research that emphasises the study of causation or association and then draws conclusions based on generalisability. It uses statistical analysis to confirm hypotheses, using numbers as an output. Findings from this group (quantitative) are limited in explaining issues relating to causation or association, which is the strength of the

second group—the qualitative researchers. Qualitative research is often exploratory, seeking to uncover unknown aspects of the research problem. Narrative data is analysed in the form of text and words (Teddlie and Tashakkori, 2009).

In the continuum of research approaches (see Figure 5), the mixed methods approach does not favour quantitative or qualitative approaches, instead giving priority to both, especially in applied research projects (Teddlie and Tashakkori, 2009) such as this thesis. However, the priority or weight given to qualitative approaches in comparison to quantitative approaches within mixed methods research varies depending on the research questions, so they may or may not have an equal weight within a study (Creswell and Plano Clark, 2011).



Figure 5: Research approaches

3.3 Rationale

The mixed methods philosophy is often one of pragmatism, focusing on “what works” in answering research questions (Teddlie and Tashakkori, 2009). The aim in this PhD thesis is to provide a clear picture of the reasons for late presentation in the study context, and the use of a single research approach (qualitative or quantitative) was judged to be insufficient for achieving this end.

The aim of this thesis is to discover *what* factors are associated with late presentation among women with breast cancer and *why* these factors may affect women’s presentation time in seeking medical care and diagnosis. Mixed methods optimally address the research question. This thesis has multiple objectives, and each objective required a certain method, population, and type of data collection (see Table 3). All of the objectives, however, are linked with each other by time and task, so a mixed methods approach was used to provide a comprehensive explanation of women’s late-presentation for breast cancer diagnosis. This involved triangulating qualitative data with quantitative results in order to provide a contextual understanding of why

and how the quantitative figures might occur, thus enhancing the analysis of the research problem (Bryman, 2006).

From an academic point of view, the mixed methods approach suits the need to understand complex health problems and fulfil the researcher’s curiosity about the reasons behind the research problem (see section 6.6 on the researcher role in the qualitative study). From a personal development point of view, the mixed methods approach enabled the researcher to learn and apply different research methods and skills that are important for academic development (Teddlie and Tashakkori, 2009). In addition, using the mixed methods approach allows the thesis findings to be communicated and disseminated to a wider range of people—those with quantitative, qualitative and mixed methods backgrounds.

Table 3: Thesis objectives and questions, required data and methods

Research objective	Research question	Data needed to identify	Research method
To review evidence on the factors influencing late-presentation breast cancer in the Middle East.	What factors are involved in late presentation in the Middle East?	Factors that influence late presentation.	Literature review.
To conduct a quantitative study in order to examine factors associated with late-stage diagnosis of female breast cancer in Saudi Arabia.	What factors are associated with late-stage diagnosis of female breast cancer?	Factors associated with late-stage diagnosis of breast cancer.	Quantitative (using data from SNCR).
To conduct an in-depth qualitative study in order to explore factors influencing late-presentation for female breast cancer in Saudi	Why are the relevant factors associated with women’s late presentation for the diagnosis of breast	Barriers to and facilitators for seeking medical care after the recognition of breast cancer	Qualitative (interviews with patients).

Research objective	Research question	Data needed to identify	Research method
Arabia.	cancer?	symptoms.	
To integrate findings from the systematic review, using quantitative and qualitative results to build an overview of what factors influence late-presentation female breast cancer and how.	What is the evidence regarding factors associated with late presentation from the thesis data?	A review using the quantitative and qualitative results.	Integrating the evidence from the thesis findings.

3.4 The implementation of the mixed methods approach

Data quality has special importance in public health research. Health research is frequently instigated by problems that need solutions, with the results being used to articulate healthcare policy, and thus the power of findings is therefore far-reaching. It is therefore, critical that the evidence reflects the actual situation (Rychetnik et al., 2004). This led me to think about innovative methods for investigating research problems that affect health, in particular, for the late-presentation female breast cancer.

This PhD thesis used an “explanatory sequential mixed method design” (Creswell and Plano Clark, 2011). This involved two distinct sequential phases: data collection and analysis in a quantitative study, followed by data collection and analysis in a qualitative study. The mixed methods design adopted here is helpful for sorting quantitative variables according to their importance, and the subsequent qualitative results help explain and expand on the quantitative results. This design also suits researchers with quantitative backgrounds (Creswell and Plano Clark, 2011). The following sections describe the process of the thoughts behind the research plan and its implementation.

3.4.1 Development of the study design for the thesis

A study design (version I) (see Figure 6) was designed for answering the research inquires, and provided a strategy for addressing late-presentation breast cancer diagnoses in women without being restricted to the existing literature, and for moving beyond the mere description of the problem. Although the existing literature provides the source of key information about the problem, results, models and theories from the literature may be misleading because their description might be incomplete or inappropriate (Maxwell, 2013).

Several theoretical models are used to explain the reasons for the late presentation of breast cancer patients in the existing literature. Lim (2011) has reviewed and compared the models used to explain breast cancer delay, including: the Total Patient Delay model (Andersen et al., 1995), the Judgement to Delay model (Facione et al., 2002), the Passive Detection and Help-Seeking model (de Nooijer et al., 2003), the Understanding Patient Delay model (Bish et al., 2005), the Care-Seeking Behaviour model (Reifenstein, 2007), the Prolonged Patient Delay model (Rauscher et al., 2010), and the Help-Seeking Behaviour and Influencing Factors framework (O'Mahony et al., 2011). These models often utilise behavioural theories and constructs, and investigate individual and sociocultural interactions (Lim, 2011). However, there are (again) a variety of different features used to assess delays, and thus a number of questions arise regarding the contexts to which these models are applicable and the extent to which they are generalisable to other populations or cultures (Lim, 2011). Most of these models and theories are designed within Western cultural contexts, and are thus might not globally applicable.

Walter et al. (2012) reviewed the literature for studies which used Andersen's Model of Total Patient Delay in cancer diagnosis delay. They found that there was variation in how the model was understood and applied in these studies with differences in the 'time interval' or 'delay' and this did not facilitate international comparison between them.

As a result of their review, they proposed a Model of Pathway to Treatment. This model provides a theoretical perspective for studies which examine delay in diagnosis. It acknowledges the distinction between stages or 'intervals' from symptom detection, to first medical consultation, to diagnosis and to treatment.

These intervals can be determined by specific events, for example, the detection of bodily changes to perceived reasons to discuss symptoms with healthcare professionals determined the 'appraisal interval'. It differentiates between patients' pathways to treatment, and recognises that pathways might not be linear or similar in their starting points. The complexity of factors that could influence pathways to treatment is acknowledged. Factors can be related to the patient, healthcare professional and system or disease specific characteristics (Walter et al., 2012).

Models based on behavioural theories, such as the Health Belief Model (Becker, 1974), are commonly used for understanding behaviour and for informing behavioural change. However, one of the most striking limitations of such behaviourally-based models is their focus on individual cognition, which takes the behaviour away from its societal context (Pasick and Burke, 2008). There is currently a growing interest in understanding the socio-cultural components that affect health and behaviour, and such an understanding may be best achieved by employing a qualitative approach (Pasick and Burke, 2008).

This thesis adopts an applied approach to research, with an emphasis on context-specific evidence that is based on the fact that countries might show variations in the barriers that they have regarding early presentation and survival (Forbes et al., 2013). Using a mixed methods approach without the predetermination of behavioural theories enables new insights to be brought to bear through contextual constructs as a result of the "lack of the road map" (Pasick et al., 2009), because this provides the opportunity to learn about the problem through applying a variation of research methods (Pasick et al., 2009). Therefore, a study design was designed to answer the study questions, using empirical evidence and researcher experience in the study context to enhance the consciousness of late-presentation breast cancer (Maxwell, 2013). This study design utilises the benefits of a mixed methods approach, and was planned and implemented to achieve the central aim of the thesis.

Figure 6 illustrates the first version of the study design used in this thesis. This design started by reviewing evidence about the factors associated with late presentation (Phase I), which guided the selection of the quantitative approach to answer the question of what factors are associated with late presentation of female breast cancer in Saudi Arabia (Phase II), which in turn informed the selection of representative women to participate in the qualitative study (Phase III), which sought

to answer the questions of *why* and *how* these factors affect late presentation. It was planned that the evidence from phases I, II and III would be integrated to synthesise evidence (Phase IV).

The methods implemented in each phase were different in terms of their approach, their participants, the time at which they were undertaken, their results (as shown in Table 4), and their strengths and limitations. The combination of these methods and the sequence of their implementation helped to build better insights into the problem, to acquire stronger evidence to answer the *what* and *why* questions, to overcome biases and limitations in each phase, thus providing more generalisable findings (Phase IV) and to develop the researcher's research skills.

Table 4: Comparison between the three phases of research in the thesis

Sequence	Phase I	Phase II	Phase III
Method	Systematic review	Quantitative	Qualitative
Target population	Women with breast cancer in the Middle East.	Women with breast cancer in Saudi Arabia.	Saudi female breast cancer patients.
Results	General overview of factors associated with late presentation.	Main effects of factors on late stage at diagnosis.	Factors affect late presentation and diagnosis.

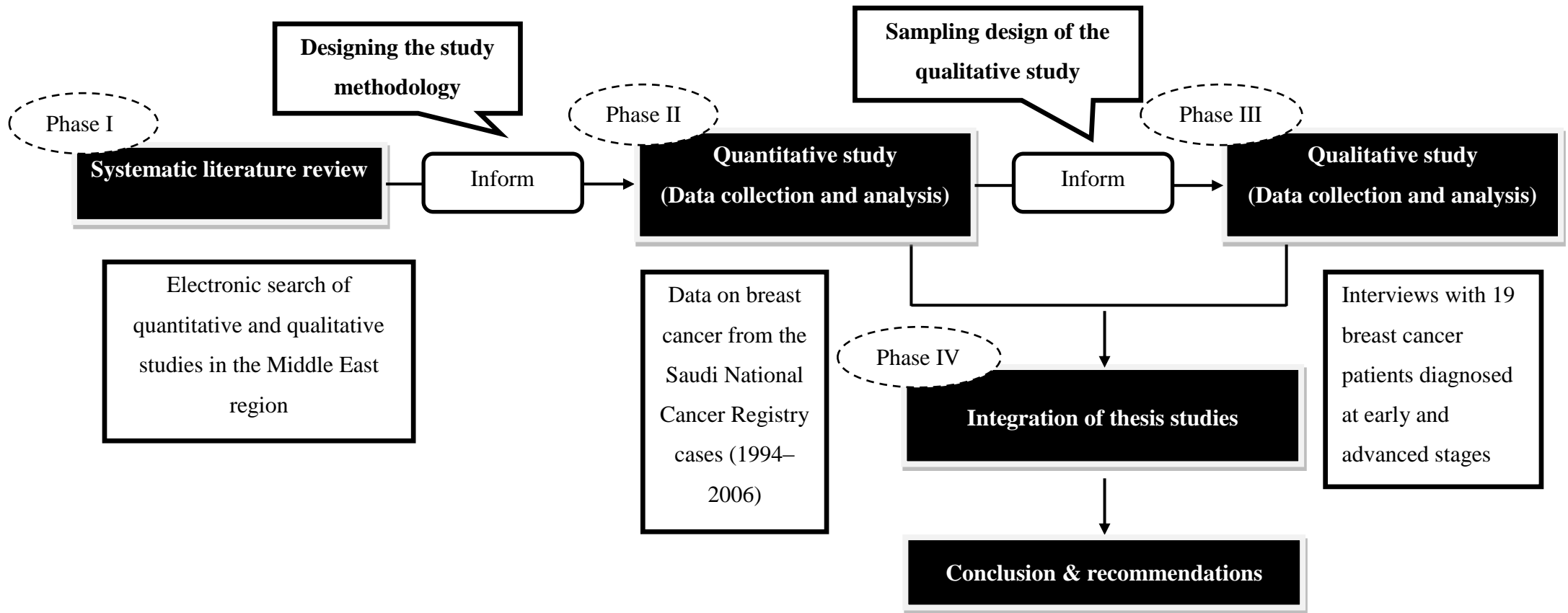


Figure 6: The PhD study design (version I)

3.4.2 Phase I

The first phase comprised a literature survey of the evidence that could be found for answering the research questions. This phase addressed the first objective of the thesis—to seek possible causes of late presentation in contexts similar to those experienced by Saudi Arabian women, and to base evidence on the existing literature. Thus, a systematic review of the possible determinates of late presentation in Middle Eastern countries was conducted. Chapter 4 describes phase I in detail.

This review in phase I had two purposes: the first to systematically search the literature in order to identify whether the evidence provided by these studies was similar or different to the study context and to findings in the wider literature; the second to confirm the originality of the thesis.

The review established that no previous studies have been conducted in Saudi Arabia, and that qualitative research is not commonly employed in this area. The review is part of the thesis, so the results of the review were used to inform the selection of the methods for phases II and III.

3.4.3 Phase II

Given that little was discovered about the research problem in Saudi Arabia from the literature review, it was considered to be important to develop a general idea of what factors might be associated with late presentation. So it was decided that a quantitative study should be conducted before the qualitative inquiry was undertaken. It was decided that cancer census data would be retrieved from the SNCR in Saudi Arabia, as such data was the most expansive data set that could be accessed on breast cancer in Saudi Arabia, and its use would enable an examination of the association between covariate and late-stage diagnoses together with the trends seen over time.

The quantitative approach that was employed in this phase provided evidence of the effects of specific factors on the stage of breast cancer at diagnosis from a large number of participants, thus providing powerful generalisable estimations. Using the SNCR enabled a quick collection of data with little cost, but the data set was subject to availability. This phase focused on answering the question: ‘what are the main effects of age, place of residence, nationality, year of diagnosis and marital status on the late-stage diagnosis of female breast cancer?’

This phase informed the next phase. Generalisable findings from the phase-II quantitative study were used to select a small representative sample for phase-III—the in-depth qualitative study that was used to further investigate the reasons for late-presentation. Chapter 5 describes phase II of the study in detail.

3.4.4 Phase III

Several factors that were considered to have an effect on the stage of breast cancer at the time of diagnosis emerged in phase II. After examining the associations between these factors, an idea of the problem at the macro level began to form, and it became clear that contextual understanding would be important. Thus, the results of the quantitative study were used to inform the sampling strategy of phase III of the study—the qualitative study. The main objective of the qualitative study was to provide in-depth understanding from a patient's perspective on the reasons that might lead to late presentation by answering the *why* questions. Therefore, in this phase, women diagnosed with breast cancer were interviewed, and their narratives used to expand the findings of the quantitative results and put the problem of late presentation into context. Chapters 6 and 7 describe phase III in detail. This phase of the study located patterns of late-presentation among participants by age at diagnosis, which lead to a further research question about the quantitative data: 'how do age, place of residence, nationality, year of diagnosis interact and affect the stage of female breast cancer at the time of diagnosis?'

After analysing and reporting the qualitative data, there were two options: either to follow the study design (version 1) and draw evidence-based findings and interpretations from phases I, II and III, or to re-examine the quantitative data and look at *how* the covariates interact with the stage of cancer at diagnosis. The first option would have been more straightforward, but the second option reflects the flexibility of the mixed methods approach, and also had the potential to enhance the validity of the thesis's inferences using the qualitative data. Although there was a risk of this latter approach being too time-consuming, it was chosen and, as a result, phase IV of the study design (version I) was modified.

3.4.5 Phase IV

According to version I of the study design for the thesis (see Figure 6), the results from the phase-II and phase-III studies were supposed to integrate and thus help to clarify the examination and interpretation of the problem of late presentation.

However, a modification of the study design (see Figure 7) was made following the results of phase III—the qualitative study. Phase IV consist of two parts:

Part I: several themes that emerged from the qualitative data suggested that there was an interaction between factors, especially with respect to age. Both qualitative and quantitative research were given the same priority in this thesis, and to produce a holistic understanding of the problem, the quantitative data was re-analysed to examine the *interactions* between the covariates and the stage of breast cancer at the time of diagnosis. This led to a clearer understanding of the characteristics of women who are at higher and lower risks of late-stage diagnosis.

Part II: to produce the best available understanding of the problem, the re-analysed results from the quantitative data, the qualitative results (phase III) and the systematic review (phase I) were integrated. The integration of the results brought different data together, as described in Table 4, with the aim of answering the thesis question illustrated in Table 3. The diversity of forms of data, methods and sources from which it was collected enabled the research problem to be viewed from different perspectives, although the variety of research questions, participants, methods and data used made it challenging to develop conclusions to the thesis (i.e. to integrate and interpret the findings). Inferences from the mixed methods employed in the thesis enhanced the understanding of the factors associated with late-presentation by women with breast cancer, and increased the transferability of the findings for the future, as well as in relation to other settings with similar characteristics to those of the context of the current study (Teddlie and Tashakkori, 2009). This is because the quantitative data was large enough to be representative, and was analysed using different methods to provide greater confidence about the generalisability of the findings. The qualitative findings provided details that enhanced the inferences and made them more likely to be transferable (Teddlie and Tashakkori, 2009). Chapter 8 describes Phase IV in detail.

Although the methods used in this thesis started with the explanatory sequential mixed method design, as a result of the reanalysis of the quantitative data the study is no longer best categorised as being simply sequential. In fact, the term ‘spiral’ would be better suited to describing the methodology of this thesis. The research moves in circles of quantitative-qualitative-quantitative, but each time on a higher level. As shown in Figure 7, the PhD study design (version II), the analysis of the thesis was

an ongoing process, although it was conducted in a sequence of phases in order to build better inferences. Starting from a first base, the analysis of the evidence then went through a circular series of steps using different data and methods.

The literature review for the study was conducted in 2010 and then rerun in 2014 to ensure that the evidence was consistent and up to date. The quantitative data was analysed using two statistical regression methods during phase II to enhance its validity. The qualitative data was collected and incorporated into the quantitative findings, then systematically thematically analysed (phase III). As a result of this, the quantitative data was then re-analysed (phase IV) using statistical methods (classification trees) different to those used in phase II to integrate quantitative and qualitative findings. The analysis process was abductive, placing the deductive and inductive processes together (see Table 5). All the data collected in this study was used to inform the thesis's conclusion, enabling the thesis objectives to be addressed (see Chapter 8).

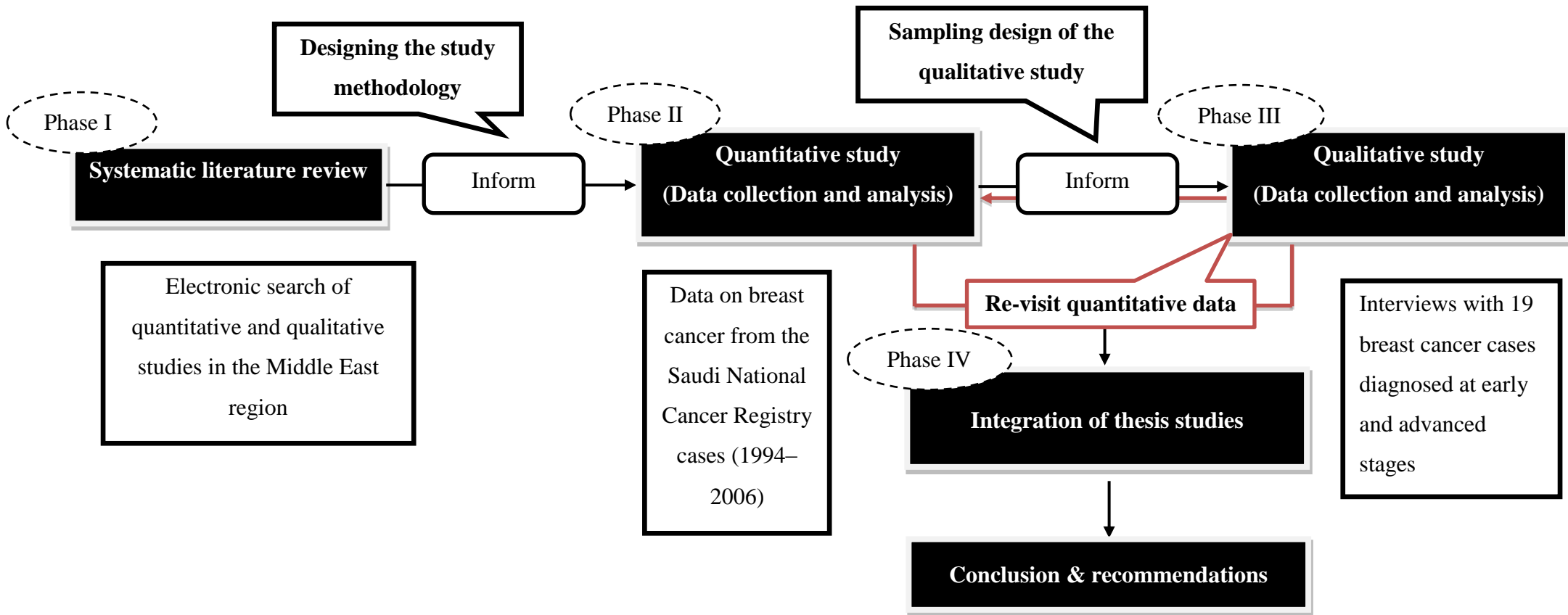


Figure 7: The PhD study design (version II)

Table 5: Description of the PhD study stages and methods

Study Stage	Method	Output
1 - Systematic review	Electronic search of the literature.	Overview of the problem of late presentation in the Middle East. Input into study methodology.
2 - Quantitative study	Data collection	Data on breast cancer patients 1994-2006.
3 - Study analysis	Univariate and multivariate analyses to ascertain the relationship between a variety of different factors and the stage of breast cancer at the time of diagnosis.	Descriptive data on breast cancer patients. Models for factors that influence late-stage diagnosis.
4 - Development of a sampling strategy for the qualitative study.	Purposive sampling based on the findings of the quantitative study. Development of an interview guide.	
5 - Qualitative study	Face-to-face interviews with selected cases.	Nineteen interviews
6 - Study analysis	Thematic analysis	A model for explaining late presentation.
7 - Re-think the quantitative data	Re-visit quantitative data and re-analyse.	Characteristics of women at higher and lower risk of an advanced-stage diagnosis.
8 - Integration of	Interpretation of the	Discussion of the results.

Study Stage	Method	Output
quantitative and qualitative studies.	findings from phases I, II, and III.	Recommendations for health education interventions.

3.5 Summary

This chapter described the sequential mixed methods design used in this thesis. The rational for the use of mixed methods is given along with the philosophy of this approach. The four phases of the research are explained and in particular how they will provide a comprehensive understanding of late presentation of breast cancer from both clinical and patient perspectives to yield guidance for implementation of breast cancer care in Saudi Arabia. The following chapters present these outlines, results and analysis of the different phases of the research in detail.

Chapter 4 Phase I: Late presentation female breast cancer in the Middle East—a systematic review

4.1 Introduction

This chapter undertakes the first phase of this mixed methods PhD—the systematic review. During the development of the study design, two questions were raised: (1) to what extent has the problem of late presentation been examined in contexts similar to the study setting? And, (2) are the factors associated with late presentation similar to those in other cultures, such as those in the Western World? These questions led to the need to review the relevant literature in order to locate evidence of factors associated with the late presentation and diagnosis for breast cancer in the Middle East (see Figure 8).

The systematic review was used as a method for summarising and analysing evidence from studies on late presentation that look at places similar to the study setting, and to thus also identify the extent to which the problem has been investigated. A systematic review of the literature represents a quick and cost-effective way of gathering a large amount of data (Mulrow, 1994). This review focuses on factors associated with late-presentation breast cancer among females and the methods used to investigate this problem.

The review was conducted to inform the other phases (II, III and IV) of this thesis (see Chapter 3), and thus it was conducted and published (Alhurishi et al., 2011) prior to the quantitative and qualitative studies. In addition, it has been cited in articles relevant to cancer in the Middle East (Brown et al., 2012, González Jiménez et al., 2012, Taha, 2013, Taha et al., 2012).

The results of the first systematic review (Alhurishi et al., 2011) underlined the need for this research due to the lack of published studies on the study setting. In addition, the results indicated that quantitative methods were the dominant type of research enquiry in this area. In the quantitative studies reviewed, increasing age and lower educational levels were identified to be strongly associated with late presentation, whilst employment status was found to have no association with late presentation (Alhurishi et al., 2011).

In order to improve the integration of the data produced in this thesis and the conclusions reached through integrating it (see Chapter 8), the original review that was undertaken needed to be updated to account for the possibility that new evidence had emerged between the time of publishing the review (2011) and integrating the evidence (2014). This chapter presents the updated systematic review.

4.2 The aim of the review

This systematic review summarises the literature concerning factors associated with the late presentation and diagnosis of female breast cancer in the Middle East and records the methods used to examine this issue. The review seeks to discover what evidence exists for a variety of factors associated with the late presentation and diagnosis of breast cancer among women in the Middle East.

4.3 Methods

4.3.1 Studies selection

Studies (using quantitative or qualitative methods) were eligible for inclusion in the review if they met the inclusion and exclusion criteria presented below.

4.3.1.1 Inclusion criteria

- 1- The population of the study is female breast cancer patients who lived in one of the countries listed in Table 6.
- 2- The study provides a clear definition of late/delayed presentation.
- 3- The study focused on causes or factors associated with delay or late presentation for breast cancer.
- 4- The study was conducted after 1970, but follow-up of cases was not required.
- 5- The study used either quantitative or qualitative methods.

4.3.1.2 Exclusion criteria

- 1- The study included male breast cancer cases, benign diseases, or breast cancer cases for those living in countries other than those listed in Table 6.
- 2- The study was conducted before 1970.
- 3- The study did not have a clear definition of delayed presentation.

- 4- The study was a quantitative one that made no attempt to correlate late presentation for breast cancer with its possible causes.

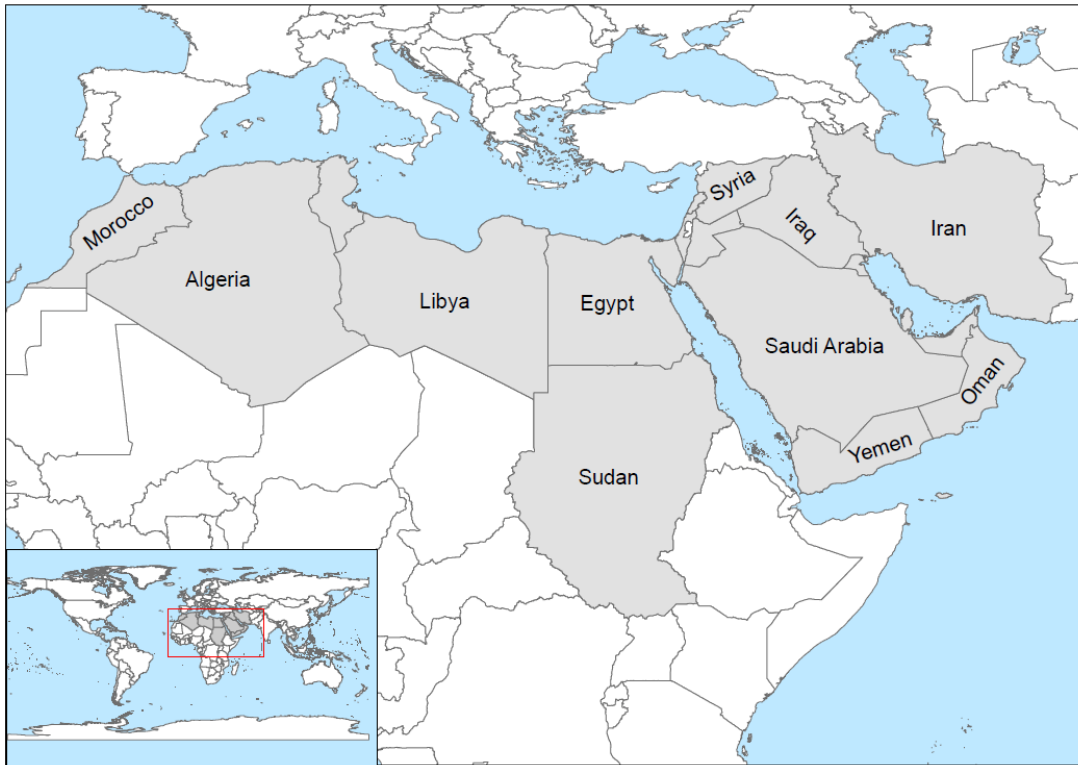


Figure 8: Map of the Middle East⁸

4.3.2 The search strategy

Published studies were identified using the search strategy presented in Table 6. This strategy was developed through identifying keywords used in similar studies, discussion with supervisors, examining published systematic reviews, attending a systematic review course, and discussion with a librarian.

The search strategy contains four main terms: breast cancer, late presentation, Middle East and seeking behaviour. Table 6 describes the synonyms used for searching. The Middle East countries chosen were those that are either near to Saudi Arabia or share similar culture, religion and level of economic development (or both).

The first search was conducted numerous times between January and March 2011 using multiple sources (Alhurishi et al., 2011). In May 2014, the search was rerun to update the previous review.

⁸ Source: GIS base maps, modified by Suad Al Manji in GIS software, 2014.

The searches focused on published literature and used electronic databases comprising PubMed; Online OVID databases (BIOSIS, EMBASE, Global Health, MEDLINE and PsycIFNO); ISI Web of Knowledge (see Appendix A); and the Cochrane Library. The search terms presented in Table 6, using abbreviation of terms, for example Saudi* and present*, were combined using Boolean operators (and/or).

Table 6: Searching strategies

Breast cancer	Middle East	Late presentation	Seeking medical attention
Breast tumour	Eastern	Delay	Help seeking
Breast neoplasm	Mediterranean	Late present	behaviour
Breast carcinoma	Saudi	Early present	Waiting times
	Kuwait	Postpone	Motivation
	Qatar	Wait	Priorities
	Bahrain	Hesitate	Consultation
	Oman	Defer	Use of health
	Emirate	Early stage	services
	Egypt	Late stage	Access to care
	Sudan	Advanced stage	Symptoms duration
	Algeria	Late action	Symptoms
	Morocco	Early action	attribution
	Tunis		Sick role
	Libya		Lag-time
	Palestine		Seeking advice
	Lebanon		Barrier
	Iraq		Time-factor
	Syria		Seek or ask or
	Yemen		Look Near care or
	Iran		attention or Assist
	Jordan		or help

Since the public health literature on observational studies is widespread (Jackson and Waters, 2005) and the possibility of finding publications in languages other than

English is high—particularly in the Middle East (Habibzadeh, 2006)—other search methods were also used. Medical Journals in the Middle East were identified using the World Health Organization website⁹, as most of these journals are indexed and could be accessed through searches in the above databases. Thus, it was anticipated that recent publications could be identified from searching the medical databases above.

Online thesis libraries (ProQuest and EThOS) and popular search engines (Google and Google Scholar) were also used. In addition, manual searches were also used, which involved looking at the reference lists of key sources. The searches were conducted using the English language.

4.3.3 The output of the search strategy

An updated search was run, and 2,491 studies were located (PubMed (n=1121); Online OVID databases (BIOSIS (n=107), EMBASE (n=710), Global Health (n=81), MEDLINE (n=203) and PsycINFO (n=23)); ISI web of knowledge (n=239); Google website (n= 1) and manual searching (n=6)). Figure 9 shows the flow for the studies selection process undertaken in this review. After duplicate removal, a total of 1,815 studies remained. From their titles, 37 studies were identified as being relevant for inclusion in the review. After the abstracts had been screened, a further 19 of these 37 were excluded.

The final eligibility of these remaining 18 studies to be included in this review was then assessed, with a further six being excluded in total, either because they did not meet the inclusion criteria as no attempt to correlate late presentation for breast cancer with its possible cause was made (Abdelhadi, 2008, Aboserea et al., 2011, Ahmad, 2004, Landolsi et al., 2010) (see Appendix A), or because they had been located through manual searches and were non-retrievable (Corbex and McEwan, 2010, Elzawawy, 1987).

Thus, 12 studies were included in this review, of which ten used quantitative methods (Abdel-Fattah et al., 1999, Al Saad and Alsayed, 2012, Corbex, 2009, El-Zawawy, 1991, Elzawawy, 1999, Ermiah et al., 2012, Harirchi et al., 2005, Montazeri et al., 2003, Mousa et al., 2011, Stapleton et al., 2011) and two used qualitative methods (McEwan et al., 2014, Rastad et al., 2012).

⁹ <http://applications.emro.who.int/library/imjournals/Default.aspx?id=2> Accessed 29 May 2014.

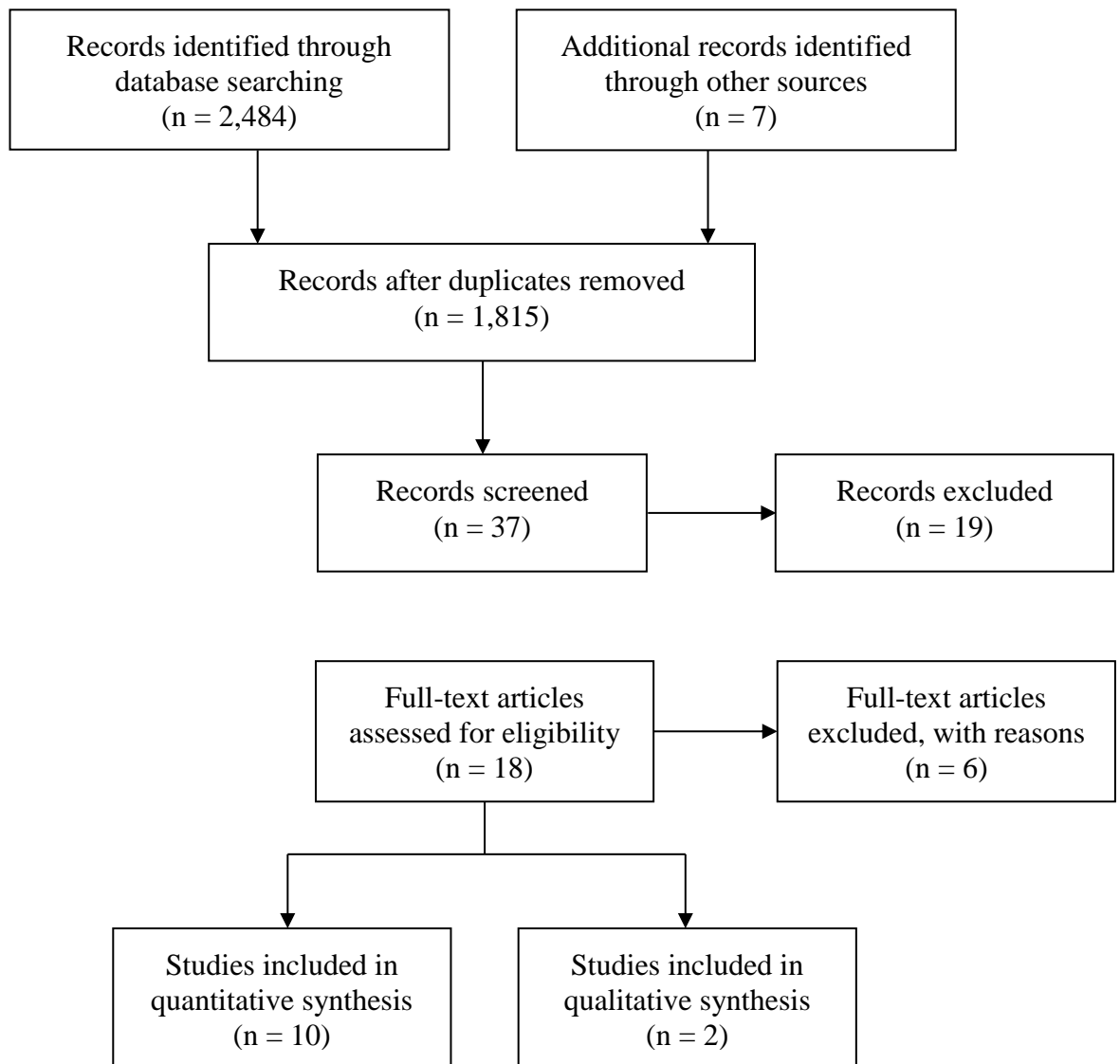


Figure 9: Flow chart of the studies searching and selection

4.3.4 Quality assessment

4.3.4.1 Quantitative studies

Different methods exist for assessing the quality of observational studies in systematic reviews (Shamliyan et al., 2010). Unlike randomised controlled trials, there is no consensus on how to assess the quality of studies included in reviews of observational studies, and there is no transparent measure for differentiating between poor methods and poor reporting (Shamliyan et al., 2010).

To overcome the potential bias produced through poor quality studies, each quantitative study was assessed using a modified version of the elements from the Agency for Healthcare Research and Quality to rate the quality of individual observational studies. This comprised of a clear study question, a defined study population, an examination of the comparability of participants, an assessment to exposure to interventions, an outcome measurement, statistical analysis, the results, discussion and information about funding and sponsorship (West et al., 2002). Additional items were added (see Table 7) based on Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations (Von Elm et al., 2007b).

Each study was given a weighed score out of 30, as shown in Table 7. A score of 24 or above was considered to be indicative of high quality, while a score between 15 and 23 was considered to be representative of moderate quality and a score of less than 15 was deemed to indicate low quality.

None of the studies were excluded as a result of the quality assessments, and Table 7 shows the quality assessment scores for the quantitative studies included in this review. Two studies were scored in the high quality range and the rest were considered to have moderate quality. All of these studies are included in the evidence synthesis.

Generally, the studies included are of good quality, and use female patients that have been diagnosed with breast cancer patients in their studies. A common issue noticed among these studies is that they did not utilise the expected sample size that would be sufficient for generalising that factors are associated with late presentation in breast cancer. Montazeri et al. (2003) reflected on the generalisability of the findings and the possibility that they may have less power due to their small sample sizes. The power of the study findings was not commonly mentioned in the rest of the included studies, perhaps because of the limited number of available breast cancer patients, and it is possible that researchers recruited as many as they could for their studies. For example, Harirchi et al. (2005), in their cross-sectional study, reported that two hundred breast cancer patients from a health facility that had been diagnosed at stages IIb, III or IV had agreed to participate in their study over the course of a year (April 2000 to April 2001).

Table 7: Quality assessment of quantitative studies

Item	Weighed score	(Abdel-Fattah et al., 1999)	(Al Saad and Alsayed, 2012)	(Corbex, 2009)	(El-Zawawy, 1991)	(Elzawawy, 1999)	(Ermiah et al., 2012)	(Harirchi et al., 2005)	(Montazeri et al., 2003)	(Mousa et al., 2011)	(Stapleton et al., 2011)
1. Title and abstract are clear and appropriate.	1	1	1	1	1	1	1	1	1	1	1
2. Study question and aim are clear and focused.	1	1	1	1	1	1	1	1	1	1	1
3. Study population is female breast cancer patients.	1	1	1	1	1	1	1	1	1	1	1
4. Sample size is justified.	1	1	0	0	0	0	1	0	1	0	0
5. Subjects are comparable.	1	1	1	1	1	1	1	1	1	1	1
6. Inclusion & exclusion criteria are appropriate.	1	1	0	0	1	1	0	1	1	0	1
7. Criteria are applied equally to all groups.	1	1	0	0	1	1	0	1	1	0	1
8. Exposure exists.	1	1	1	1	1	1	1	1	1	1	1
9. Methods are standards and valid.	1	1	1	1	1	1	1	1	1	1	1
10. Outcome measure: outcome variables, predictors and confounders are clear.	3	3	2	2	2	2	1	2	2	2	3
11. Efforts to address bias are described.	1	0	0	0	0	0	1	1	0	1	1

Item	Weighed score	(Abdel-Fattah et al., 1999)	(Al Saad and Alsayed, 2012)	(Corbex, 2009)	(El-Zawawy, 1991)	(Elzawawy, 1999)	(Ermiah et al., 2012)	(Harirchi et al., 2005)	(Montazeri et al., 2003)	(Mousa et al., 2011)	(Stapleton et al., 2011)
12. An explanation for how the sample size was arrived at is provided.	1	1	0	0	1	1	1	0	1	0	1
13. Statistical analysis: test is appropriate.	1	1	1	1	1	1	1	1	1	1	1
14. Statistical analysis: univariate analysis or multivariate analysis (or both) are provided.	3	3	1	1	1	1	2	1	3	3	1
15. Studies have statistical power.	1	0	0	0	0	0	0	0	0	0	0
16. Results: the number of participants at each stage is provided, together with non-participation rates and the reasons for these.	2	2	1	1	2	2	2	2	2	2	2
17. Descriptive data is provided	1	1	1	1	1	1	1	1	1	1	1
18. Main results are provided	1	1	1	1	1	1	1	0	1	1	1
19. Other results are provided.	1	1	1	1	0	0	1	0	0	1	1
20. Discussion: summary of the key results is given.	1	1	1	0	1	1	1	1	1	1	1
21. Bias and limitations are addressed.	1	0	0	0	0	0	0	1	1	1	0

Item	Weighed score	(Abdel-Fattah et al., 1999)	(Al Saad and AIsayed, 2012)	(Corbex, 2009)	(El-Zawawy, 1991)	(Elzawawy, 1999)	(Ermiah et al., 2012)	(Harirchi et al., 2005)	(Montazeri et al., 2003)	(Mousa et al., 2011)	(Stapleton et al., 2011)
22. Interpretation of the findings is provided.	1	1	1	1	1	1	1	1	1	1	1
23. The study has generalisability.	1	1	0	0	0	0	0	1	1	0	1
24. Funding or sponsorship has been provided.	1	1	0	1	0	0	1	0	0	1	0
25. Ethical issues, including approval, have been addressed and secured.	1	0	1	0	0	0	1	0	0	0	1
Total Weighed score	30	26	17	16	19	19	22	20	23	22	24

4.3.4.2 Qualitative studies

The trustworthiness of the results in the included studies was evaluated to explore the extent to which these studies could contribute to this review. The Critical Appraisal Skills Programme's (CASP) qualitative research checklist (Critical Appraisal Skills Programme (CASP), 2014) was used to assess the reporting in the qualitative studies. Each study was given a weighed score out of 34, as shown in Table 8. A score of 26 or above is considered to indicate high quality, a score of 17 to 25 to indicate moderate quality, and a score of less than 17 to indicate low quality. Table 8 presents the total scores for the quality assessments of the qualitative studies, which were all scored to be of acceptable quality, even though there was significant variation in the scores.

Table 8: Quality assessment of qualitative studies

Item	Weighed score	(Rastad et al., 2012)	(McEwan et al., 2014)
Was there a clear statement of the aims of the research?	3	3	3
Is a qualitative methodology appropriate?	2	2	2
Was the research design appropriate to address the aims of the research?	1	0	1
Was the recruitment strategy appropriate to the aims of the research?	3	1	3
Was the data collected in a way that addressed the research issue?	7	3	3
Has the relationship between researcher and participants been adequately considered?	2	2	1
Have ethical considerations been taken into account?	3	1	3
Was the data analysis sufficiently rigorous?	6	1	4
Is there a clear statement of the findings?	4	2	4
How valuable is the research?	3	2	1
Total Weighed score	34	17	23

4.4 Data analysis

4.4.1 Quantitative studies

It was difficult to draw evidence of factors that influenced late presentation from the selected studies using meta-analysis because of differences in how late presentation was defined (as described in section 4.5.1), together with differences in the factors that were included in the studies (Ramirez et al., 1999). Conclusions about the direction of effect of factors on late presentation were drawn using Ramirez et al. (1999) classification of 'evidence strength'. This classification weighs the number of studies and the sample sizes of those studies in relation to their effects on late presentation. The direction of evidence (strength) was assessed in terms of one of three categories: strong, moderate or insufficient.

A 'strong' association between a factor and late presentation can be said to exist if a high proportion of studies supports the association, there are a large number of patients to support the effect, and there is a low chance that a new and large study will have contradictory results.

A 'moderate' association between the factor and late presentation exists if at least two studies support the association, but it is possible that a new large study could affect the conclusion.

An 'insufficient' evidence to support the association of a factor and late presentation if only one study supports the effect of the factor, or when the numbers of studies for and against the effect of the factor are equal.

4.4.2 Qualitative studies

Meta-ethnography (Noblit and Hare, 1988) was used to synthesise evidence from qualitative studies by identifying common themes and concepts from each study included in the review. The themes or concepts in each study are then examined to see if there are contradictions and to explain objections in results, before a general interpretation from the results of the studies can be drawn (Dixon-Woods et al., 2005). Meta-ethnography is a commonly used method (Britten et al., 2002, Campbell et al., 2003, Elmir et al., 2010, Malpass et al., 2009), and has previously been utilised in systematic reviews to understand cancer patient's health-seeking behaviours and delays (Smith et al., 2005).

4.5 Results

This section presents the results of the review. In total, 12 studies (quantitative, n=10 and qualitative, n=2) were found to be relevant and thus included in the review (see Table 9). None of the included studies was conducted in Saudi Arabia, but included studies from Egypt (n=7), Iran (n=3), Bahrain (n=1) and Libya (n=1). The evidence explored in this review comes from studies that investigated factors associated with late-presentation breast cancer among women, and were published between 1991 and 2014.

These studies examined the effect of certain factors on late-presentation breast cancer among female patients at various points, from recognition of breast cancer symptoms to seeking medical care (point I); to diagnosis (point II); to treatment (point III), as illustrated in Figure 10.

There was no common definition used for late presentation or diagnosis with breast cancer (see Table 9). However, the majority of the included studies focused on point I of late presentation, which commonly invoked more than three months between systems recognition and contact with medical practitioners as the marker for late presentation. The disparity that is seen in the length of time that is classified as late presentation for point I in Middle Eastern studies perhaps reflects the tension between global scientific findings on the significance that delaying more *three* months has for breast cancer survival rates (Richards et al., 1999a) and the need to reduce the time for presentation in the Middle East, where seeking medical care in less than *one* month from the self-recognition of symptoms has been viewed as being critical (Harirchi et al., 2005).

The lack of a standardised cut-off point was also common for Point II of the medical care process, which was assessed using four weeks (Abdel-Fattah et al., 1999), three weeks (Ermiah et al., 2012) and two weeks (Mousa et al., 2011) as cut-off points. Another way to examine factors associated with point II of late presentation was to use the *stage at breast cancer diagnosis*, which might reflect on the time from seeking medical care (point I) to the point at which a definite diagnosis is made (point II). Point III of late presentation was given little attention in the literature (Corbex, 2009, McEwan et al., 2014).

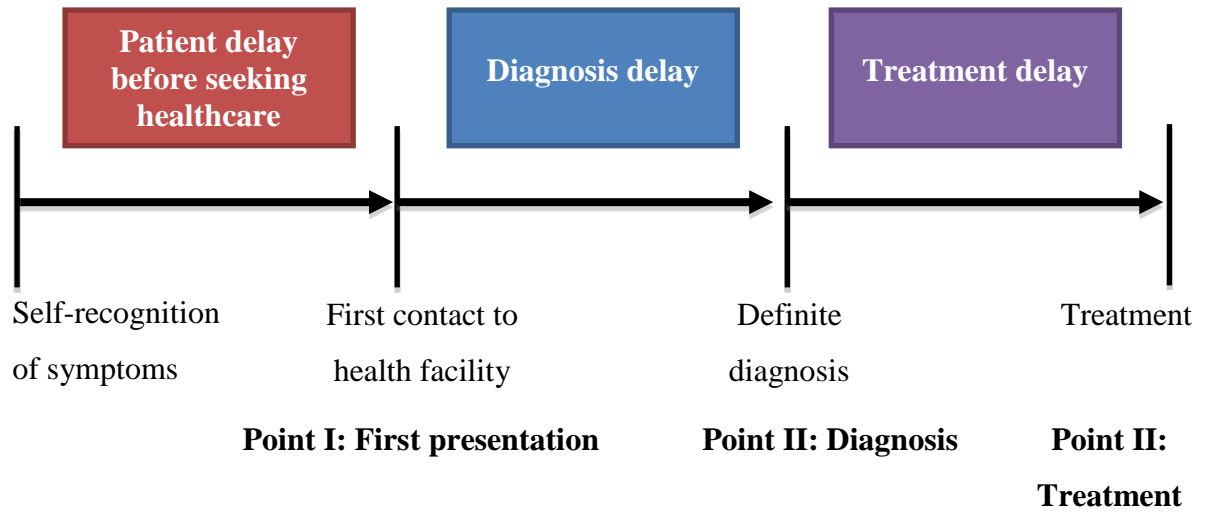


Figure 10: Points of late-presentation breast cancer among females journey from seeking healthcare to treatment

Table 9: Description of the review studies

No.	Study	Sample size	Methods	Country	Late-presentation point	Criteria
1	(El-Zawawy, 1991)	N=80	Quantitative	Egypt	Patient delay	Three months
2	(Elzawawy, 1999)	N=182	Quantitative	Egypt	Patient delay	Three months
3	(Montazeri et al., 2003)	N=190	Quantitative	Iran	Patient delay	Three months
4	(Harirchi et al., 2005)	N=200	Quantitative	Iran	Patient delay	One month
5	(Corbex, 2009)	N=204	Quantitative	Egypt	Patient, diagnosis and treatment delay	Patient delay: one month Treatment delay: fourteen days
6	(Abdel-Fattah et al., 1999)	N=565	Quantitative	Egypt	Patient and diagnosis delay	Patient delay: three months Diagnosis delay: four weeks
7	(Mousa et al., 2011)	N=163	Quantitative	Egypt	Patient and diagnosis delay	Patient delay: three months Diagnosis delay: two weeks
8	(Ermiah et al., 2012)	N=200	Quantitative	Libya	Patient and diagnosis delay	Patient delay: three months

						Diagnosis delay: three months
9	(Stapleton et al., 2011)	N=345	Quantitative	Egypt	Diagnosis delay	Early stage breast cancer: stages I and II. Late stages: stage III and IV.
10	(Al Saad and Alsayed, 2012)	N=161	Quantitative	Bahrain	Diagnosis delay	Early breast cancer (T1, T2, N0-N1, M0), locally advanced (T3, T4, N0-N2, M0), advanced or systematic (T1-T4, N0-N3, M1)
11	(Rastad et al., 2012)	N=10	Qualitative	Iran	Patient delay	Three months
12	(McEwan et al., 2014)	N=15	Qualitative	Egypt	Patient, diagnosis and treatment delay	Three months.

4.5.1 Results from the review of the evidence from the quantitative studies

Table 10 lists the factors that are associated with late-presentation, point I. Strong evidence from four studies (n=1,168) supported the hypothesis that there is an association between education and late-presentation breast cancer (Abdel-Fattah et al., 1999, Ermiah et al., 2012, Harirchi et al., 2005, Montazeri et al., 2003), although one study (n=163) did not find a significant association (Mousa et al., 2011). The latter study understood education in terms of either having or not having a bachelor's degree, however, whereas the other studies understood it with reference to a wider range of features, such as being literate or not (Abdel-Fattah et al., 1999, Ermiah et al., 2012, Harirchi et al., 2005, Montazeri et al., 2003). Illiteracy still exists in the Middle East¹⁰ (UNESCO, 2003), and so the association between late presentation for diagnosis with breast cancer and education may not concern women's levels of formal higher education, but rather whether they are literate or illiterate.

Moderate evidence suggests that age is associated with late presentation for female breast cancer (n= 1,027) (Abdel-Fattah et al., 1999, El-Zawawy, 1991, Elzawawy, 1999, Ermiah et al., 2012). In contrast, two studies did not support the likelihood of this association (Montazeri et al., 2003, Mousa et al., 2011). However the net sample (n= 366) was smaller compared to the supportive studies (as shown in Table 10).

There was moderate evidence for an association between knowledge about breast cancer (n=404) and late presentation (Corbex, 2009, Harirchi et al., 2005), and similarly with breast self-examination (n=765) (Abdel-Fattah et al., 1999, Ermiah et al., 2012). This relationship was examined in two studies, and both provided evidence supporting the association.

There was moderate evidence from four studies (n=1,027) of no association between marital status and late presentation (Abdel-Fattah et al., 1999, El-Zawawy, 1991, Elzawawy, 1999, Ermiah et al., 2012). Two Iranian studies suggested that marital status is associated with late presentation, but marital status was categorised differently in these studies. In one of them, being divorced or widowed was significantly associated with late presentation compared to being married or single (Montazeri et al., 2003). A later study classified women as being married or single, and found that single women less likely to delay compared to married ones (Harirchi

¹⁰ 70 million illiterates people

et al., 2005). This finding indicates the likelihood that socio-cultural elements influence whether marital status has an impact on late presentation.

Similarly, there was moderate evidence to suggest that employment status is not associated with late presentation, with three studies (n=825) (Abdel-Fattah et al., 1999, El-Zawawy, 1991, Elzawawy, 1999) reporting no link, whilst one study found it to be significantly associated with late presentation (Ermiah et al., 2012).

Breast cancer symptoms were found not to be associated with late-presentation for diagnosis with breast cancer in studies on a total of 931 women (Abdel-Fattah et al., 1999, Montazeri et al., 2003, Mousa et al., 2011), whilst a study on 200 women found a link between having breast lump or having other breast cancer symptoms (Ermiah et al., 2012). There was also insufficient evidence to draw conclusion about the effects of many other factors (see Table 10).

Table 11 presents evidence gathered from the included studies about factors associated with late-stage diagnosis (point II of late presentation for breast cancer diagnosis). The evidence strongly suggested that the type of healthcare that is sought is significantly associated with late presentation (n=1,275) (Abdel-Fattah et al., 1999, Corbex, 2009, Mousa et al., 2011, Stapleton et al., 2011), and that age is not associated with late-stage diagnosis (n=1,232) (Abdel-Fattah et al., 1999, Al Saad and Alsayed, 2012, Mousa et al., 2011, Stapleton et al., 2011).

There is a moderate level of evidence to suggest that types of breast cancer symptoms, having lump vs other symptoms and no pain, are associated with late-stage diagnosis (n=1,108) (Abdel-Fattah et al., 1999, Ermiah et al., 2012, Stapleton et al., 2011). However, Mousa et al. (2011) did not find this association based on their study of 163 women.

Education was not associated with late-stage diagnosis based on the moderate level of evidence provided by 543 women (Mousa et al., 2011, Stapleton et al., 2011). However, Ermiah et al. (2012) found the opposite relationship to hold in a study of 200 women. In addition, there is a moderate level of evidence to suggest that a family history of breast cancer is not associated with late-stage diagnosis (n=324) (Al Saad and Alsayed, 2012, Mousa et al., 2011).

The evidence from these studies was not sufficient for drawing conclusions concerning the association between late-stage presentation and numerous factors (as

presented in Table 11). Similarly, there was insufficient evidence to draw any conclusion about factors associated with point III of late presentation, as it was investigated in only one study (Corbex, 2009).

Table 10: Factors associated with the first point of late presentation: from discovery of symptoms to seeking medical attention

Factors	Association with late presentation		Direction and strength of association established
	Significantly associated	Not associated	
Education	N=1,168 (Abdel-Fattah et al., 1999, Ermiah et al., 2012, Harirchi et al., 2005, Montazeri et al., 2003)	N=163 (Mousa et al., 2011)	Strong association
Age	N= 1,027 (Abdel-Fattah et al., 1999, El-Zawawy, 1991, Elzawawy, 1999, Ermiah et al., 2012)	N= 366 (Montazeri et al., 2003, Mousa et al., 2011)	Moderate association
Breast self-examination	N=765 (Abdel-Fattah et al., 1999, Ermiah et al., 2012)		Moderate association
Knowledge about symptoms	N=404 (Harirchi et al., 2005) (Corbex, 2009)		Moderate association
Marital status	N= 403 (Harirchi et al., 2005, Montazeri et al., 2003)	N= 1,027 (Abdel-Fattah et al., 1999, El-Zawawy, 1991, Elzawawy, 1999, Ermiah et al., 2012)	Moderate evidence of no association
Employment status	N=200 (Ermiah et al., 2012)	N= 827 (Abdel-Fattah et al., 1999, El-Zawawy, 1991,	Moderate evidence of no association

		Elzawawy, 1999)	
Breast cancer symptoms	N=200 (Ermiah et al., 2012)	N= 931 (Abdel-Fattah et al., 1999, Montazeri et al., 2003, Mousa et al., 2011)	Moderate evidence of no association
Place of residence	N= 200 (Harirchi et al., 2005)	N= 163 (Mousa et al., 2011)	Insufficient evidence
Access to physician in place of residence	N=200 (Harirchi et al., 2005)	None	Insufficient evidence
Low economic status	N=200 (Harirchi et al., 2005)	None	Insufficient evidence
Menopause status	None	N=200 (Ermiah et al., 2012)	Insufficient evidence
Breastfeeding	N=200 (Ermiah et al., 2012)	None	Insufficient evidence
Oral contraceptives	N=200 (Ermiah et al., 2012)	None	Insufficient evidence
Number of children	None	N= 203 (Montazeri et al., 2003)	Insufficient evidence
Family history of breast cancer	N=204 (Harirchi et al., 2005, Montazeri et al., 2003) (contradictory)	N=200 (Ermiah et al., 2012)	Insufficient evidence
History of benign breast disease	N=200 (Ermiah et al., 2012)	N= 203 (Montazeri et al., 2003)	Insufficient evidence

History of chronic illness	None	N= 200 (Harirchi et al., 2005)	Insufficient evidence
Not disclosing symptoms	N=204 (Corbex, 2009)	None	Insufficient evidence
Knowledge about prevalence	None	N=200 (Harirchi et al., 2005)	Insufficient evidence
Knowledge about the main way of diagnosis	N=200 (Harirchi et al., 2005)	None	Insufficient evidence
Attitudes about prevention and treatment	None	N=200 (Harirchi et al., 2005)	Insufficient evidence
Attitude toward breast self-examination	N=200 (Harirchi et al., 2005)	None	Insufficient evidence
Familiarity with breast self-examination	None	N=200 (Harirchi et al., 2005)	Insufficient evidence
Not Receiving education about breast cancer after discovering a lump	N=204 (Corbex, 2009)	None	Insufficient evidence

Table 11: Factors associated with the second point of late presentation, breast cancer diagnosis

Factors	Association with late presentation		Direction and strength of association established
	Significantly associated	Not associated	
Type of health care	N= 1275 (Abdel-Fattah et al., 1999, Corbex, 2009, Mousa et al., 2011, Stapleton et al., 2011)	None	Strong association
Age	None	N= 1232 (Abdel-Fattah et al., 1999, Al Saad and Alsayed, 2012, Mousa et al., 2011, Stapleton et al., 2011)	Strong evidence of no association
Type of symptoms	N= 1108 (Abdel-Fattah et al., 1999, Ermiah et al., 2012, Stapleton et al., 2011)	N= 163 (Mousa et al., 2011)	Moderate association
Education	N= 200 (Ermiah et al., 2012)	N= 543 (Mousa et al., 2011, Stapleton et al., 2011)	Moderate evidence of no association
Family history of breast cancer	None	N= 324 (Al Saad and Alsayed, 2012, Mousa et al., 2011)	Moderate evidence of no association
Health insurance	N=565 (Abdel-Fattah et al., 1999)	None	Insufficient evidence
Place of residence	None	N= 163 (Mousa et al., 2011)	Insufficient evidence

Breast self-examination	N= 200 (Ermiah et al., 2012)	None	Insufficient evidence
History of benign disease	N=200 (Ermiah et al., 2012)	None	Insufficient evidence
Oral contraceptives	N=200 (Ermiah et al., 2012)	None	Insufficient evidence
Marital status	None	N= 161 (Al Saad and Alsayed, 2012)	Insufficient evidence
Having children	None	N= 161 (Al Saad and Alsayed, 2012)	Insufficient evidence
Employment	None	N= 343 (Stapleton et al., 2011)	Insufficient evidence
Treatment status	N= 343 (Stapleton et al., 2011)	None	Insufficient evidence
History of mammogram	None	N=343 (Stapleton et al., 2011)	Insufficient evidence
History of clinical breast examination	None	N=343 (Stapleton et al., 2011)	Insufficient evidence
Knowledge of breast self-examination	N=343 (Stapleton et al., 2011)	None	Insufficient evidence
Social, financial and time	None	N=343 (Stapleton et al., 2011)	Insufficient evidence
Physician misdiagnosis	N=204 (Corbex, 2009)	None	Insufficient evidence

4.5.2 Results from evidence review of qualitative studies

There have been two original studies in the Middle East on late presentation using qualitative methods (McEwan et al., 2014, Rastad et al., 2012), and these are published in oncology-related journals. They collected qualitative data in total from 25 participants through interviews, and both looked at how women recognise their symptoms and seek medical care. There are several reasons for late presentation, and these can be grouped into two categories: patient-related and healthcare-related.

4.5.2.1 Patient-related factors

An important element relating to late presentation is whether breast cancer patients successfully recognise breast changes, interpret them as being serious, and relate them to breast cancer.

The false interpretation of symptoms is common and leads women to postpone seeking medical advice (McEwan et al., 2014, Rastad et al., 2012). Incorrect interpretation of symptoms might result from poor knowledge or misconceptions about breast cancer (McEwan et al., 2014, Rastad et al., 2012), and the prevalence of late presentation might increase when women underestimate the risk of having breast cancer.

As Rastad et al. observed, this happens when patients think:

I thought that it [cancer] could occur to others but I didn't think that it would occur to me (Rastad et al., 2012 p.4513).

The possibility of late presentation might also increase due to the fear of 'saratan' (McEwan et al., 2014) (as illustrated in Chapter 2). This fear may result from women hearing the experiences of other people diagnosed with cancer (McEwan et al., 2014, Rastad et al., 2012). Some women might feel happier or less afraid by postponing seeking medical care and thus not knowing whether they have breast cancer than they would be were they to have a diagnosis of breast cancer confirmed (Rastad et al., 2012).

In addition, family or work commitments can be barriers to the prompt seeking of healthcare. A woman might have several roles—as a mother, wife, daughter, and sister (Rastad et al., 2012)—and these competing roles and the priorities they are perceived as generating may provide some explanation for late presentation.

Close family contact and support might encourage women to present early if they notice symptoms. McEwan et al. (2014) relay their finding that none of the participants in their study reported being discouraged by close family or friends. This may be explained by the fact that Muslims are encouraged to look after their health and to seek medical care if needed (as discussed in Chapter 2). In addition, social networks might play a fundamental role in receiving breast cancer-related advice and information. Depending on the advice received, social networks may even facilitate early presentation (McEwan et al., 2014).

4.5.2.2 Healthcare-related factors

Two issues relating to healthcare may play role in the late presentation for and/or late diagnosis of breast cancer in the Middle East. The first one is related to the health systems found in the different countries in this region. In Egypt, for example, financial considerations have been linked to late presentation, in particular the cost of healthcare and transportation to health facilities (McEwan et al., 2014). However, financial matters are unlikely to have a significant bearing in all Middle Eastern countries, such as in the Gulf States, for example, where healthcare is free for all nationals.

Moreover, the process of navigating through the healthcare system to receive the proper diagnosis could be an issue for some women, who may not be sure where to go to check their breast cancer symptoms, which may be located a long distance away from them (McEwan et al., 2014).

The second healthcare issue relating to late presentation and diagnosis is health professional-related. Misdiagnosis has been reported to be an issue that has led to a number of advanced stage diagnoses and treatment delays (McEwan et al., 2014, Rastad et al., 2012). Moreover, patient-doctor communication can also contribute to a delay in diagnosis or treatment. Women sometimes fear having a lack of knowledge and certainty about what could happen after they seek healthcare, and health professional might worsen the situation if they do not communicate with patients well, as the following quote from McEwan et al. highlights:

He spoke in dry manner. I was frightened ... He said that we will do this and that and maybe the breast will be removed. Maybe we cut a bit away. It was a shock (McEwan et al., 2014 p.5).

The variation in healthcare systems could help to explain the difference in issues such as financial burdens. The ability to afford health costs was mentioned in one study (McEwan et al., 2014), but not in the other one (Rastad et al., 2012). The cost of healthcare might be unique to certain countries, particularly where it is not provided free of charge.

4.6 Discussion

Research into late-presentation and diagnosis for breast cancer among women in the Middle East is in its infancy, going back only as far as the 1980s, although the international literature on late presentation for breast cancer goes back as far as 1932 (Ramirez et al., 1999). Perhaps the growing interest in research in this area can be attributed to the combination of the alarming rises in the incidence of breast cancer and the fact that it is often diagnosed at advanced stages (World Health Organization, 2009).

This review included an additional six quantitative and two qualitative studies compared to the previously published one (Alhurishi et al., 2011). No standard definition of late presentation was seen in the literature, although there were distinctions between the seeking of healthcare, and diagnosis and treatment for cancer (as shown in Table 9 and Figure 10).

The present review indicated the complexity of breast cancer and the possibility that multiple factors might be associated with the late presentation, diagnosis and treatment of it in the Middle East. There was no unified approach for examining factors associated with breast cancer in these studies, and therefore drawing conclusions from all the different factors addressed in them was challenging. However, all the studies shared the idea of examining late-presentation breast cancer in women with confirmed diagnoses.

The heterogeneity in definitions of late presentation, as well as in the variables (or factors) examined in relation to late presentation and the categories within each variable prevented a meta-analysis from being conducted. Instead, each variable's direction of effect was assessed, and this approach thus diverged from previous reviews in this area (Facione, 1993, Ramirez et al., 1999). In addition, these studies recruited a small number of diagnosed women, which made it difficult to draw firm

and reliable conclusions—a problem that is common in studies of breast cancer delay (Ramirez et al., 1999).

4.6.1 Late-presentation breast cancer

There is moderate evidence that types of symptoms are not associated with late presentation by breast cancer patients. This may be because seeking medical treatment revolves less around women's recognition of symptoms than their mistaken interpretations of these symptoms as being unrelated to breast cancer, as described in the qualitative synthesis. Many women may have a low awareness about breast cancer and its symptoms, and this might interfere with the timely seeking of medical care due to faulty interpretations that the symptoms are not an indication breast cancer. This factor is well-documented across cancer help-seeking studies (Smith et al., 2005). Perceptions of illness can also be influenced by the type of symptoms, their severity, pain, previous experiences of benign diagnoses, and beliefs about symptoms.

The role that misconceptions play in preventing the timely seeking of medical care is supported by moderate evidence from the quantitative syntheses, which suggest that not practicing breast self-examination and being less aware of cancer symptoms, is moderately associated with late presentation.

Women's lack of awareness in Middle eastern countries could be explained by the strong association between lower education levels and late presentation—in terms of being literate vs. illiterate, as this relationship does not hold when illiteracy is not a factor in educational levels (Mousa et al., 2011). Illiteracy is assumed to be higher among older women than younger women in Middle Eastern countries, and this might explain the moderate association between older age and late presentation, as noted in the quantitative evidence. The association between older age and late presentation in the Middle East fits with the published literature in this area (Ramirez et al., 1999).

It is also a possibility that lower education levels might prevent individuals from accessing correct health messages, resulting in misconceptions and fears about breast cancer, as reported in the qualitative synthesis. This could also interfere with the timely seeking of medical care. The literature supported the association between fewer years of education and breast cancer treatment-seeking delays (Ramirez et al., 1999).

A synthesis from the qualitative studies will provide further explanations concerning the effects that patient-related and healthcare-related factors have on late presentation. One important factor that may explain why some patients take a long time to seek medical attention is the issue of how breast cancer patients interpret symptoms and what makes them consider symptoms serious enough to seek healthcare. Fears about cancer or embarrassment are commonly cited as causal barriers to seeking treatment in qualitative studies of cancer (Smith et al., 2005). Dubayova et al. (2010) examined the role of fear in cancer and acute myocardial infarction, with 6 out of the 15 studies they reviewed focussing on breast cancer, and their review provides some candidate explanations about how fear might affect delays in seeking healthcare. Fear can either encourage or act as a barrier to help-seeking behaviour, depending on the reasons for the fear and how the patient copes with it (Dubayova et al., 2010). The relationship between fear and help-seeking is linked with differences in the perceptions of symptoms. Thus, women might have different symptoms and experience different sensations from the same symptoms, and this may be a factor in their “fight or flight” in coping with fear (Dubayova et al., 2010).

The quantitative synthesis in this study did not support the association between marital status and late stage diagnosis as in those in other parts of the world (Ramirez et al., 1999).

One of the challenges for understating the effect of marital status is that there are differences in how studies categorise marital status, with some using the simple alternatives married vs. unmarried, and others using the more detailed list of married, single, widowed and divorced. However, the qualitative synthesis illustrates the positive role that family members and other close people have on health-seeking behaviours, and perhaps it is thus no longer important to know if a female patient is married or not if she receives proper support and encouragement from her family to seek medical care.

4.6.2 Late diagnoses of breast cancer

In this review, some studies move beyond point I of late presentation in exploring the factors associated with late diagnoses of breast cancer. While patients might play role in late diagnosis, the quantitative synthesis did not show support for a relationship between age, education, family history and late diagnosis, although it

did show that type of healthcare provision is associated with late diagnosis, possibly as a result of the variations in availability and quality of healthcare services and in Middle Eastern countries. The qualitative synthesis explains the role that healthcare plays in late diagnosis in terms of the cost of healthcare and the fact that referrals to health specialists might present an obstacle to early diagnosis.

While types of breast cancer symptoms are not associated with late presentation (point I), they are however moderately associated with late diagnosis (quantitatively). This might (qualitatively) explain the reasons for misdiagnosis by healthcare professionals, who might have a low awareness about breast cancer and its epidemiology in the Middle East.

There was no consistency in the sets of factors that different studies examined, leading to insufficient strengths in the associations made between many of them. As a result, this review cannot confirm the magnitude of the effect of these factors on late presentation, and cannot thus inform future policy and interventions using such data. However, it can make suggestions about factors that should be prioritised for future research and interventions. Older women and women with lower educational levels are more likely to present later compared to others, and these facts might be important for generating hypotheses for new research in this area.

As noted, none of the included studies described the power of their studies during the quality assessment, and future studies need to be clear in reporting their sample size and powers in order to strengthen evidence for future policies.

A majority of the studies that were included focused on the patients' opinions in order to understand the reasons for late presentation, with a few studies focussing on further points in the diagnosis and treatment of the patients. Future research would benefit from exploring the points further on in the treatment process of late presentation patients, and focusing on key players that might influence late presentation other than the patients.

While the qualitative synthesis provided here provides some understanding of the reasons for late presentation, it was only based on two studies. Although the main reasons for late presentation did not differ from those found in other studies (Smith et al., 2005), more qualitative studies could provide a better understanding of the contextual factors relating to late presentation in the Middle East.

4.7 Strengths and limitations of the research review

One of the strengths of this review compared to the one that was previously undertaken by the author is its *interpretive synthesis*, which brings qualitative and quantitative evidence together (Dixon-Woods et al., 2005). The process of data analysis was carried out without previously determining the empirical evidence, and the definition of late-presentation breast cancer was not fixed in advance either, with the synthesis bringing evidence and summarising data in relation to the definitions that were adopted.

The systematic review provided an efficient research method for locating and understanding recent studies on late-presentation breast cancer among women in countries similar to the context of the study, and assisted in weighing the consistency and generalisability of the evidence. The review utilised comprehensive searches to reduce bias through locating studies using specific inclusion and exclusion criteria, and by allowing evidence to be gathered from a wide range of methods.

A number of limitations of the review need to be highlighted, however, in order to make its scope clear. First, the searches were mainly conducted electronically and in the English language. There are several languages used across Middle Eastern countries, and it was difficult to search for evidence in all of them (Habibzadeh, 2006). It is possible that evidence published in languages other than English was not located, and therefore not included. A challenge for conducting systematic reviews in Middle Eastern countries is the difficulty of locating studies, as some journals are not published electronically (Habibzadeh, 2006).

Second, the analysis of the results from the quantitative studies produced likelihoods of strength of the effects of the various factors explored on late presentation. However, it did not provide estimates of the magnitude and likelihood of risk for any of the factors explored in relation to late presentation, because a meta-analysis was not undertaken. Therefore, the evidence that was generated from this review was insufficient to inform policies for addressing the problem of late-presentation breast cancer.

4.8 Output of phase I

The updated systematic review indicates the shortage of studies that exist in this research area in Middle Eastern countries. The lack of evidence from quantitative or qualitative studies in Saudi Arabia about factors associated with late presentation by women with breast cancer therefore emphasised the value of conducting further research in this area, as well as the originality of this thesis.

In addition, the benefits of using qualitative methods to provide an in-depth understanding of the reasons for late presentation by breast cancer patients provided through the quantitative evidence were clearly shown. In Egypt, a qualitative study on late presentation was conducted to provide greater understating of quantitative studies (McEwan et al., 2014), indicating the value of employing mixed methods in this thesis.

4.9 Summary

The purpose of this chapter was to review evidence about factors associated with late presentation by female breast cancer patients. Ten quantitative studies and two qualitative studies were located. Following the analysis of the evidence from those studies, it was seen that older age and a lower education level were associated with an increased probability of late presentation. The variation in defining the outcome—late presentation—and the independent variables did not facilitate the calculation of the estimated effects of these factors. However, some factors were addressed in the qualitative studies, and were overlapped with the findings of the broader literature.

As the effects of factors such as age were not determined in this review, it is important to discover what effects age and other factors had in Saudi Arabia to help healthcare professionals identify women who are at higher at risk of presenting late for the diagnosis and treatment of breast cancer. In addition, the contexts that influence late presentation need to be understood in order to guide future interventions to tackle this problem. Hence, qualitative methods should also be utilised in such research.

Chapter 5: Phase II—Late-stage diagnosis of female breast cancer in Saudi Arabia, a quantitative study

5.1 Introduction

This chapter describes the second phase of in this mixed methods PhD—the quantitative study. This study addresses the second objective of the thesis: To analyse registry data from Saudi Arabia to find factors associated with late-stage diagnosis of breast cancer. To examine this issue, data from the SNCR in Saudi Arabia (1994–2006) was analysed in order to identify significant factors associated with late-stage tumours at the point of breast cancer diagnosis. Previous studies have used data from the SNCR to investigate the prevalence of breast cancer, to calculate breast cancer survival rates and to predict the future incidence of breast cancer (Alghamdi et al., 2013, Hamdan et al., 2011, Ibrahim et al., 2008). This study is original in that no previous published study has used this valuable data source to examine the *problem* of late presentation and diagnosis.

This chapter starts with a recap on the study's importance, aims and objectives, together with the methods used, including the key variables and strategies for analysing the data. It then outlines the study's findings, beginning with the descriptive data, before providing the results, detailing the factors that were found to be associated with late-stage diagnoses of breast cancer using ordinal and binary logistic regressions, and assessing their impact on the following phase of the thesis (as previously described in section 3.4, Chapter 3). A summary of the key findings is provided at the end of the chapter.

5.2 Rationale

The systematic review of the literature on late presentation for breast cancer in the Middle East (see Chapter 4) highlighted deficiencies in the research in this area in the Gulf States, and in Saudi Arabia in particular. This chapter addresses the second objective of the thesis—to provide useful information about the *main effect* of the factors that have been found to influence breast cancer at diagnosis. This information about the stage of breast cancer diagnosis is macro-level data as it uses data from the SNCR in Saudi Arabia.

5.2.1 The aim of the study

The aim of this phase of the PhD work is to identify risk factors associated with late-stage breast cancer diagnosis using SNCR data for the period 1994–2006.

5.2.2 Objectives

- 1- To capture patterns of breast cancer diagnosis and to profile female patients presenting with breast cancer.
- 2- To investigate potential risk factors and protective factors (age, marital status, nationality, year of diagnosis and place of residence) associated with the stage of cancer at diagnosis, and to identify potential risk factors for late presentation using ordinal and logistic regression analyses.
- 3- To establish the strengths and limitations of the data and the analysis.

5.3 Study questions

This study seeks to address the following questions:

- 1- Is there a relationship between the stage of breast cancer and the time of diagnosis?
- 2- What factors are associated with late stage diagnosis?
- 3- Are older women more likely to be diagnosed with more late stages of breast cancer?
- 4- Does the stage of breast cancer at diagnosis vary over time?
- 5- Is a patient's location associated with stage of cancer at diagnosis?
- 6- Is there any relation between late-stage diagnosis and patients' nationalities?
- 7- Is marital status associated with late-stage diagnosis?

5.4 Methods

5.4.1 Study design

This is an observational 'routine database study' as the data was obtained from a routine database system (Dos Santos Silva, 1999). This type of study design is useful in research because it provides information about a large population over time (Dos Santos Silva, 1999). It is low cost, the data collection can be performed quickly as it is already available, and it can be used to produce new research hypotheses (Hess, 2004). On the other hand, the data is reliant on the precision of the data collection,

and not all the information that is required can necessarily be secured (Hess, 2004). It is important to note that this study did not examine how the factors identified *caused* late stages of breast cancer, but rather sought for *associations* between different factors and stages of breast cancer.

In order to examine the association between age, year of diagnosis, place of residence, nationality, marital status and the stage of breast cancer at the time of diagnosis, the study required a large sample in order to produce statistically meaningful relationships. The best source from which to obtain a large data sample for this study was found to be the SNCR, which provides census data for all cancer patients. Registration of cancer is compulsory. So, in theory, all cancer patients will be documented, although reality may not reflect the ideal. The process of cancer registration starts by identifying cancer patients who sought medical diagnosis using medical records. However, it provides data for all the breast cancer patients that are likely to be available for analysis. Therefore, there should be very little selection bias.

In 2011, anonymised data was requested from the SNCR for all patients diagnosed with breast cancer since 1994. Information about the patients was requested based on its availability in the cancer registry, which was ascertained on the basis of the SNCR's data abstraction form. Data was available from 1994 to 2006 when the request for data was made on 29 January 2011.

5.4.2 Cancer registration

Cancer registries are organisations that systematically collect, analyse, report and interpret data on cancer patients. They can be either hospital-based registries, which register cancer cases in a particular hospital, or population-based registries, which register new cancer cases in a defined population (Dos Santos Silva, 1999).

Population-based registries are valuable sources of data regarding statistics concerning cancer mortality and morbidity, which can help to guide cancer prevention and control. There are over 200 population-based registries across the world, with more of these being found in developed countries than in developing ones (Dos Santos Silva, 1999).

Several variables that are collected by the registries depend on data feasibility. Preferably, data should be collected from multiple sources that provide cancer

diagnoses and treatments, such as hospitals and diagnostic departments. Death certificates are also important to confirm whether cancer was the cause of death. Personal identification numbers are usually used to link cancer-related information to individual cases in order to remove duplicate cases, although some registries might use different ways to link data, such as names (Parkin, 2006).

5.4.3 Cancer registration in Saudi Arabia

The second chapter of this thesis provided an outline of healthcare provision in Saudi Arabia. Part of cancer care is the registration of cancer-related data, and as the SNCR is a population-based registry under the management of the Ministry of Health—which made reporting cancer cases mandatory in 1994 (Al-Eid and Garcia, 2012)—the SNCR has since prepared periodic reports to disseminate cancer-related statistics.

Data collected by the SNCR includes patient information data, such as names and personal identification numbers, as well as contact information, such as phone numbers and addresses. The demographic data they collect comprises the patient's age at diagnosis, sex, marital status and nationality, whilst the cancer-related information they collect comprises the date of the diagnosis; topography; morphology; tumour stage, behaviour and grade; laterality and basis of diagnosis; reporting and hospital referral; and follow-up information, such as patient status and death. Cancer topography and morphology are identified and coded according to the International Classification of Diseases of Oncology 3rd edition (Fritz et al., 2000). The SEER guidelines are used for tumour-stage coding (Young et al., 2001), and the sources of information are mainly clinically related (such as the names of hospitals), although death certificates are also included and can locate cases that are not clinically identified (Al-Eid and Garcia, 2012). CanReg software, developed by the IARC, is used for data entry and reporting (Al-Eid and Garcia, 2012).

Cancer-related data was collected by trained SNCR registrars and abstracted from cancer patients' records based on their clinical or histopathological diagnoses using both active and passive methods. Data was collected from Ministry of Health hospitals, governmental and private hospitals, clinics and laboratories from all over the Kingdom (Al-Eid and Garcia, 2012, Hamdan et al., 2011), covering an estimated population of 28,376,355 (Central Department of Statistics and Information, 2010c). The main SNCR office is located in Riyadh city at the KFSH&RC, and there are also regional branches: the Central, Eastern, Western, Southern, Madinah and Northern

branches. There are also institution-based registries¹¹ operated in the KFSH&RC, Armed Forces Hospitals, National Guard Hospitals, the Security Forces' Hospital, and the King Abdulaziz University Hospital (Al-Eid and Garcia, 2012).

All of the above offices operate under the supervision of the main SNCR, which is in charge of quality assessment, the verification of data, accuracy and data unification, and comprehensive data collection (Al-Eid and Garcia, 2012). For example, it is in charge of removing duplicate cases through the checking of personal numbers entered on these records and ensuring that data is only entered for one personal number (Al-Eid, 2011). The quality of the data produced by the SNCR is high, with data inconsistencies being very low (Hamdan et al., 2011)

5.4.3.1 Heterogeneity in breast cancer registration in the GCC

The ASIR for Saudi women in 2004 was 15.4/100,000 (Alghamdi et al., 2013). It is relatively close to the overall ASIR in GCC states, which was 18.2/100,000 women during 1998–2005, ranging from 53.4 in Bahrain to 14.8 in Saudi Arabia (Al-Madouj and Al-Zahrani, 2009). This reflects the low heterogeneity in the cancer registration undertaken by the SNCR, as the incidence of breast cancer fits with that in GCC states at large, which might indicate that the rates of non-registration are similar.

5.4.4 Participants

This study included adult female residents in Saudi Arabia who had been diagnosed with breast cancer and registered by the SNCR during 1994–2006.

5.4.4.1 Inclusion criteria

Adult women aged 18 years or greater that were diagnosed with breast cancer during 1994–2006 and who were resident in Saudi Arabia were eligible for inclusion in this study.

5.4.4.1 Exclusion criteria

Male breast cancer cases were excluded from the study because of its low incidence amongst men, the differences in prognosis (Muller et al., 2012), and the possible differences in factors effecting late presentation compared to female patients (Smith

¹¹ These are operated in medical institution which provides oncology care other than the Ministry of Health.

et al., 2005). Women under the age of 18 years, those living outside Saudi Arabia, and those diagnosed before 1994 were also excluded from the study.

5.4.5 Variables

5.4.5.1 The dependent variable

The dependent variable is represented by the stage of cancer found at time of the breast cancer diagnosis. Ideally, the dependent variable would represent ‘appraisal interval’ (note that the term ‘patient delay’ is no longer recommended, another acceptable term is ‘help-seeking interval’), the time point when first bodily changes and/or symptoms are noticed and the time at which the patient first contacts a health-care professional about their condition (Weller et al., 2012). This ideal information is not captured by the SNCR. The stage of breast cancer at the time of diagnosis covers four time points. These are: symptom recognition, presentation to healthcare, referral and diagnosis. Cancer stage seems to be an appropriate measure to use because of its impact on survival. In Europe and the US, variations in breast cancer mortality rates were mainly ascribed to the differences stages found at diagnosis (Sant et al., 2004), which have been identified as being associated with survival and delay time (Richards et al., 1999b). Moreover, differences in survival rates relating to the stage of cancer at diagnosis have also been reported in Saudi Arabia, even though this difference was not found to be statistically significant there (Ravichandran et al., 2005).

Using stage of cancer at diagnosis also overcomes the lack of accuracy that would feature if the interval between identification of symptoms and first contact with healthcare was used, due to the recall bias of participants (Partridge et al., 2012) and the fact that participants might not define delay in an identical way (Andersen et al., 2009). It also takes into account the fact that breast cancer is not homogenous, in that some cancers might progress faster than others as a result of their different pathways or levels of aggressiveness (Al-Kuraya et al., 2005). Therefore, using ‘stage at diagnosis’ is more likely to provide an accurate estimate of late presentation. Stage at diagnosis was assumed to reflect on time from recognition of breast cancer symptoms to seek medical investigations.

The SNCR uses the SEER summary stage system (Al-Eid and Garcia, 2012, Young et al., 2001). Stage at diagnosis is regarded as an ordinal outcome measure, with the

localised stage being more serious than in-situ, regional stage worse than localised and distant stage worse than regional. Stage at diagnosis is ordered based on the severity of disease prognosis and chances of survival (Howlader et al., 2012). The order of these variables helps in identifying the characteristics of women who are at a higher risk of being diagnosed at late stages of breast cancer.

The SNCR record the tumour behaviour as being either in-situ or malignant (the latter referring to the localised, regional and distant stages). The frequent detection of the in-situ stage in the US is attributed to the increase in the use of mammography screening, which can detect abnormalities in the breast before any problem could otherwise be detected by women or health professionals (American Cancer Society, 2011). Screening can also help to detect invasive or malignant breast cancers at earlier stages, at which point their progression can be stopped and they are less likely to be fatal (Esserman et al., 2013).

The fact that all lesions at the in-situ stage may not progress to invasive breast cancers (Erbas et al., 2006), together with the low percentage of this stage that are seen in Saudi Arabia, raises questions about whether it is appropriate to include this stage in the analysis. However, it is possible that in-situ lesions will progress to invasive cancers; therefore it is worth including this stage in the first ordinal regression analysis. Nonetheless, the possibility that in-situ lesions may not all have progressed to invasive cancers was considered, and led to the development of regression models with and without the in-situ stage (see section 5.4.8.3).

5.4.5.2 Dependent variables

The SNCR provides data on age, year of diagnosis, place of residence, nationality and marital status, and these were thus used as independent factors in this study. Their independent effects were examined in relation to the stage of the cancer at diagnosis.

(1) Age at diagnosis

Age was coded as a continuous variable in the SNCR. In order to examine the main impacts of patients' ages at diagnosis on the stage at diagnosis, ages were categorised into three ranges; <40, 40–49, 50+, and unknown (for those who did not have an age entered at the time of diagnosis).

These categories were used to achieve a parsimonious and efficient model. They took into account the potentially non-linear effect of age, the likelihood that a significant number of diagnoses would be made at a younger age range in Saudi Arabia than in Western countries (Ravichandran et al., 2005), and the likelihood that a high percentage of breast cancer patients would fall into the age range 40–50 years (Abulkhair et al., 2010b).

The mean age at diagnosis was 47.2, the median was 45 and the mode was 40, with the age range being set between 18–100 years. The number of patients diagnosed with breast cancer at an age of 81 years or over constituted 1.4% of the total cases. It was not possible to verify whether patient-given ages of 100 years were accurate, as there was no official registration of birth in Saudi Arabia 100 years ago, but these possible inaccuracies in age do not provide a problem for the analysis, as ages were categorised into ranges.

Missing data was partially overcome as cases were not dropped from the analysis due to missing age. The ‘unknown’ missing data category was difficult to interpret in terms of its impact on other covariate estimates in the regression.

(2) Year of diagnosis

To achieve greater parsimony and efficiency in investigating the main effect of the year of diagnosis on the stage at diagnosis, this variable was categorised into four ranges based on three years trends: 1994–1996, 1997–1999, 2000–2002 and 2003–2006.

The SNCR started to collect cancer data in 1994 (Al-Eid and Garcia, 2012). The data from the first period—1994–1996—was consistent with the published epidemiology study by Ravichandran et al. (2005). During the period 1997–1999, cancer registration was expected to improve. Cancer diagnosis and treatment improved from 2000 (De Angelis et al., 2014), when the new SEER staging guidelines were published, providing more accuracy in staging, and these changes were applied by the SNCR from 2001 (Al-Eid and Garcia, 2012). Therefore, it was important to investigate whether there were changes over the subsequent 2000–2002 and 2003–2006 periods. This categorisation process also considered the improvement in cancer registration between the early years that the SNCR started collecting data and the most recent period provided (2003–2006).

(3) Place of residence

The SNCR codes 'place of residence' in terms of administrative regions. To understand the main effect of place of residence, or region, on the stage of cancer at diagnosis, this variable was categorised in relation to the availability and distribution of advanced oncology care. From the 13 administrative regions in Saudi Arabia, advanced oncology care is only found in three, as already noted—in Riyadh, Makkah and the Eastern regions (Ibrahim and Ezzat, 2010). These regions had the highest breast cancer incidence (Al-Eid and Garcia, 2012), with other regions—Madinah, Northern, Qassim, Jazan, Ha'il, Najran, Baha, Aseer, Tabuk and Jouf—having a lower number of breast cancer patients (Al-Eid and Garcia, 2012). The higher incidence of breast cancer in regions with advanced oncology care could be attributed to higher population density in these regions (Central Department of Statistics and Information, 2010b), but could also be attributed to the presence of facilities for detecting and treating breast cancer.

Thus, to achieve parsimonious and efficient models, place of residence was categorised in terms of 'regions with advanced oncology care' (Riyadh, Makkah and the Eastern region), 'regions without advanced oncology care', and 'unknown'.

Errors in coding place of residence were very low. Since place of residence is coded according to regions, this covers wide urban and rural areas. Although nomadic people still exist in Saudi Arabia, there numbers are very small (Al-Yousuf et al., 2002).

Missing data was partially overcome by not dropping cases from the analysis due to missing places of residence. The 'unknown' missing data category was difficult to interpret because of its impact on other covariate estimates in the regression.

(4) Nationality

As this thesis focuses on Saudi Arabian nationals, nationality was categorised as 'Saudi Arabian' for all Saudi nationals, 'non-Saudi' for all non-Saudi nationals, and 'unknown' if the nationality was not reported.

Missing data was partially overcome here by not dropping cases from the analysis due to missing nationality. The 'unknown' missing data category was difficult to interpret because of its impact on other covariate estimates in the regression.

(5) Marital status

In this study, marital status was categorised as ‘married’, ‘unmarried’ or ‘unknown marital status’. The ‘married’ category represented those with valid married status, with ‘unmarried’ including single, divorced and widowed women, and ‘unknown’ representing unreported marital status. For parsimony and to create an efficient model, single, divorced and widowed women were collapsed together because of the small number of members in each category.

This categorisation aimed at producing consistency with categories used in the literature that was examined in the systematic review (Alhurishi et al., 2011) and within the international literature (Ramirez et al., 1999) in order to investigate any significant effects of marital status on the stage of cancer seen at diagnosis.

The registry data provides little evidence of any association with marital status, but this might be due to the large number of those in the ‘unknown’ category (28.6% of the total). There is thus a lack of evidence to suggest that marital status has any association with the diagnosis of breast cancer. These results led to the exclusion of this variable from the regression models, as the results were not easy to interpret. (This will be explained further in results section 5.6.2)

5.4.6 Study size

The study size was determined by the number of breast cancer cases registered by the SNCR. Between 1994 and 2006, there were a total of 12,863 breast cancer patients registered in Saudi Arabia, of whom 304 were male patients, comprising 2.3% of the total number. Data related to male breast cancer was excluded from the study. There were thus 12,559 female breast cancer patients. However, for the analyses, only those who had a valid stage at diagnosis (n=10,663) were included, and thus a total of 1,896 further cases were excluded from the study (see Figure 11).

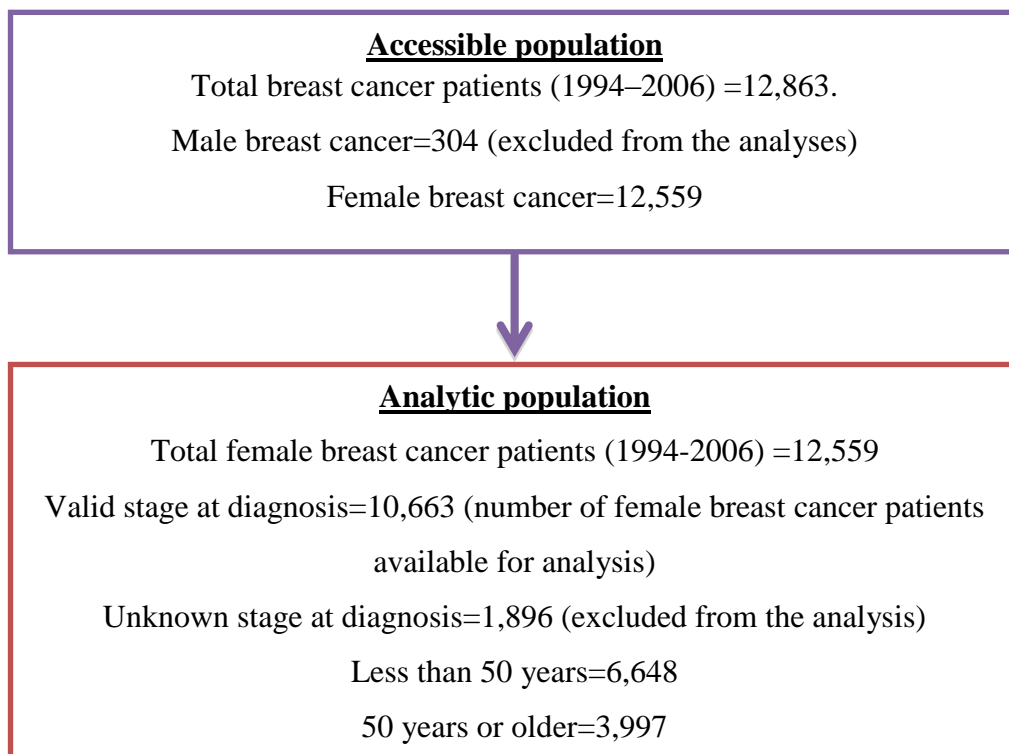


Figure 11: Flow chart of the study sample size

5.4.7 The study's power

The power of the study is “the probability of obtaining a statistically significant result, i.e. a *P*-value below certain pre-established significance level (usually 0.05) if the true magnitude of the effect is as anticipated” (Dos Santos Silva, 1999 p. 334-335). The statistical power of this study was calculated to ensure that the number of participants recruited for this study was appropriate for meeting its objectives—i.e. that the available number of female breast cancer patients was enough to determine the relationship between predictors and stage of cancer at diagnosis. The power of the study was calculated in order to detect the association between the most important predictors—age and outcome, and stage at diagnosis.

Table 12 shows the number of female patients diagnosed with breast cancer at early and late stages for women younger than 50 years and women aged 50 years or older as reported by Ravichandran et al. (2005). The proportion of women under the age of 50 that were diagnosed with breast cancer at late stages was 56.6%, compared to 62.5% of the women diagnosed with breast cancer at the age of 50 or over. A difference of 5.9% is expected to be clinically relevant. The cases with breast cancer from the SNCR were anticipated to be 10,000, with 6,000 of them among younger women and 4,000 of them among older ones.

The statistical power of this study was calculated by comparing two proportions using Java Applets for power and sample size (Lenth, 2006-9). The power to detect a 5.9% difference in stage at diagnosis (early vs. late stages) between older and younger women was 100%, bearing in mind that normality was not assumed in the calculations. This power concludes that there will be good power to detect differences due to all risk factors included in this study. Thus, the study findings are informative and clinically important.

Table 12: Cross tabulation between age and stage at diagnosis

Variables	Early stages (Localised)	Late stages (Regional and distant)	Total
Age 50 and over	36	60	96
Under the age of 50	72	94	166
Total	108	154	262

Source: (Ravichandran et al., 2005)

5.4.8 Statistical methods

The analysis and model-fitting was performed using the Statistical Package for Social Science (SPSS) version 20 (IBM Corp., Released 2011). The first step in this process was to check data completeness, and then to perform a descriptive analysis and a regression analysis.

5.4.8.1 Step 1: Data completeness

‘Missingness’ is a common problem that arises for data analysis, and thus observing any patterns in missing data is crucial (Tabachnick and Fidell, 2013). Missing data can be a challenge for studies that utilise registry data, like this one (Gliklich and Dreyer, September 2010). An examination of the missing data was conducted before the data analyses in order to examine the magnitude of missing data and assess its impact on the study findings, as missing data can lead to biased results. Thus, deciding how to reduce the inconsistency in the data and the results also needed addressing.

For all variables, an unknown value was categorised as a missing value, and placed in the ‘unknown’ category, and was treated for all variables except stage at diagnosis, the outcome variable. Table 13 shows the percentage of missing data in

each variable. Marital status has the highest percentage of missing values (28.6%), followed by stage at diagnosis (15.1%).

Table 13: Frequency of missing data for female breast cancer (n=12,559)

Variables	Missing		Percentage
	Yes	No	
Stage at diagnosis	1896	10663	15.1
Year of diagnosis	0	12559	0
Place of residence	939	11620	7.5
Age at diagnosis	39	12520	0.3
Nationality	244	12315	1.9
Marital status	3591	8968	28.6

A cross-tabulation of jointly missing data that occurs for more than 1% of the total number of patients shows the numbers of jointly missing variables for individual cases. It illustrates that marital status and place of residence were missing more often than any other paired set of variables (See Table 14). The high percentage of missing marital status data might perhaps be attributed to the time-consuming nature of the process of extracting data from patient records. Marital status may not be clearly reported in medical notes, and therefore registrars might find it difficult to extract. The best way to check marital status is via personal identification cards, which are usually located at the end of medical records. It is conjectured that information about marital status is most likely missed out as a result of the time constraints on the active data extraction process and the fact that such data is not easily locatable from patients' records.

Table 14: Cross tabulation of missing data analysis for the study cohort¹²

Missing Pattern						Frequency
Year of diagnosis	Age at diagnosis	Nationality	Place of residence	Marital status	Stage at diagnosis	
				×		2115
					×	1130
			×	×		683
				×	×	525

With respect to dependent variables, cases were omitted from the analysis only if the stage of cancer at diagnosis was not available, as it would be difficult to meaningfully compare unknown tumour stage cases with those in which the stages were known. The stage of the cancer at the time of diagnosis was unknown for 1,896 patients, so these patients were excluded from the analyses. It seems possible that cases that had valid tumour stages were better recorded than those with unknown stages at diagnosis, and it is possible that estimates could differ if patients with unknown stages were added to the analysis.

As there was no control for missing data, relying on cases with valid stage tumours at diagnosis, removing cases with an unknown stage at diagnosis from the analysis and keeping the ‘unknown’ category for of all independent variables permitted the use of all cases, therefore reducing any bias from complete data analysis because missing data was not missed randomly ($P < 0.001$).

5.4.8.2 Step 2: Descriptive statistics

Descriptive analysis was used to outline the characteristics of female breast cancer, with the Chi-Square (χ^2) test being calculated to determine the unadjusted independent effect of important factors—namely age, year of diagnosis, place of

¹² Patterns with less than 1% cases (126 patients or fewer) are not displayed.

residence, nationality and marital status—on the stage of breast cancer seen at diagnosis, as this could be different from when the analysis is adjusted. The figures were investigated in order to locate patterns in the disease. After that, a description of the cohort in relation to tumour stages at diagnosis and the factors associated with this was provided.

5.4.8.3 Step 3: Regression analysis

The associations between the potential factors related to developing breast cancer and the stages at diagnosis were examined using ordered logistic regression analysis. Logistic regression modalities are multivariable analyses that can help to identify the relationship between being diagnosed at a late stage of breast cancer (outcome) and the predictors (independent variables), with the independent effect of each variable being adjusted to the other covariates (Tabachnick and Fidell, 2013). This form of analysis is commonly used in statistics relating to public health and epidemiology (Levy and Stolte, 2000), and is useful when the distribution of dependent variables is not linear with those of independent variable(s) (Tabachnick and Fidell, 2013). The regression analysis looks at how independent variables contribute to the outcome (i.e. the stage of the tumour at the time of diagnosis).

5.4.8.3.1 Ordinal regression

Ordinal regression is the first choice of method for explaining the association between late stage diagnoses of breast cancer and the potential factors associated with this. The outcome variable—the stage at diagnosis—is ordered as follows: (1) in-situ, (2) localised (3) regional and (4) distant stage. This order is based on the tumour's potential impact on disease progression and survival (Howlader et al., 2012), and therefore using ordinal regression is recommended (Bender and Grouven, 1997).

The benefit of ordinal regression is that it has more power than logistic regression. The Proportional Odds Model (POM) (McCullagh, 1980), sometimes referred to as ordinal logistics or cumulative odds (Scott et al., 1997), is the most popular model used for analysing ordinal data (Bender and Grouven, 1997), and is used in epidemiology (Ananth and Kleinbaum, 1997). The POM builds an assumption about the relationship between the outcome and independent variables, and presents the

results in a clear and simple way (Bender and Grouven, 1997), and it is important that the proportional odds assumptions are checked.

The paralleled logit or log odd surfaces must be tested to ensure that the assumption of the POM is valid. If the test of parallel lines is not significant, this indicates that the odds ratio is constant across all the cut points of outcome and the stage at diagnosis, and it is thus usually considered that the POM is valid. Although POM is widely used, it must however be remembered that it is sensitive to sample size (Gameroff, 2005).

An ordinal regression model (Model 1) was built after excluding marital status. The model identified variables that significantly influence late-stage breast cancer among females. Risk factors and protective factors were then considered. The results of the ordinal regression can be misleading if assumptions about the parallel lines of the categorical variable are not appropriate (Bender and Grouven, 1997). The test of parallel lines was thus examined in Model 1, and it was assumed that the assumption about parallel logit surfaces was significant, and therefore that the POM might not have been valid and the results could be misleading (see section 5.6.2.1) (Ananth and Kleinbaum, 1997).

There are two options for dealing with assumption violations. The first option is to ignore the test of the assumption because the sample size is large, and therefore a small violation in the assumption of the parallel line test can be significant. The second is to apply separate logistic regression models by fitting partial POMs (Peterson and Harrell, 1990).

The second option was chosen for the analyses and, as a result, four models were developed. In model 2, the in-situ stage was excluded (see section 5.6.2.2) and the analysis confined to invasive breast cancer because of the uncertainty about the potential progress from in-situ to invasive cancer (Erbas et al., 2006). The model looked at a group of the total sample in order to reduce the risk of assumption violations (Peterson and Harrell, 1990). However, after testing the goodness of fit, the POM assumptions seemed to be violated (see Tables 15). Another solution to avoid this problem would be to fit a partial POM or else to use binary logistic regression models utilising dichotomised responses for ordinal variables (Bender and

Grouven, 1998), although this latter solution is not recommended as it would produce statistical loss (Gameroff, 2005).

There was in this initial analysis no intention to examine the interactions between factors. The number of interactions between 6 factors will be large and potentially complex (West, 2012). If the factors could have been represented by single parameters then the number of parameters to represent interactions would be 15, for two-way interactions, plus 20 for three-way interactions, plus 15 (4-way), plus, 6 (5-way), plus 1 (6-way). That is a total of 64 parameters. The situation though is more complex than this since age needs to be represented with more than a single parameter: non-linear effects of age may well be important and to deal with this age might be categorised into several, say m , categories requiring $m-1$ parameters. There are similar problems in handling year of diagnosis where multiple categories will be required. As an initial analysis therefore, only the main effects (the factors) were considered.

The model might have been developed later to include interactions once evidence to support relevant interactions had been gathered, for example from the qualitative stage of this research. A much more fruitful approach however was selected, that of modelling using a classification tree. This is detailed in Chapter 8. Note that the classification tree has the advantage of identifying important potential interactions in an efficient manner driven from the data. The intention here is that these can be compared to the findings from the qualitative work.

5.4.8.3.2 Sensitivity analyses

A sensitivity analysis was conducted to ensure that the POM was valid to examine whether the results were consistent. Since the POM's assumptions were violated, separate binary logistic regression models were employed to carefully analyse the data and assess the assumptions about the effect of covariates on stage progression. The outcome variable was categorised in a dichotomised response. Three models were developed. Model 3 was produced to investigate the association between late stages of breast cancer (localised, regional and distant), very early stages of it, and its in-situ stage. Model 4 was run to investigate the association between late stages (regional and distant), early stages, the in-situ stage and the localised stage. Model 5 investigated the association between covariates among women diagnosed at

metastasised stages i.e. very late stages (distant) and those diagnosed at other stages (in-situ, localised and regional) (see section 5.6.2.1). After this, the goodness of fit was assessed for each model.

5.5 Ethical considerations

The joint ethics committee of the Leeds Institute of Health Sciences, the Leeds Institute of Genetics, Health and Therapeutics, and the Leeds Institute of Molecular Medicine at the University of Leeds reviewed this study on 21 April 2011 (Ref no. HSLTLM/10/015; see Appendix B). The SNCR accepted the study application and permitted data release and use for this study (see Appendix C).

Breast cancer data was anonymised during data collection, analysis and reporting. Identifiable data, such as patient names, full addresses, and medical record numbers were neither requested nor collected. As no personal identifiable data was accessed, data was not being linked to individuals, and patient confidentiality was thus maintained. The data was stored at the University of Leeds M drive to ensure its security.

5.6 Results

This section presents the findings of the second phase of this PhD—the quantitative study. A general description of the profile of female breast cancer is provided, and then the results of the cross-tabulation between the stage of breast cancer stage at diagnosis and the covariates—age, diagnosis year, place of residence, nationality and marital status—is provided. Finally, ordinal regression and binary logistic regression models are presented.

5.6.1 Results of the descriptive analysis

This section describes the overall characteristics of the participants in the study of female breast cancer in Saudi Arabia during the period 1994–2006 in terms of the stage of breast cancer at diagnosis, age, place of residence by region, nationality, marital status, and the year that the diagnosis was made. Then the cross-tabulation of the stage of breast cancer among female patients by key factors is provided.

5.6.1.1 Profile of the 10,663 female breast cancer patients participating in the study

This section gives a general description of the 10,663 patients who were living in Saudi Arabia and over the age of 18 when they were diagnosed with a valid stage breast cancer between 1994 and 2006.

The majority of these patients were assumed to be alive at the time of diagnosis, except from the five patients who were registered through their death certificates. The data produced on breast cancer by the SNCR from death certificates alone is low because of the poor reporting of causes of death (Ansary et al., 2012) and the lack of follow-ups on cancer patients.

Of the 10,663 patients, 2.3% were diagnosed at the in-situ stage, with the highest percentage of diagnoses being made at the regional stage (51.5%), followed by the localised stage (28.6%) and the distant stage (17.7%) (see Table 15). The percentage of women by age group varied. Being diagnosed under the age of 51 represented 65.6% of the cohort with one third of women aged between 41 and 51 years old. The percentage for women aged 51 years or older was 34.2% with a 4% increase in the percentage of women aged 51–60 years (19%) compared to those older than 60 (15.2%).

Most female breast cancer patients were married at the time of diagnosis (62.5%), Saudi nationals (67.5%), and from regions that had advanced oncology care (73.4%). There was an increase in the number of cases registered over time, with the number of cases nearly doubling by the period 2003–2006 (4,399 cases) from when the SNCR started providing data in 1994 (1,904 cases, 1994–1996) (see Table 15).

Table 15: Distribution of the 10,663 female breast cancer patients in Saudi Arabia by age, marital status, stage at diagnosis, nationality, location and year of diagnosis during the period 1994–2006.

Variable	N (%)	Variable	N (%)
Stage at diagnosis		Nationality	
In-situ	242 (2.3%)	Saudis	7,198 (67.5%)
Localised	3,047 (28.6%)	Non-Saudis	3,328 (31.2%)
Regional	5,491 (51.5%)	Unknown	137 (1.3%)
Distant	1,883 (17.7%)	Years of diagnosis	
Age at diagnosis		1994–1996	1,904 (17.9%)
18-30	701 (6.6%)	1997–1999	2,041 (19.1%)
31-40	2878 (27%)	2000–2002	2,319 (21.7%)
41-50	3424 (32.1%)	2003–2006	4,399 (41.3%)
51-60	2025 (19%)	Place of residence	
Older than 60	1617 (15.2%)	Regions with advanced oncology care	7,831 (73.4%)
Unknown	18 (0.2%)		
Marital status		Other regions	2,033 (19.1%)
Married	6,660 (62.5%)	Unknown	779 (7.5%)
Unmarried	1,135 (10.6%)		
Unknown	2,868 (26.9%)		

5.6.1.2 Characteristics of the 10,663 female breast cancer patients in relation to stage at diagnosis, together with covariates

The following sections provide descriptions of female breast cancer by stage at diagnosis, together with age, year of diagnosis, place of residence, nationality and marital status.

5.6.1.2.1 Characteristics of the 10,663 female breast cancer patients in relation to tumour stage and age at diagnosis

A cross-tabulation of the 10,663 patients' stages of breast cancer and ages at diagnosis shows that women aged 50 years or over were diagnosed at late stages more often than younger women. The percentage of distant stage diagnoses were higher among older women (19.9%) compared to those aged less than 40 (17.5%), with women aged 40–49 having the lowest distant stage diagnoses (15.2%). This latter age group also had the highest percentage of regional stage diagnoses (see Table 16).

The association between age and stage at diagnosis was significant (Pearson $\chi^2=23.256$, $df=9$ and $P<0.001$). However, it was not linear (see Figure 12).

To provide greater understanding about the age profile of women, age groups were cross tabulated by year of diagnosis. This shows that there was decrease in the percentage of women diagnosed at 40 years or younger over time while there was increase of 4.3% for women aged between 41 and 50 years since 1994. For those aged 51 or greater the profile remains similar over time (see Tables 15 and 16).

Table 16: Description of the 10,663 female breast cancer patients in relation to stage at diagnosis and age (1994–2006)

Age at diagnosis	Stage at diagnosis			
	In-situ N (%) ¹³	Localised N (%)	Regional N (%)	Distant N (%)
Less than 40	61 (2%)	911 (29.3%)	1589 (51.2%)	545 (17.5%)
40–49	89 (2.5%)	1022 (28.9%)	1892 (53.4%)	539 (15.2%)
50 or greater	91 (2.3%)	1105 (27.6%)	2004 (50.1%)	797(19.9%)
Unknown	1 (5.6%)	9 (50%)	6 (33.3%)	2 (11%)
Total	242 (2.3%)	3047 (28.6%)	5491 (51.5%)	1883 (17.7%)

Table 17: Distribution of the 10,645¹⁴ female breast cancer patients in Saudi Arabia by age and year of diagnosis during the period 1994–2006.

Year of diagnosis	Under 30 N (%)	31–40 N (%)	41–50 N (%)	51–60 N (%)	Older than 60 N (%)
1994–1996	154 (8.1%)	557 (29.3%)	565 (29.7%)	350 (18.4%)	278 (14.6%)
1997–1999	151 (7.4%)	591 (29%)	609 (29.8%)	383 (18.8%)	307 (15%)
2000–2002	136 (5.9%)	626 (27%)	762 (32.9%)	436 (18.8%)	359 (15.5%)
2003–2006	260 (5.9%)	1104 (25.2%)	1488 (34%)	856 (19.5%)	673 (15.4%)

¹³ Percentage within a diagnosis year

¹⁴ The unknown category (n=18) was excluded for this table.

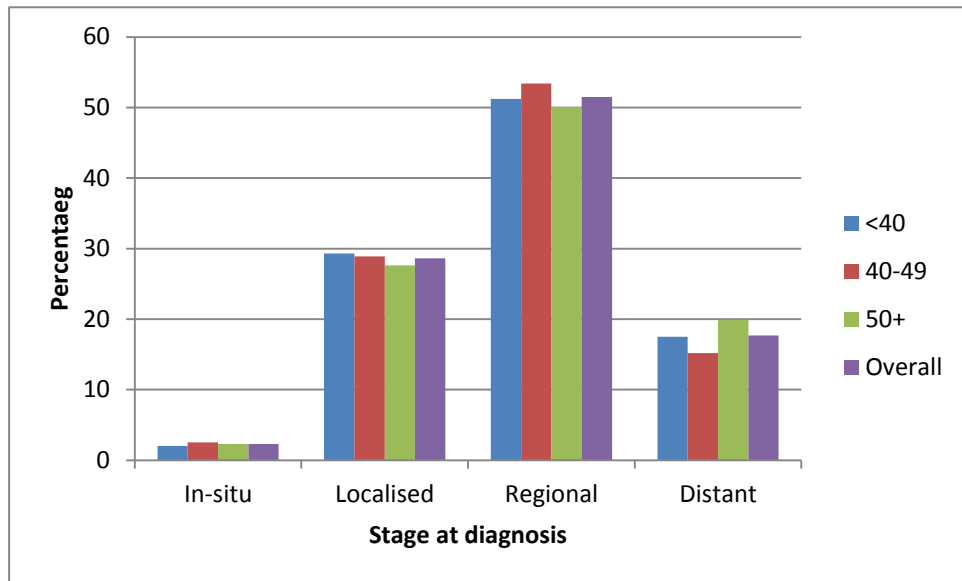


Figure 12: Distribution of female breast cancer cases in relation to age and stage at diagnosis (1994–2006)

5.6.1.2.2 Characteristics of the 10,663 female breast cancer in relation to stage of cancer and year of diagnosis

From the time at which the SNCR started collecting data (1994–1996), the percentage of women diagnosed with distant stage breast cancer has been reduced by nearly half—from 30.1% in 1994–1996 to 15.4% in 2003–2006 (see Table 18). Figure 13 shows the changes in the pattern of the disease at the stage at diagnosis. Stage at diagnosis appears to be very different during 1994–1996 to the patterns seen in later years, where there was a sharp increase in the numbers and percentages of cases diagnosed at the regional stage and a decrease in the percentages of cases diagnosed at the localised and distant stages, with an overall increase in the numbers of cases diagnosed. This indicates decline in late stages at diagnosis from 1994–1996. There was a significant relationship between stage at diagnosis and years of diagnosis (Pearson $\chi^2=330.70$, $df=9$ and $P<0.001$).

The increase in the number of breast cancer patients might be explained by (the combination of) a number of reasons. These include improvement in cancer registration over time; the massive improvement in healthcare, which might have led to improvements in the detection and diagnosis of breast cancer; the disease itself, breast cancer, might have evolved over the period of interest due to changes in diet and lifestyle (Al-Foheidi et al., 2013, Alothaimen et al., 2004) and/or an actual

increase in the incidence of breast cancer, especially given population growth. In 2006, an increase of 5,756,300 in the population has been estimated compared to the estimated population in 1994, 17,790,342¹⁵, when the SNCR started.

Table 18: Distribution of the 10,663 female breast cancer patients by tumour stage and year of diagnosis (1994–2006)

Year of diagnosis	Stage at diagnosis			
	In-situ N (%)	Localised N (%)	Regional N (%)	Distant N (%)
1994–1996	24 (1.3%)	631 (33.1%)	704 (37%)	545 (28.6%)
1997–1999	24 (1.2%)	499 (24.4%)	1203 (58.9%)	315 (15.4%)
2000–2002	49 (2.1%)	651 (28.1%)	1275 (55%)	344 (14.8%)
2003–2006	145 (3.3%)	1266 (28.8%)	2309 (52.5%)	679 (15.4%)
Total	242 (2.3%)	3047 (28.6%)	5491 (51.5%)	1883 (17.7%)

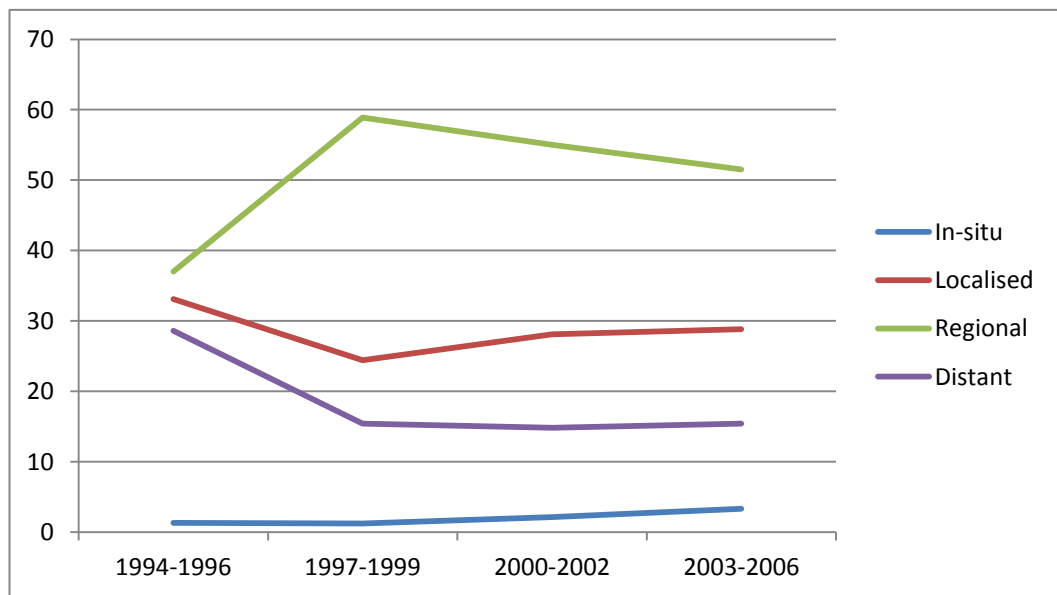


Figure 13: Percentage distribution of the 10,663 of female breast cancer patients by tumour stage and year of diagnosis

¹⁵ These estimations were calculated based on published data from the Central Department of Statistics and Information, Saudi Arabia, <http://www.cdsi.gov.sa>.

5.6.1.2.3 The characteristics of the 10,663 female breast cancer patients' tumour stages at diagnosis in relation to their places of residence

Table 19 shows the variation in the distribution of breast cancer cases in relation to the patients' tumour stages at diagnosis and their places of residence. Breast cancer patients that lived in regions with less advanced oncology care had a higher percentage of advanced, distant stage tumours (19.6%) compared to those that lived in regions with more advanced oncology facilities. A significant relationship between regions and tumour stage at diagnosis was found (Pearson $\chi^2=177.625$, $df=6$ and $P<0.001$)

Table 19: Distribution of the 10,663 female breast cancer patients in relation to tumour stage at diagnosis and place of residence (1994–2006)

Place of residence	Stage at diagnosis			
	In-situ N (%)	Localised N (%)	Regional N (%)	Distant N (%)
Regions with advanced oncology care	187 (2.4%)	2282 (29.1%)	4092 (52.3%)	1270 (16.2%)
Regions without advanced oncology care	37 (1.8%)	514 (25.3%)	1084 (53.3%)	398 (19.6%)
Unknown	18 (2.3%)	251 (31.4%)	315 (39.4%)	215 (36.9%)
Total	242 (2.3%)	3047 (28.6%)	5491 (51.5%)	1883 (17.7%)

The univariate analysis was rerun after excluding the unknown category. The result indicated an association between stage at diagnosis and place of residence (Pearson $\chi^2=21.888$, $df=3$ and $P<0.001$).

5.6.1.2.4 Characteristics of the 10,663 female breast cancer patients in relation to tumour stage at diagnosis and nationality

Table 20 represents the study cohort in relation to tumour stage at diagnosis and nationality. A greater percentage of non-Saudis were diagnosed at the localised stage (30.6%) than Saudis (27.6%). However, a higher percentage of Saudi nationals were diagnosed at regional (52.2%) and distant stages (18.1%) than non-Saudis (49.8% and 16.9%, respectively). This factor was significantly associated with stage at diagnosis (Pearson $\chi^2=20.421$, $df=6$ and $P<0.002$).

For better accuracy on the effect of marital status, a univariate analysis was conducted to investigate the difference between the ‘married’ and ‘unmarried’ categories, without including the ‘unknown’ category.

Table 20: Description of female breast cancer cases in relation to stage at diagnosis and nationality (1994–2006)

Nationality	Stage at diagnosis			
	In-situ N (%) ¹⁶	Localised N (%)	Regional N (%)	Distant N (%)
Saudis	149 (2.1%)	1987 (27.6%)	3756 (52.2%)	1306 (18.1%)
Non-Saudi	91 (2.7%)	1019 (30.6%)	1657 (49.8%)	561 (16.9%)
Unknown	2 (1.5%)	41 (29.9%)	78 (56.9%)	16 (11.7%)
Total	242 (2.3%)	3047 (28.6%)	5491 (51.5%)	1883 (17.7%)

The univariate analysis was rerun after excluding the unknown category. The results indicated an association between stage at diagnosis and nationality (Pearson $\chi^2=16.301$, $df=3$ and $P<0.001$).

¹⁶ Percentages of cases in the respective nationality groups.

5.6.1.2.5 Characteristics of the 10,663 female breast cancer patients in relation to tumour stage at diagnosis and marital status

The percentages of married women who were diagnosed at localised (27.1%) and regional (55.5%) stages were higher than those for unmarried women (26.8% and 51.6%, correspondingly). On the other hand, the percentage of unmarried women that were diagnosed at the distant stage (18.5%) was higher than that for married women (15%), as shown in Table 21. There were many patients with an unknown marital status, and this group had the highest percentage of distant stage tumours at diagnosis (23.4%).

Through examining the χ^2 , it was found that marital status was significantly associated with the stage of cancer at diagnosis (Pearson $\chi^2=177.6$, $df=6$ and $P<0.001$).

Table 21: Description of female breast cancer in relation to tumour stage at diagnosis and marital status (1994–2006)

Marital status	Stage at diagnosis			
	In-situ N (%) ¹⁷	Localised N (%)	Regional N (%)	Distant N (%)
Married	156 (2.3%)	1807 (27.1%)	3695 (55.5%)	1002 (15%)
Unmarried	35 (3.1%)	304 (26.8%)	586 (51.6%)	210 (18.5%)
Unknown	51 (1.8%)	936 (32.6%)	1210 (42.2%)	671 (23.4%)
Total	242 (2.3%)	3047 (28.6%)	5491 (51.5%)	1883 (17.7%)

Because of the difficulty in interpreting the results of the univariate analysis, due to the high percentage of cases without a valid marital status, the univariate analysis was rerun after excluding the ‘unknown’ category (n=2868, 26.9%), as shown in Table 20, and the results indicated an association between stage at diagnosis and marital status (Pearson $\chi^2=12.291$, $df=3$ and $P<0.006$).

¹⁷ Percentage within marital group

5.6.2 Results of the regression analyses

Two POMs were run in the third step of the analysis, and all of the factors included (age, year of diagnosis, place of residence and nationality) were found to be significantly associated with tumour stage at diagnosis.

The initial POM tested the independent effect of covariates on tumour stage at diagnosis. Marital status was originally included, and was significant only for the unknown category. However, it was hard to interpret its effect, given the high percentage of cases in the ‘unknown’ category; therefore it was removed from the regression analyses (see Appendix D).

5.6.2.1 Model 1: POM for the effect of covariates on tumour stage at diagnosis for the 10,663 female breast cancer patients surveyed

Ordinal regression analysis was conducted on the tumour stage seen at the point of diagnosis as an outcome in relation to the four predictor variables: age, year of diagnosis, location and nationality. It included a total of 10,663 patients whose tumour stage at diagnosis was known (as described in the ‘missing data analysis’ section).

Table 22 presents the associations of each variable with tumour stage at diagnosis using the ordinal regression model and adjusting for other covariates. For all factors, a Proportional Odds Ratio (POR) greater than 1 indicates a greater likelihood that the variable had an effect on the stage’s progression.

The risk of being diagnosed at late stages of breast cancer was significantly higher among women whom were diagnosed during 1994–1996 (POR=1.303, 95% CI=1.160–1.463) and 1997–1999 (POR=1.24, 95% CI=1.125–1.374) when compared to those diagnosed during 2000–2002 and 2003–2006. In addition, those living in regions with less advanced oncology services were at a greater risk of late-stage diagnosis (POR=1.214, 95% CI= 1.105–1.333) compared to those living in regions with more advanced oncology services. Moreover, the risk of late-stage diagnosis was also significantly greater for women aged 50 years or older (POR=1.23, 95%, CI=1.506–1.210) compared to those younger than 50 years. However, this risk was significantly reduced among non-Saudi nationals (POR=0.848, 95% CI=0.778–1.080) in comparison to Saudi nationals.

A method that can be used to test the model's fitness is Pseudo R^2 , which was low in this model (Nagelkerke=1%). This indicates that the model explains a relatively small proportion of variation in tumour stage at diagnosis. Such a value is expected, as there are many factors associated with late presentation, as described in Chapter 4. The McFadden value (0.4%) confirms the possible effect of multiple factors on tumour stage at diagnosis, as the model can be better with predictors than without them. This stresses the need for phase III of this PhD—the qualitative study—which will examine other potential factors likely to be associated with late-stage breast cancers at diagnosis.

The parallel line test provides another way for testing the model's appropriateness. Testing the parallel line at a significance level of 0.05 shows that the assumption of equal odds for each threshold is rejected (in this model, for tumour stage), as $P < 0.001$.

The results of the POMs were presented here regardless of the parallel line test because it is very sensitive to large sample sizes (Peterson and Harrell, 1990), like those seen in this study ($n=10,663$). The main effect of the predictors on moving from one stage to another is the main interest of this study. Therefore, the results from the POMs are worth reporting. However, for POMs to be considered further exploration of the models is required. Therefore, another POM was run after the in-situ cases had been excluded (Model 2), and separate binary logistic regression models (3, 4 and 5) were also produced. The results of these models are presented in the following section.

Table 22: Model (1) POM for factors associated with later breast cancer tumour stages at diagnosis for the 10,663 female patients surveyed.

Factors	Adjusted ordinal regression	
	<i>P</i>	POR, (95% CI)
Age at diagnosis		
Unknown	0.040	0.375, (0.148–0.954)
Less than 40	0.001	0.830, (0.744–0.926)
40–49	0.000	0.807, (0.731–0.832)
50 or greater	1 (Reference)	
Year of diagnosis		
1994–1996	0.000	1.298, (1.155–1.458)
1997–1999	0.000	1.240, (1.122–1.371)
2000–2002	0.271	1.055, (0.959–1.160)
2003–2006	1 (Reference)	
Place of residence		
Unknown	0.025	1.217, (1.025–1.446)
Other regions	0.000	1.217, (1.108–1.336)
Regions with advanced oncology care	1 (Reference)	
Nationality		
Unknown	0.639	0.921, (0.656–1.294)
Non-Saudi	0.000	0.853, (0.782–0.931)
Saudi	1 (Reference)	
Test for parallel lines: $\chi^2=327.090$, $df=20$ & $P<0.001$		
Pseudo R²: Cox and Snell=0.009, Nagelkerke=0.010 & McFadden=0.004		

5.6.2.2 Sensitivity analysis

In addition to the main effect analysis, other models (2, 3, 4 and 5) were run to check the consistency of the results as well as whether the models are sensitive to the way the dependent variables are reported or, in the case of the in-situ, whether the study size is large enough to run these models (Von Elm et al., 2007a). The following models offer more details about the effect produced by the various factors.

The second model was produced to assess the predication of late stages for three categorical outcomes (localised, regional and distant). The effects of the year of diagnosis, place of residence, age and nationality are similar to those seen under the first model (see Table 23). Similarly, this model's fitness was comparable to the first model.

Table 23: Model (2) POM for factors associated with later tumour stages of the 10,421 female patients diagnosed with invasive breast cancer

Factors	Adjusted ordinal regression	
	<i>P</i>	POR, (95% CI)
Age at diagnosis		
Unknown	0.006	0.399, (0.149–1.063)
Less than 40	0.000	0.820, (0.734–0.917)
40–49	0.000	0.812, (0.734–0.899)
50 or greater	1 (Reference)	
Year of diagnosis		
1994–1996	0.002	1.203, (1.069–1.353)
1997–1999	0.004	1.16, (1.047–1.284)
2000–2002	0.810	1.012, (0.918–1.115)
2003–2006	1 (Reference)	
Place of residence		
Unknown	0.009	1.263, (1.060–1.504)
Other regions	0.000	1.207, (1.097–1.327)
Regions with advanced oncology care	1 (Reference)	
Nationality		
Unknown	0.412	0.864, (0.611–1.223)
Non-Saudi	0.001	0.864, (0.791–0.945)
Saudi	1 (Reference)	
Test for parallel lines: $\chi^2=292.857$, $df=10$ & $P<0.001$		
Pseudo R²: Cox and Snell=0.007, Nagelkerke=0.008 & McFadden=0.004		

The separate logistic models help to ascertain greater details concerning the associations evident from the registry data. A binary logistic regression model (3) which examined the main effects of age at diagnosis, year of diagnosis, place of residence and nationality on very early stage tumours (in-situ, n=242) in comparison to other breast cancer stages (n=10421) showed that only the year of diagnosis was significantly associated with the tumour stage at diagnosis.

The risk of being diagnosed at later stages of invasive breast cancer reduced over time, from 3.42 (95% CI 2.016–5.827) in 1994–1996, to 2.935 (95% CI 1.897–4.539) in 1997–1999, to 1.595 (95% CI 1.148–2.215) in 2000–2002, compared to 2003–2006 (see Table 24). The percentage of women diagnosed at the in-situ stage increased in 2003–2006 to more than double those diagnosed at 1994-1999 (see Table 25).

However, when the outcome (tumour stage at diagnosis) was dichotomised to early stages (in-situ and localised, n=3,047) vs. late-stages (regional and distant, n=7,374), year of diagnosis, place of residence and nationality were significantly associated with late stages of breast cancer at diagnosis (see Model 4, Table 26). The risk of being diagnosed at a late stage of female breast cancer significantly reduced in women diagnosed in or after 2000, for patients living in regions with advanced oncology care, and for non-Saudi nationals.

Model 5 shows the effect of covariates on very late stages of breast cancer at diagnosis, namely at the distant stage (n=1,883) vs. other stages (n=8,538). In this model, the year of diagnosis, the place of residence, the nationality and the age at diagnosis were all significantly associated with very late stages of cancer at diagnosis. Strong evidence of an association between older age and stage at diagnosis occurs only at the distant stage. Table 27 shows that patients diagnosed during 1994–1996 (Odds ratio 2.064 95% CI 1.784–2.387), patients living in regions with fewer oncology services (Odds ratio 1.215, 95% CI 1.070–1.380), and patients that were Saudi nationals were at greater risk of late stage of breast cancer at diagnosis.

These models (3, 4 and 5) show the differences in effect size of the main effects of the covariates on the tumour stage in female breast cancer diagnoses, because the

direction is the same. Therefore, there is some validity in these models, which is worth reporting.

Table 24: Model (3) Factors influencing late-stage diagnoses of breast cancer for the 10,663 female patients surveyed (1994–2006) (in-situ vs. others)

Factors	Adjusted binary regression	
	<i>P</i>	Odds Ratio (95% CI)
Age at diagnosis	0.426	
Unknown	0.273	0.259 (0.023–2.903)
Less than 40	0.345	1.172 (0.843–1.631)
40–49	0.764	0.955 (0.709–1.287)
50 or greater	1 (Reference)	
Year of diagnosis	0.000	
1994–1996	0.000	3.427 (2.016–5.827)
1997–1999	0.000	2.935 (1.897–4.539)
2000–2002	0.005	1.595 (1.148–2.215)
2003–2006	1 (Reference)	
Place of residence	0.141	
Unknown	0.162	0.639 (0.341–1.196)
Other regions	0.187	1.275 (0.889–1.828)
Regions with advanced oncology care	1 (Reference)	
Nationality	0.079	
Unknown	0.261	2.627 (0.488–14.15)
Non-Saudi	0.061	0.762 (0.572–1.013)
Saudi	1 (Reference)	

Table 25: Cross tabulation between in-situ stage and years of diagnosis

Years of diagnosis	In-situ stage at diagnosis N (%)
1994-1996	24 (9.9%)
1997-1999	24 (9.9%)
200-2002	49 (20.2%)
2003-2006	145 (59.9%)
Total	242 (100%)

Table 26: Model (4) Factors influencing late stage diagnoses of breast cancer for the 10,663 female patients surveyed (1994–2006)

Factors	Adjusted binary regression	
	<i>P</i>	Odds Ratio (95% CI)
Age at diagnosis	0.138	
Unknown	0.035	0.343 (0.127–0.929)
Less than 40	0.315	0.949 (0.856–1.051)
40–49	0.351	0.954 (0.864–1.053)
50 or greater	1 (Reference)	
Year of diagnosis	0.000	
1994–1996	0.037	0.871 (0.765–0.991)
1997–1999	0.000	1.387 (1.233–1.562)
2000–2002	0.108	1.094 (0.981–1.220)
2003–2006	1 (Reference)	
Place of residence	0.001	
Unknown	0.059	1.204 (0.933–1.461)
Other regions	0.001	1.216 (1.089–1.357)
Regions with advanced oncology care	1 (Reference)	
Nationality	0.002	
Unknown	0.858	1.037 (0.697–1.544)
Non-Saudi	0.000	0.838 (0.759–0.925)
Saudi	1 (Reference)	

Table 27: Model (5) Factors influencing very late-stage (distant stage) diagnoses of breast cancer for the 10,663 female patients surveyed

Factors	Adjusted binary regression	
	<i>P</i>	Odds Ratio (95% CI)
Age at diagnosis	0.000	
Unknown	0.813	0.829 (0.177–3.896)
Less than 40	0.007	0.844 (0.747–0.955)
40–49	0.000	0.735 (0.650–0.830)
50 or greater	1 (Reference)	
Year of diagnosis	0.000	
1994–1996	0.000	2.064 (1.784–2.387)
1997–1999	0.940	1.006 (0.869–1.164)
2000–2002	0.542	0.957 (0.831–1.102)
2003–2006	1 (Reference)	
Place of residence	0.001	
Unknown	0.017	1.309 (1.050–1.630)
Other regions	0.003	1.215 (1.070–1.380)
Regions with advanced oncology care	1 (Reference)	
Nationality	0.021	
Unknown	0.135	0.655 (0.377–1.140)
Non-Saudi	0.014	0.849 (0.746–0.967)
Saudi	1 (Reference)	

5.7 Output of phase II

The regression analyses of the main effects of covariates (age, year of diagnosis, place of residence and nationality) on the stage of breast cancer at the point of diagnosis were significant. However, as shown from the POMs, the low Nagelkerke & McFadden values (presented in Tables 22 and 23) indicate that these models were not sufficient to fully explain the reasons for the late stages of breast cancer seen at diagnosis. Thus, a qualitative study was conducted to overcome the shortcomings of this data collection and analysis. The significance of the role of age, place of residence, year of diagnosis and nationality from the quantitative study informed the sampling strategy for participants for the qualitative study, which is described in the next chapter.

5.8 Strengths and limitations of the study

A major strength of this study is that the registering of cancer cases is compulsory in Saudi Arabia, and this means that the analysis of the census data provides a general picture of female breast cancer across Saudi Arabia. The data collection performed in routine data-based studies using such sources and methods can be quick, and a large sample can be exacted (Dos Santos Silva, 1999). The SNCR collects cancer-related data from the entire Kingdom, and as this data collection process is compulsory, the data obtained covers almost all of the diagnosed patients.

However, there are a number of important limitations to this form of research, which need to be considered here. First, in routine data-based studies, a limited number of variables are available (Dos Santos Silva, 1999). This study used data from the SNCR and, as a result, the effects of certain factors could not be measured. For example, the time interval between the recognition of symptoms and first medical contact is not measured by the SNCR. Neither do they report on screening practices, or record any data about the educational levels or backgrounds of patients. Therefore, the analysis of factors influencing the stage of breast cancer at the point of diagnosis is limited to age, marital status, location, year of diagnosis and nationality, and thus potential compounding factors were not available in this data, or

in the information produced by routine-data based studies in general (Dos Santos Silva, 1999).

Second, the retrospective nature of this area of the study limits the ability to look further for other possible determinants of late stage diagnosis. There is no follow-up information available for these patients, and tracking them would not be easy. For example, there is no link between the SNCR and the death registry, and therefore it would have been necessary to track the patients to produce a survival analysis.

Third, the pattern of late presentation in recent years could not be analysed using SNCR data due to the unavailability of data acquired by it after 2006 when the data was collected. Changes in the trend of late presentation for breast cancer since 2006 are possible, so this represents a further limitation to the use of SNCR data. Al-Rikabi and Husain (2012) also point out the possibility that there has been an increase in the number of breast cancer cases due to increased awareness together with a greater uptake of screening services. They found a shift in the distribution of breast cancer cases after reviewing breast tissue specimens since 2007. The SNCR cancer registration is ongoing, and data for breast cancer cases diagnosed after 2006 would be available were an application to be submitted for more updated data.

Fourth, there is no control on data quality and missing data. Thus, SNCR data completeness and quality might be an issue (Al-Zahrani et al., 2003). Missing data for some factors led to a reduction of the number of cases to those with valid stage tumours at diagnosis. The completeness of the data is generally good, however, with the exception of marital status. The SNCR tries to improve the quality of its data, and has been successful in doing so over time (Al Sayed et al., 2010).

5.9 Summary

This Chapter described the quantitative study, which was the second phase in the thesis. It identified the main effects of age, year of diagnosis, place of residence, nationality and marital status on the stage of female breast cancer seen at the point of diagnosis using census cancer data from the SNCR.

Different logistic regression models (ordinal and binary) were fitted and demonstrated the significant association between a number of factors and later stages of breast cancer at the time of diagnosis, comprising the increasing age of women, a

diagnosis made between 1994–1999, residing in regions with less advanced oncology care, and being a Saudi national. The various models applied provide details about the association between the covariates and stage at diagnosis.

The models included factors as main effects only and did not include interactions between factors. Including interactions for the initial analysis without guidance from other research would have very greatly inflated the number of model parameters and reduced robustness as a consequence.

Older women were at a higher risk of late stage at diagnosis is in line with literature about the association between older age and late presentation of breast cancer (Abdel-Fattah et al., 1999, El-Zawawy, 1991, Elzawawy, 1999, Ermiah et al., 2012, Ramirez et al., 1999) and late diagnosis (Arndt et al., 2001). Some studies from the Middle East however did not support this result (Abdel-Fattah et al., 1999, Al Saad and Alsayed, 2012, Mousa et al., 2011, Stapleton et al., 2011) and these studies were varied in how they assess this association (see Chapter 4). Marital status is not a useful predictor for late presentation in this study and as indicated in the literature (Ramirez et al., 1999) (Abdel-Fattah et al., 1999, El-Zawawy, 1991, Elzawawy, 1999, Ermiah et al., 2012). The place of residence has been identified as a risk factor for advanced breast cancer. The disparity of stage of diagnosis by location has been recognised (Nguyen-Pham et al., 2014).

It is anticipated that reporting of cancer stage changed from 2000 onwards, after it was modified by the SEER. This might provide more precise data about late presentation compared to the early years of SNCR's data collection (1994–1999).

These factors explain *some* of the characteristics that are linked with late presentation for female breast cancer in Saudi Arabia, but Chapters 6, 7 and 8 will provide a more in-depth exploration of the reasons for late-presentation.

Chapter 6 Phase III: Late-presentation female breast cancer in Saudi Arabia: a qualitative study

6.1 Introduction

This chapter describes the methods used to undertake the third phase of this thesis—the qualitative study. Its aim is to provide an in-depth contextual understanding of the factors that influence late presentation for investigations and diagnoses for female breast cancer in Saudi Arabia.

Public health guidelines in Saudi Arabia are commonly based on evidence gathered from epidemiological studies. These studies use quantitative methods to describe health problems and to produce generalisable conclusions about health issues. Our understanding of the role that social factors play in complex public health issues like cancer require comprehensive, in-depth evidence to be attained (Jack, 2006). A qualitative approach investigates why and how a problem develops through identifying the relevant contextual factors and influences, and is thus able to improve our understanding of the reasons for individual behaviours (Jack, 2006).

A qualitative approach is useful for explaining issues related to help-seeking and late presentation for diagnosis with cancer (Smith et al., 2005), and has been successfully used in numerous studies (Burgess et al., 2001, Gould et al., 2010, Lam et al., 2009, McEwan et al., 2014, Norsa'adah et al., 2012, O'Mahony et al., 2011, Rastad et al., 2012). While several attempts have been made to explain delays in presenting for breast cancer symptoms, as explained in Chapter 4, all of the studies that have done so were not conducted in Saudi Arabia.

Although phase II of this study revealed some of the characteristics of women that are connected with a high risk of being diagnosed with breast cancer after the disease has reached an advanced stage, it provides neither a holistic view of the current causes of late presentation nor an in-depth understanding of this research problem. Thus, this qualitative study was used in order to try to fill in many of the gaps in this area. This third phase of the thesis informs health professionals, policymakers, and the general public about the concerns of potential breast cancer patient identifies,

supports for and barriers to timely care, examines factors influencing early presentation and provides suggestions for future research in this area.

6.2 Aim of the study

This study investigates the factors that influence late presentation for breast cancer investigations and diagnoses amongst women in Saudi Arabia.

6.3 Study objectives

The main objectives of this study are to:

- Explore lay-understandings of breast cancer and its progression.
- Explore the reasons for seeking or not seeking immediate medical care after symptoms recognition.
- Explore the barriers to and the facilitators of the seeking of timely medical attention for breast cancer investigations.
- Map the healthcare-seeking pathway of breast cancer patients.
- Develop an explanatory model of the factors that influence women in seeking medical attention following symptoms discovery.

6.4 Methods

6.4.1 Study design

The third phase of this study used a qualitative research approach. Qualitative health research is a special form of qualitative research (Morse, 2011), and is recognised as a valid method for obtaining information (Popay and Williams, 1998) on how people react to symptoms and seek healthcare (Morse, 2011). It can access information that is not accessible through quantitative methods, helping to gather in-depth, detailed information from small groups of people, thus generating textual rather than numerical data (Holloway, 2005, Patton, 2002).

6.4.2 Methods of data collection

Data collection methods can be broadly classified into the two categories of the collection of naturally occurring data, which can be done using methods such as observation; and data generation through research intervention, which can be done using methods such as interviews and focus groups (Ritchie and Lewis, 2003). The

observation of naturally occurring data helps to develop an understanding of behaviour in context (Ritchie and Lewis, 2003). This study explored the pathways available for Saudi women to seek medical care, and the factors that help or impede their search. However, it would be difficult to identify participants that are experiencing breast cancer symptoms and then simply observe their care-seeking behaviours. Moreover, other methods could possibly generate more data. Patton (2002) notes that although observing feelings, thoughts and intentions is difficult, asking persons about them is possible. Morse (2011) stresses that patients often remember significant health-related events, such as illnesses, and that hospitalisation is difficult to forget. Patient recall is thus an effective way of gathering material on which good qualitative research can be based, because the emotions felt on recall are a reflection of the emotions felt when the events happened, and thus interview validity is retained (Morse, 2011).

The main proven methods for retrospectively gathering information on events are participant focus groups and individual interviews. Both have been used in medical help-seeking studies for cancer, but interviews are more common in this area (Smith et al., 2005). Focus groups are often used for the quick and cost effective gathering of information (Patton, 2002), and are acceptable in the context of cancer studies because participants usually like talking with others who share their health concerns. However, the number of questions that can be used in focus group studies are restricted by the group structure, and may thus limit the depth of individual responses (Patton, 2002). Arranging meeting times suitable for all eligible participants can also be problematic. Furthermore, fear of embarrassment may prevent people from talking about certain issues in these contexts, so, in practise; the individual interview is generally then a preferred method of data collection for such studies.

This study generated qualitative data from individual stories using 'semi-structured interviews' (Corbetta, 2003), which enable the interviewer to focus the interview on issues related to the study whilst simultaneously allowing free conversation to occur. The interviewer is able to clarify ambiguities by asking the interviewee follow-up questions (Corbetta, 2003). Thus, different participant responses can be clarified as actual differences in participants' reactions to questions, rather than variations produced by different interpretations of the wording or a lack of comprehension on the part of the interviewees (Barriball and While, 1994).

Semi-structured interviews were thus chosen because they were the best suited to achieving the aim of this study. Interviews with eligible participants were scheduled at the convenience of the patients, who were often able to participate in the study before or after visiting the hospital for treatment. Although data collection using one-on-one interviews may be expensive and time consuming (Teddlie and Tashakkori, 2009), they provide a more private conversation than focus groups, and allow more details to be gathered from each individual (Ritchie and Lewis, 2003).

In this study, all the participants took part in one interview conducted in spoken Arabic—the native language of all the participants. All interviews were conducted by the researcher, one-on-one, in a private setting at the oncology centre. The collaboration of the KFSH&RC's oncology centre during data collection and its provision of facilities for conducting this research are both greatly appreciated.

6.4.3 Interview guide

An 'interview guide' approach (Patton, 2002) was used, which comprises a list of questions and/or issues to be explored during the interview. The list ensures that the interviewer utilises the interview time effectively and covers all the planned topics. It also helps keep interviews systematic, comprehensive and focused, whilst allowing the interviewer to be flexible during questioning and to explain or to ask about issues in more depth (Patton, 2002).

The interview guide was developed following a thorough literature review (see Chapter 4). The guide aimed to capture information on types of symptoms identified; perceptions, knowledge, and recognition of symptoms; health-seeking behaviours; the social networks of participants; and the length of time that passed between respondents discovering symptoms and seeking healthcare. The guide also explored facilitators of and barriers to the seeking of medical care, together with women's suggestions for health education and promotion (see Appendix E). Open-ended questions were used to obtain participants' views in a way that minimised "the imposition of predetermined responses" (Patton, 2002).

The interview guide was initially written in English so that it could be discussed with the researcher's supervisors. It was then translated into Arabic, and revised by two female medical practitioners who were fluent in both Arabic and English in order to ensure the translation's accuracy. The Arabic version of the interview guide was then pilot-tested with a woman who was Saudi by birth before the interviews were begun.

No changes were made to the interview guide after the pilot test. Rather, the pilot helped to assess what terms or phrases would be most easily understood by the participants, and to ensure that no medical or technical terms that could have been difficult for the participants to understand were used. In the first four interviews of this study, the researcher continued to note which words and expressions best conveyed the meaning of the questions, and thus enhanced their cultural appropriateness.

6.4.4 Study participants

The inclusion criteria for the study were that participants be female, Saudi nationals, age 18 or older, and had been diagnosed with breast cancer between two and six months before the interview. Patients who had received a cancer diagnosis within two months of the interview date were excluded from the research population in order to minimise emotional distress, as these patients could still be in the shock phase of the disease, and their emotions could also colour their responses compared with those of the other participants. Patients who had prior experience of cancer were also excluded, as were those with cognitive or psychiatric problems that could interfere with their ability to communicate and express their disease experience and/or their ability to provide informed consent to be interviewed.

6.4.5 The sampling strategy

An innovative form of purposive sampling was undertaken using empirical evidence from the quantitative study to select information-rich participants. Factors found to be significantly associated with the stage of the tumour at the point of the breast cancer diagnosis in Chapter 5 were considered to be relevant characteristics for guiding the purposive sampling. These included: stage at diagnosis, age, and place of residence.

(1) Stage of tumour at breast cancer diagnosis

The tumour stage at diagnosis was used as a proxy of the time between noting symptoms and seeking medical care. It was assumed that those who sought medical care promptly were more likely to be diagnosed at an early stage.

Participants with a cross-section of cancer stages—from early and advanced—were recruited. Stages I and II were classified as ‘early-stage’ breast cancer, and stages III and IV as ‘advanced-stage’ using TNM staging system, as prognosis and survival

differ for early- and advanced-stage cases (Sant et al., 2003, Walters et al., 2013b). Moreover, the recruitment of participants with cancer at all stages allowed for the investigation of similarities and differences in seeking healthcare in relation to stage at diagnosis.

(2) Age

The systematic review carried out in this thesis presents evidence about the impact of age on late presentation for breast cancer investigations from the existing literature in the Middle East (see Chapter 4). These findings agreed with the wider literature in this area (Ramirez et al., 1999). Moreover, the quantitative study in this thesis—which gives information specific to Saudi Arabia—confirmed that age has a significant effect on the stage of breast cancer at diagnosis. Thus, participants were recruited from different age groups in order to capture more information. An age of 50 is considered to be the boundary between older and younger women because routine mammography screening is more likely to be effective from this age (US Preventive Services Task Force, 2009). This age precedes the menopause for most women.

(3) Place of residence

The results from the quantitative study indicated that regions are important predictors of how advanced the stage of breast cancer is at the point of diagnosis. Thus, one sampling criterion that was used was whether or not the patient resided in the Riyadh region or not. This criterion allowed for the exploration that the impact of living in a region with advanced oncology care has on health-seeking behaviour.

The quantitative study in this thesis found nationality (Saudi vs. non-Saudi) to be significantly associated with the stage of breast cancer seen at the time of diagnosis, with Saudi women being more likely to be diagnosed at later stages of breast cancer than non-Saudi women. Since the focus of this study was on Saudi nationals, non-Saudi women were excluded from the qualitative study.

The year that the breast cancer diagnosis was made was not considered to be a relevant factor since all potential participants would have been diagnosed within relatively short period, and thus was not a criterion for sampling participants. The time gap between data collection for the qualitative study (2011) and the quantitative study (1994–2006) also made a criterion for year of diagnosis unfeasible, as those who were diagnosed at very advanced stages in 2006 might not still be alive, and

women that were still alive would be less likely to recall events as accurately as those diagnosed in the last two to six months.

Non-significant factors were considered to be non-relevant and therefore excluded. For example, marital status had no significant impact on presentation for breast cancer investigations in the Middle East (See Chapter 4). It was not associated with stage at diagnosis in the quantitative study, and consequently it was not considered to be a relevant sampling criterion (see Chapter 5). A married woman was equally as likely as an unmarried woman to present late. This is explored further in the discussion section (Chapter 8).

A sampling frame was designed, incorporating stage at diagnosis, age and region of residence (see Appendix F). It was designed to recruit a sample of up to 24 participants, and 19 women were actually recruited, with each participant having multiple characteristics, as presented in Table 28. Another four potential participants were approached, but refused to participate. A description of the participants is provided in Chapter 7 – the results chapter.

Table 28: Characteristics of the study sample based on the sampling frame

Characteristics	Number of participants
Early stages, younger than 50 years and from Riyadh region	2
Early stages, younger than 50 years and from regions other than Riyadh	1
Early stages, 50 years or older and from Riyadh region	3
Early stages, 50 years or older and from regions other than Riyadh	1
Advanced stages, younger than 50 years and from Riyadh region	3
Advanced, younger than 50 years and from regions other than Riyadh	4
Advanced, 50 years or older and from Riyadh region	2
Advanced stages, 50 years or older and from regions other than Riyadh	3

6.4.6 The study setting

The study took place in a single health institution—the KFSH&RC in Riyadh, Saudi Arabia. This institution has one of the most advanced oncology centres in the country, and accepts referrals of national and international cancer patient. The institution provides tertiary level healthcare, and is accredited by the World Health Organization as a collaborating centre for cancer prevention and control (KFSH&RC, 2011). A multidisciplinary team conducts patient assessment and treatment according to disease-specific guidelines there (Mohiuddin, 2011), and the clinical sections comprise medical oncology, radiation oncology, adult haematology/oncology and bone marrow transplantation, palliative care, and a research unit (Mohiuddin, 2011). The KFSH&RC hosts the SNCR and the Cancer Registry of the GCC countries (KFSH&RC, 2011).

According to the KFSH&RC Tumour Registry (2012), a hospital-based registry that has operated since mid-1975 up through 2011, the institution treated 72,557 cancer patients. Patients were mainly referred from the Riyadh (35.5%), Eastern (14.8%), and Makkah regions (11.5%) (Mehmood et al., 2012).

During 2011, when the data collection for this qualitative study was conducted, a total of 2,527 cancer cases were diagnosed at KFSH&RC, with 1,436 of these being females. Breast cancer was the dominant type of female cancer, constituting 16.7% of the total cancer cases, male and female, in 2011. Among females, breast cancer comprised 38% of all cancer cases. Looking at the general referral pattern of cancer patients to KFSH&RC in relation to location, most female breast cancer cases were referred from the Riyadh region (39.7%), followed by the Aseer (10.3%) and Eastern regions (9.6%) (Mehmood et al., 2012).

Participants for the current study were selected from this institution because it is one of the largest oncology centres in Saudi Arabia, and it was considered likely that a sufficient number of participants for the study could be recruited from the institution's referrals. KFSH&RC accepts cancer patients from throughout the country, so despite varying referral patterns, any eligible patient from these regions was offered the opportunity to join the study. This reduces the risk of attaining an insufficient number of study participants and a bias toward recruiting patients only eligible for specific healthcare services (see Chapter 2).

Generally, the oncology team was very supportive and friendly with both the patients and the researcher. Given their heavy workload, they were very helpful and answered all the researcher's questions concerning their patients' journeys through diagnosis and treatment.

6.4.7 Data collection

Nineteen participants agreed and signed consent forms to participate in the study between September and December 2011. Within qualitative studies, this sample size is considered sufficient to draw evidence (Guest et al., 2006), and is within the range of sample sizes used in published qualitative studies on cancer help-seeking (Smith et al., 2005). A small sample size is common in qualitative research due to the intensiveness of the data collection and analysis process (Popay and Williams, 1998). The in-depth nature of this qualitative research allows the gathering of a large amount of data from participants, whose numbers were restricted based on the time available for the data collection. Moreover, at the end of the study, saturation was reached with this number of interviewees, and a larger group would most likely have yielded no new information.

Eligible participants were identified by hospital staff members—usually either by the patient's oncologist or the breast cancer nurse acting as the patient's caregiver. The oncology centre was visited at times when potential participants could be met. The hospital contact would meet the researcher with a list of patients, and the researcher would then select potential study participants who met the sampling criteria. The hospital contact would then approach the selected patients and introduce the researcher to those that showed interest in the study. An information sheet (see Appendix G) which describes the study was given to potential participants. Interview dates and times were then arranged at the convenience of each willing participant. Each interview began with the researcher welcoming the study participant and introducing herself in order to build rapport, to put the interviewees at ease, and to establish natural conversation (Kvale, 2007). Each participant was told that her experience with the disease was valuable for understanding late presentation for investigations and diagnoses, and that the researcher would not judge her experience in any way (Patton, 2002).

After this, the study objectives would be described, including the various ethical standards that the study upheld (such as maintaining the patient's confidentiality and

anonymity), and the topics that would be covered in the interview. The purpose of audio recording would then be explained, and the participant's written consent would be requested. The participant would also be asked if she had any further questions.

The participant signed a consent form (see Appendix H) on the day of the interview and in the presence of the researcher before the recorded interview started. If the participant agreed, the interview was audio recorded; otherwise, the interview was recorded by hand in written notes. Five participants agreed to their interviews being audio recorded. During the other interviews, the participants' answers to questions were written out by the researcher while they were talking. Decisions—about not audio record interviews—were respected without any requests for justifications being made. Even though the confidentiality of the interviews was explained to all the participants, perhaps women might refuse audio recordings because they have little awareness about or familiarity with interviews in qualitative research and audio recording for research purposes.

As Long (2005) has noted, Saudi culture emphasises the value of personal trust, and the Saudi public is suspicious about the credibility of ideas and opinions expressed in the media. The participants in this research might have linked the idea of audio recording with media interviews, and there is a possibility that they may have felt they would have to be more careful about what to say if the interviews were audio recorded.

Some women might be careful when they talked about their personal experiences even if their interviews were not audio recorded. For such cases, extra reassurance and explanations about confidentiality and the use of these data for research purposes were provided. For example, one participant interrupted the interview and asked about the confidentiality of the data, even though her interview was not being audio recorded and confidentiality was explained thoroughly earlier. She was reassured again that all data would be anonymised, and an example was given to her: even the names of the healthcare facilities that the women first visited would be anonymised. After this reassurance, she then talked more freely.

At the beginning of the recorded interviews, background demographic information was collected, comprising the woman's age, marital status, number of children, education, employment, and family history of breast cancer or other types of cancer. The questioning did not follow the same sequence in each interview, nor did it always follow the sequence laid out in the interview guide. Interviews usually

continued with an open question like “Please tell me about the first symptoms you noticed”. Participants’ conversations were followed to ensure that the interview remained focused on issues related to symptoms and healthcare-seeking behaviour. Most questions were open-ended in order to encourage the participant to talk, with probes and follow-up questions being used to clarify new issues that arose. For example, when participants were asked about barriers to seeking medical care, some participants had not considered the existence of barriers before, so the researcher tried to clarify by giving examples, such as transportation to a health facility or holding other responsibilities.

Leading questions were rarely used with the participants. The purpose of leading questions is to ascertain whether an event or issue is pertinent (Kvale, 2007). For example, if a woman spoke of seeking care at a health facility, and the researcher was not sure which facility she meant, the participant would be asked if she meant a PHC or a private clinic.

At the end of the interview, the participants were asked if they had anything they would like to add, and the times that each interview started and ended were noted.

6.4.8 Data analysis

‘Applied thematic analysis’ (Guest et al., 2012) was used to analyse the qualitative data. This method of analysis was chosen because it provides a systematic, credible, and transparent way of identifying relevant themes from qualitative or textual data. It is currently the predominant method for analysing data in research projects with an applied qualitative focus (Guest et al., 2012).

Qualitative data analysis is a complex and lengthy process because participants responses are neither systematic nor homogeneous (Patton, 2002). Thematic analysis seeks to recognise patterns or themes in the data (Braun and Clarke, 2006), using a phenomenological approach to investigate perceptions and lived experiences. The method characterises and then summarises these for the purpose of applying the findings to the research question. Thus, *applied* thematic analysis is used for applied research projects that aim to provide practical solutions to problems (Guest et al., 2012).

6.4.8.1 The analysis process

The analysis explores the textual data with the aim of build a coherent and consistent story from it. To achieve this, common features were identified through a series of

steps, and these features defined by using themes. The themes emerged in response to textual data from participants' interviews that represented shared ideas (Guest et al., 2012). The data analysis involved four stages: familiarisation, text segmentation, re-contextualisation, and writing up.

(1) Familiarisation

The first stage of the data analysis began with the researcher becoming fully familiar with the data (Patton, 2002). This process commenced during the data collection phase, through the researcher's interaction with the participants, and developed further through listening to their interviews and writing up the field notes (Braun and Clarke, 2006). After the last interview was completed, the process of transcribing each audio recording and writing up the written interviews was performed. During transcription, the data was coded, with a number being assigned to each participant in order to preserve informants' anonymity and to ensure that no data was able to lead back to them. For audio-based data, the accuracy of each transcript was checked against the audio or written recording before the analysis commenced.

The analysis of the data focused on the research question that this applied qualitative study was designed to explore the barriers and facilitators that exist for the seeking of medical care after the self-recognition of breast cancer symptoms has occurred. The anonymous transcripts and notes were read and re-read in order for the researcher to become familiar with the data. This stage was helpful for understanding the study context and detecting differences in the women's narratives. At the end of this first stage, a map was drawn up for each participant, referred to as a "medical care-seeking pathway". This step helped to identify general and specific themes and topics (Ritchie and Lewis, 2003).

(2) Text segmentation

The second stage of the data analysis involved text segmentation, which is an analysis mapping tool that allows the assessment of data quality and helps in exploring themes in terms of their similarities, differences, and inter-relations (Guest et al., 2012). The text from each transcript was broken into segments, and the data was coded by assigning a code to each segment. A code describes the component of a theme and sets its boundaries, whereas a theme represents a general feature occurring in the data (Guest et al., 2012).

Qualitative data was systematically coded by importing one transcript at a time into NVivo (version 9), a software package for qualitative data analysis (QSR International Pty Ltd, 2010) that assists in the management of non-numeric data by facilitating data organisation, retrieval and tracking.

To limit the possibility of the loss of content, the transcripts were analysed in their original Arabic forms, and the data was broken into text segments by identifying a beginning and an end point for each segment of each transcript. During this text segmentation and coding, the question “what does this text means to me?” (Guest et al., 2012) was recurrently considered. The process of text segmentation resulted in numerous codes, and was continued until no further codes were created.

To ensure consistency in coding, three randomly chosen transcripts were translated from Arabic into English, and the researcher’s two supervisors independently coded the three English transcripts. The researcher’s and the supervisors’ coding of the three transcripts were then compared, and after consensus on the coding of each transcript was achieved, the codes of the remaining transcripts were reviewed. A codebook was used to systematically sort texts during text segmentation and coding. This is “a structured compendium of codes that includes a description of how codes are related to each other” (Guest et al., 2012 p.50).

As the analysis became more complicated, it moved from being purely descriptive to becoming analytical through answering another question “what specific instances of meaning exist in this text?” (Guest et al., 2012 p.53). The codebook assisted in grouping the codes to develop a shared concept or theme. Table 29 provides some examples of the codes used in the codebook. The codes were sorted into potential themes by juxtaposing the codes and quotes from all interviews that shared a similar theme. Themes, with brief descriptions, were drafted for codes that shared a central idea.

Table 29: Example of codes definition from the codebook

Suggested code	Definition of elements
Breast cancer awareness	<p>Use this code for discussions of women’s knowledge about breast cancer prior to diagnosis with it.</p> <p>This can include quotes about what they knew, what they did not know, and their sources of knowledge.</p>
Misconceptions related to breast cancer	<p>Use this code for discussing women’s mistaken ideas and misunderstandings of facts related to breast cancer and the importance of seeking healthcare immediately after the discovery of symptoms. Examples can include quotes about misconceptions about breast cancer, the seeking of healthcare, and the sources of these misconceptions.</p>

Displaying data was used to enhance the understanding of the connections and explanations beyond data description (Bazeley, 2009, Miles and Huberman, 1994). Medical care-seeking pathway maps were also used to identify possible barriers and facilitators that existed for the women through identifying similarities and differences in their characteristics, mainly with respect to stage at diagnosis, age, and place of residence. The code book was modified during the analysis process as new information and thoughts emerged.

(3) Re-contextualisation

Re-contextualisation analysis is the process of theory building that is used during the refinement of data and involves linking the themes into concepts (Tesch, 1990). This step increased the complexity of the analysis by asking a third question: “are there patterns of relationship among instances of meaning in this text?” (Guest et al., 2012 p.53).

The themes emerged from the data were finalised after looking at the similarities and differences across all the transcripts. Of particular interest were comparisons between the women’s stories, as variations in opinions were expected among the

interviewed women. Where possible, negative cases were studied to enrich the analytical process—a negative case being one that does not fit with or contradicts the general pattern of the data (Guest et al., 2012, Patton, 2002).

Memos were written during the data analysis to record the analyst's thoughts about the factors that may have influenced the late-presentation for breast cancer investigations by the participants. These memos assisted in understanding the connections and relationship between themes that emerged from the data.

In addition, the researcher's discussions with supervisors that have extensive experience in qualitative research assisted in clarifying the main themes (concepts). In order to locate the main themes, differences in women's experiences of seeking medical care were compared and contrasted in relation to stage at diagnosis, age and place of residence. These comparisons revealed differences in, for example, how the seeking of medical-care varies between older and younger women with breast cancer. The narrative map of medical care-seeking for each participant pointed to events and possible factors that facilitated or impeded the seeking of healthcare. These maps helped to reveal the relationship between themes.

Each theme was then compared and assessed to ensure that, together, they presented a coherent story. During this process, new themes were created and revised, and extra data was recorded. A model was developed for this study, showing the relationship between themes experienced by at least one of the nineteen participants. A clear idea of the main themes was produced, together with an overall story shown by the data.

(4) Writing up

The written story of the qualitative findings is the final product of the research process, where data is used to tell a coherent story (Sandelowski, 1998). The writing up commences from the initial stage of the analysis and continues through each stage in which the findings are compared and contrasted and the theory is built (Ryan, 2006). Writing up the qualitative findings formed part of the data analysis of this study. Women's narratives were examined to determine each theme and how they related to others, and this helped to generate a study model (Bradley et al., 2007). The analysis process used a combination of inductive and deductive approaches, and was influenced by both data and empirical evidence.

6.4.9 Validity and reliability

Validity and reliability are important for judging the quality of qualitative studies in multidisciplinary research (Patton, 2002). In particular, the demonstration of validity and reliability is necessary for persuading others that the research findings are worth paying attention to (Lincoln and Guba, 1985).

In relation to qualitative research, validity involves “assessing what one is intending to assess” (Guest et al., 2012 p. 80). ‘Credibility’ (Lincoln and Guba, 1985) is commonly used in qualitative research to denote validity. The validity of the methodology of qualitative research is important, especially for applied research, where the findings might have an impact on policy formation.

Reliability, on the other hand, refers to “an ability to measure consistently” (Black and Champion, 1976 p.232), and qualitative research generates issues concerning reliability because a large amount of “interpretation goes into defining the data items (i.e. codes) as well as applying the codes into chunks of text” (Guest et al., 2012 p.11). It is important for qualitative research to demonstrate reliability because it helps to enhance validity.

In order to enhance credibility, various options for assessing the research problems were reviewed (see Chapters 3 and 4), and a study design was developed. Following the analysis of the quantitative data, a set of criteria was developed for the purposive sampling strategy (see Chapter 5).

The quantitative analysis aimed to discover *which* factors are associated with late presentation for breast cancer investigation and diagnosis. The characteristics that were likely to be possessed by women diagnosed at an advanced disease stage had been found at the macro level, and thus representative voices at the micro level could be selected. The qualitative analysis aimed to discover *why* and *how* the phenomenon of late presentation occurs through understanding women’s beliefs, thoughts and behaviours about the seeking of medical care when breast cancer symptoms are recognised. The qualitative approach could assist in understanding the phenomenon in this context through listening to representative experiences. By applying findings from the quantitative study to the qualitative study, findings from the qualitative analysis could thus be made more representative of the entire population, and therefore more generalisable, than if quantitative data had not been used.

Audio recordings of the interviews and verbatim transcriptions were included in the study design in order to improve the accuracy of the data (Halcomb and Davidson, 2006). However, this part of the study design was only partially utilised, since many of the participants refused to be audio recorded during their interviews. In this thesis, all the quotes from participants come from the audio recordings, while the content from written narratives is presented in the form of summarised statements. Thematic analyses of texts aimed to identify shared ideas, and this can be achieved even if verbatim transcription is not used, as verbal data can be captured by other methods, including verbatim transcription (Halcomb and Davidson, 2006).

The data was analysed by the researcher, who is Saudi Arabian by origin and birth, and it was important that the coders also had a proper understanding of the culture. Multiple coders were used to confirm coding and ensure inter-rater reliability (Barbour, 2001, Creswell and Plano Clark, 2011, Guest et al., 2012), with three transcripts being coded and analysed independently by two supervisors (JL and BP) to ensure the consistency of the coding. Differences in coding were resolved by consensus, although before arriving at a consensus, any differences were explored as a way of enriching the analysis (Potrata, 2011).

The data analysis was performed using the Arabic transcripts after the researcher and the supervisors had undertaken the calibration exercise. Thus, all the coding and the analysis of the transcripts were undertaken before the translation was conducted. The interviews were translated into English at the report writing-up stage, which involved working closely with a professional translator to ensure that the intended meanings and contexts were reproduced in the English translation (Nes et al., 2010).

6.5 Ethical considerations

The joint ethics committee of the Leeds Institute of Health Sciences; the Leeds Institute of Genetics, Health and Therapeutics; and the Leeds Institute of Molecular Medicine at the University of Leeds reviewed this study on 21 April 2011 (Ref no. HSLTLM/10/015) (see Appendix B). I applied for local ethical approval in Saudi Arabia from the research ethics committee at KFSH&RC on 21 July 2011 (see Appendix I). The ethics committee at KFSH&RC follows research ethics requirements similar to those of the National Health Service. The ethical practice in this study is in line with the ethical practice adopted by the School of Medicine at the University of Leeds, and it was audited on 19 February 2014 (see Appendix J).

The recruitment of breast cancer patients needed to be handled with care, especially when women were first approached, as they were undergoing treatment. In this study, female breast cancer patients who had been diagnosed within the last two months were not approached, as they were probably still in the shock phase, which counted against approaching them both in relation to how they would be able to manage performing interviews that soon after diagnosis and in terms of how their emotional states could have influenced their responses. During the interviews, the researcher explained to the participants that they were free to talk about whatever they thought was relevant, and that they could withdraw from the study at any time. In addition, the voluntary nature of their participation was explained. One potential participant changed her mind about wanting to participate in the study on the day of the interview. All of the women were also told that a decision to not participate would not affect the standard of care they received or their relationship with their healthcare providers.

Because the target sample was that of recently diagnosed breast cancer patients, the effects that the research could have on the interviewees were considered. Although emotional distress is possible in this kind of study, the literature has not been able to detect any “harm” from the use of interviews in such studies (Potrata, 2010), even when unstructured interviews are used (Corbin and Morse, 2003). In fact, it has been found that participants in unstructured interviews are far more likely to experience relief than distress after discussing distressing experiences (Corbin and Morse, 2003). Nevertheless, a risk management plan was drawn up to deal with the possibility that a patient might lose her ability to continue the interview due to emotional distress, even after providing informed consent. In such a case, the participant would be asked if she wanted to continue, to take a break, or to end the interview. The interviewee would be informed that they would not need to provide any explanation for their decision, whatever it was; that there would be no negative consequences for their future care; and that their decision would be respected. If the interviewee needed emotional support, standard hospital procedures and regulations for dealing with distress would be followed.

All the study participants were able to communicate in a generally calm manner, and were positive in their responses to the researcher. None of the interviews ended in tears or emotional distress. Data was stored on the University of Leeds M drive, which is secured and backed-up in password protected files. Data sets are made

anonymous by the removal of identifiers, with each participant being given a number, and any further data that might give clues to the participant's identity being either excluded in the analysis or altered through anonymisation. All the data presented in this thesis was gathered from participants.

6.6 The researcher's role and status

I am a Saudi female, born and raised in Riyadh, Saudi Arabia. As a public health specialist, I am extremely enthusiastic about developing interventions to improve early presentation for investigations and diagnoses for female breast cancer. I was brought up with supportive parents, who have always helped their children take care of themselves and find ways to improve their lives. Many members of my family work as health specialists, and we have always supported one another in our work, sometimes discussing issues in health such as revisions of health guidelines and policies, various continuing education courses, health campaigns, and advances in breast cancer care, detection and treatment. Personally, I have used both public and private healthcare in Riyadh, and am thus aware of many of their strengths and weaknesses.

Before starting this thesis, I received training at the KFSH&RC in women's health in general, and in breast cancer in particular (2004). I observed breast cancer clinics that provided in- and out-patient cancer care, including chemotherapy, radiation therapy, physiotherapy and palliative care. As a health educator, I have also been actively engaged in designing educational materials and participating in breast cancer awareness campaigns. I have also met numerous breast cancer patients in this role, and been able to discuss their experiences in discovering the disease. In the research for this thesis, I was thus able to understand participants' initial feelings when doctors told them about their diagnosis, and I was aware of the need to be careful when speaking with them to avoid making them upset. In addition, I tried to improve my interviewing skills by practising with my supervisors, and by discussing and actively engaging in qualitative data analysis using NVivo software (QSR International Pty Ltd, 2010) before commencing the data collection phase.

Being an 'insider' researcher who is a member of the research population, community, or study group can be valuable (Kanuha, 2000). For this study, I shared the participants' culture, which helped in the data collection phase as I was well situated to gain acceptance and bond with the participants (Dwyer and Buckle,

2009). One risk with being an insider researcher is the potential for the researcher's insider status to jeopardise the validity or trustworthiness of the study (Kanuha, 2000). However, as a researcher who studies in the UK and has read the literature on the topic, I have an aspect of the outsider's perspective as well.

Dwyer and Buckle (2009) suggest that instead of considering the researcher's nature in terms of binary opposites (as either an insider or outsider), there is also a space between the two perspectives that can be held, which allows the researcher to be both an insider and outsider at the same time. The most important aspect of the researcher's position is that she be open, honest and able to correctly represent participants' experiences (Dwyer and Buckle, 2009), and I made several attempts in this study to limit researcher bias and the lack of participant trust that may have been held towards me because of my position. During the data collection, I tried to encourage familiarity, and dressed in traditional female Saudi clothing¹⁸ in order to avoid any misunderstandings about my role, as well as to make it clear that I was not part of the medical team. This way, participants could better understand my role as a researcher, and also understand that talking with me would not affect their healthcare provision. Being able to speak with participants in a similar language and similar dialects was very helpful, and some women spoke about their experiences using words and phrases that I am familiar with.

After conducting an interview, I would then reflect on what had transpired during it, and kept a record of these reflections on the analysis process, which were helpful in separating my feelings and personal experiences from those of the participants (Kanuha, 2000). Thus, bias during data analysis, writing up, and interpretation was reduced. As far as possible, I tried to make sense of what the women had said during the interviews, looking through the lenses of the participants rather than my own. In addition, my supervisors—who had outsider perspectives—provided comments and feedback during the data analysis and writing up, so bias from being insider researcher should be minimal (Hewitt-Taylor, 2002).

¹⁸ During data collection, I wore a black abaya.

6.7 Summary

This chapter described the methods used in the qualitative study, the third phase in this PhD. Overall description of the study, its aim, objectives and design is provided. Furthermore, details about the process of data collection were given together with the analysis methods. Ethical issues and the role of the researcher were explained. The following chapter presents the results of this study.

Chapter 7: Seeking medical care and breast cancer investigations: women's narratives

7.1 Introduction

The previous chapter explained the methods that were used for conducting the qualitative study. This chapter presents the findings on what happens after women discover breast cancer symptoms, seek medical attention and receive their diagnosis.

The qualitative data analysis revealed five important areas concerned with breast cancer in women in Saudi Arabia: the discovery of breast cancer symptoms; knowledge, barriers and misconceptions; seeking others' advice; healthcare and help-seeking; and diagnosis and discussion on late help-seeking or late presentation.

Quotations and narratives from the participants' interviews appear throughout this chapter. In addition, late presentation is defined in relation to the study context, and a model for explaining it is proposed. Finally, the results of the study are summarised, together with its overall role in this thesis.

7.2 A description of the participants

Nineteen women agreed to be interviewed for the study, and the interviews lasted from twenty-one to sixty minutes. The participants were divided into two groups based on the stage of their breast cancer at diagnosis. Seven participants were diagnosed at early stages¹⁹ and twelve at late stages. Ten of the nineteen came from within the Riyadh region, and the participants' ages ranged from twenty-seven to sixty-one years. The analysis classified the participants in this study as either younger (below fifty years, n=10) or older (fifty or above, n=9). Some of these women were younger than forty years of age (n=6), forty years is officially recommended that women begin mammography screening in Saudi Arabia (see Chapter 2).

All participants were married, except from two, who were divorced, and participants had a number of children ranging from zero to ten. The majority of participants

¹⁹ For clinical tumours, early stages comprise stages I and II and late stages comprise stages III and IV.

(n=13) were housewives, with four in employment²⁰ and two retired. Eleven participants had a university education or diploma, whilst six had received some formal education, and two had no formal education. Fourteen participants had no family history of breast cancer, but seven of these had a family history of other types of cancer.

The length of time from self-discovery of symptoms to first medical facility sought ranged from zero days to more than a year. Nine of the participants took less than three months to seek medical care. The nineteen participants were purposively selected so that there were variations in stage at diagnosis, age, and place of residence in order to provide a diverse range of characteristics and views that would allow the research questions of this thesis to be answered.

²⁰ The term “employment” denotes full-time employment, since formal part-time employment is rare in Saudi Arabia.

Table 30: Description of the study participants

Characteristics	Early stages	Late stages	Total
Total number	7	12	19
Age			
Range	27-58 years	31-61 years	27-61
Younger than 50 years	3	7	10
50 years or older	4	5	9
Marital status			
Married	7	10	17
Unmarried	0	Two were divorced	2
Education level			
Did not receive formal education	0	2	2
Primary	1	2	3
Elementary	1	1	2
Secondary	0	1	1
Diploma	One	Two	3
University	Four	Four	8
Number of children	0-10	1-7	0-10
Place of residence			
Living in Riyadh region	5	5	10
Living outside Riyadh region	2	7	9
Employment			
Employee	3	1	7
House wife	3	10	13
Retired	1	1	2
Family history of:			

Characteristics	Early stages	Late stages	Total
Breast cancer	1	4	5
Other cancers	5	2	7
Estimated Time to presentation			
Less than three months	4	5	9
More than three months	3	7	10

7.3 Breast cancer symptoms, awareness and medical care-seeking

This section discusses the participants' decisions to seek medical investigations. Almost all of the women in this study identified a lump in their breast before being diagnosed with breast cancer, and of the three who did not find a lump; one was diagnosed without symptoms following mammography screening, whilst two detected changes in their breast size and colour.

Whereas those diagnosed early showed few symptoms other than a lump in the breast, those diagnosed at a late stage frequently had other breast cancer symptoms, such as an increase in breast size, an inverted nipple, skin thickness and redness, or an underarm lump. In addition, older participants often had comorbidities (such as gallstones or rheumatoid arthritis) that could mask breast cancer symptoms, and would seem more bothersome than a painless breast lump. Most of the women this older group were only diagnosed with breast cancer after they sought help for their comorbidities. For example, one older woman detected an increase in breast size, but because she experienced no accompanying pain and did not detect a lump, she thought that there was no point in going to the doctor with this issue. Her breast cancer was only diagnosed during a surgical consultation for gallstones when the surgeon saw a bluish, reddish discoloration near the nipple, and immediately referred her to a breast cancer specialist (Participant 17, late stage).

Younger women who were diagnosed with a late stage cancer often associated changes in their breast with reproductive health issues, such as miscarriage, breastfeeding or pregnancy. For example, a younger woman who had given birth

nine months before discovering a breast lump talked about her thoughts when she discovered the lump as follows:

I thought that it [the lump] might disappear. Sometimes the breast hardens because of menstruation. Two days before menstruation a woman feels that her breast is hard and sometimes painful. So I thought that maybe the pain was related to breastfeeding. I breastfed my child for a month from the right breast, and she did not breastfeed from the left breast. It [the left breast] was slightly larger than the other one and she did not latch onto it at all. So I thought that maybe it [the increased size of the left breast] was milk collection. It did not occur to me that it could be a disease.

(Participant 15, late stage)

The younger participants, who tended to be diagnosed with earlier stages of breast cancer, were more likely to seek medical help soon after detecting changes in their breast than the older cohort. However, although they understood that the changes might be abnormal, they did not necessarily relate them to breast cancer. For example, one younger woman detected a lump in her breast and asked those close to her for their opinions before eventually seeking medical help, but none of those she asked mentioned breast cancer (Participant 15, late stage).

The women were also frequently unaware of possible breast cancer symptoms other than a breast lump. For example, they failed to link an underarm lump or changes in breast size with breast cancer, with one participant explaining that she had seen a TV programme about breast cancer, but that she did not get worried about the lump in her underarm because she did not remember any mention of that symptom in the programme:

I did not know that the underarm had any association with it [breast cancer]. I mean, I saw on TV, when they talked about breast cancer, about breast lumps, and so on. Perhaps they talked about it [underarm lumps], but I missed it.

(Participant 2, late stage)

Those who seemed to be more aware about breast cancer, and who interpreted their symptoms as potentially serious, had a variety of reasons for seeking prompt diagnosis. For example, nearly three years before her diagnosis, one participant's sister told her about breast cancer symptoms and breast self-examination. Her sister—an educational supervisor—had attended a course on breast cancer and, after finishing the course, she had taught her family members about breast cancer and how

to perform breast self-examination, sharing written materials about breast cancer that illustrated signs and symptoms with them. When the participant herself detected an olive-size lump while taking a shower, she immediately linked this symptom to breast cancer. Because she suspected breast cancer, she promptly sought medical care (Participant 5, early stage).

Another participant attributed the lump in her breast to a physical injury. She later recognised the importance of seeking medical advice when her colleague found a lump during her postpartum period and was diagnosed with breast cancer. She believed that her colleague's experience prompted her to seek medical investigations to check whether or not the lump she had found was malignant (Participant 1, early stage). She was not the only participant who was alerted about the possibility of her own breast cancer through somebody else's experiences. One younger woman did not feel a lump in her breast, but rather noticed vein and chest tightness after her miscarriage. She thought it might be a benign tumour, because her sister's friend had similar symptoms and received that diagnosis. She decided to seek medical care immediately, to confirm that her symptoms were not dangerous (Participant 9, early stage).

In addition, periodic mammograms sometimes revealed breast cancer. An older participant who had undergone a hysterectomy and periodic mammography screening talked about her experience of receiving a coincidental diagnosis of breast cancer.

Every year I do a mammogram. Nine months before I discovered the disease, I had a mammogram and all the cells were normal. I went to a female doctor because I had a little inflammation; I had had a hysterectomy because I had ... and a benign tumour that they sampled and found was not malignant. But I had itching ... and I went to the female doctor.

(Participant 4, early stage)

The participant and the doctor spoke after the clinical examination, and the following is an account of this conversation, as recalled by the participant:

Participant: Could you do a breast examination [mammogram]?

Doctor: You did it nine months ago.

Participant: Yes.

Doctor: You don't need it. Wait for a year.

Participant: Since you did the clinical examination, let's do one too [a mammogram].

(Participant 4, early stage)

This participant knew about breast cancer from her relatives, brochures, TV, the general media and books. She later explained that insurance is an important consideration in seeking medical care:

This factor [medical insurance] helps a woman to go [to get healthcare] with confidence that she will get a quick appointment. She will be comfortable about the care because people [health workers] are providing a lot of care.

(Participant 4, early stage)

Perhaps this participant was aware of breast cancer for other reasons, and not only because she received a free mammogram. Rather, she may have learned more about breast cancer because her comorbidity increased her risk of the disease.

Several participants sought medical care promptly because they believed that the lump in their breast was abnormal. For example, one younger participant sought medical care because she found a lump, though she knew little about breast cancer.

I noticed a lump in my breast when I took a shower one day. I felt that this was something strange. First I asked my sisters, my family, like that [sic], but they did not think it important. Then, I tried to read and went to the nearest health centre.

(Participant 15, late stage)

Other younger women also sought medical advice after discovering what they perceived to be an abnormal breast lump, although they were not aware that it could be cancer. However, not all of these women were diagnosed at an early stage.

Generally, the women who were diagnosed at early stages were those who were more aware about breast cancer, regardless of age, and thus more likely to associate their symptoms with breast cancer. Many of these women were more aware about breast cancer because of those around them: one had a sister who had attended a course on breast cancer and taught her; two had friends with similar symptoms; and two were aware that they should seek medical attention immediately because their children had been diagnosed with benign or malignant tumours. Those who did not interpret their symptoms as serious, or did not realise that the symptoms could indicate breast cancer, were less likely to seek medical care promptly because of their misconceptions about breast cancer or because they did not disclose their concerns to and discuss them with significant others.

7.4 Barriers, misconceptions and medical care-seeking

Besides a lack of awareness about breast cancer, women might have encountered barriers or held misconceptions that could interfere with comprehending the risk of breast cancer or seeking prompt medical investigations.

Because a strict gender binary is the social norm in Saudi Arabia, it would be reasonable to expect that transportation issues, distance to the healthcare facility, marital status, and the gender of the healthcare provider represent important barriers to seeking timely help. Surprisingly, this study found that most women, whether diagnosed in early or late stages of breast cancer, said they encountered no such barriers while seeking medical care. Interestingly, none of the participants reported problems with transportation, with an older participant noting that there were several ways to reach the healthcare facility: going with a personal driver, with their husband, or with their children, for example (Participant 1, early stage).

The analysis detected no notable differences in healthcare-seeking behaviours between the participants based on where they lived. Additionally, none of the participating women reported being deterred from seeking medical care based on their healthcare provider's gender, or because they could not obtain permission from a legal guardian (usually a husband or close male relative). On the contrary, most women talked about being encouraged by male relatives, including their husbands and sons, to get appropriate medical advice and investigations, and reported received support from them throughout their treatment (n=16).

7.4.1 Commonly encountered barriers and misconceptions

This study did, however, find several misconceptions that delayed the participants in seeking medical attention. Many participants tended to seek help only after they started to experience pain in relation to their breast cancer symptoms, believing that if there was no pain, the condition was not serious. This was particularly common among older participants, who were frequently the ones diagnosed at late stages. For example, one older participant was diagnosed at a late stage of breast cancer only after she could no longer tolerate the pain and sought emergency medical treatment (Participant 7, late stage). Another older participant sought medical care in order to get a painkiller for the pain in her breast.

It looks like a ball [the lump], then I thought I will go [to healthcare facility] maybe they will give me something, an antibiotic. A day later I went to the Primary Health Care.

(Participant 19, late stage)

Another misconception of participants—mostly held by younger women this time—was that they would not get cancer if they had breastfed their children. Consequently, even when they noticed a symptom like a breast lump, they thought that it could not be breast cancer. One example of this was Participant 14 (late stage), who did not stop breastfeeding until she had been diagnosed. Healthcare workers may foster this belief, as this participant explained that her healthcare worker initially believed that her lump was associated with her recent breastfeeding practice. This misconception was encountered in male relatives as well. One young woman diagnosed at a late stage reported that both she and her husband thought that breastfeeding would prevent breast cancer (Participant 18, late stage). Two participants held the mistaken belief that fever is a symptom of breast cancer. One, a younger participant, mentioned that she had not experienced any fever, and therefore believed that she did not have breast cancer (Participant 16, early stage).

These were not the only misconceptions about breast cancer that might have interfered with seeking medical care quickly. The study found that some women misunderstood the risk of breast cancer, with one participant believing that if a woman had not had Hormone Replacement Therapy (HRT) she could not get breast cancer. This participant had a sister that had used HRT and later been diagnosed with breast cancer, and thought that the HRT had caused the breast cancer:

I thought about one thing. I did not continue with gynaecology after menopause. I was supposed to have replacement for that hormone—oestrogen. I did not have follow-up appointments at all after my menstrual period stopped. This is what I thought I neglected.

After menopause, my sister was prescribed patches to stick on her thigh to replace hormones—oestrogen [the sister was later diagnosed with breast cancer]. As a consequence, I was afraid that they [the patches] were the main cause of the tumour. I did not follow up [and visit a gynaecologist until much later after menopause], and look at me now! [The participant also has a diagnosis of breast cancer, despite not using HRT.]

(Participant 7, late stage)

Once women noticed their symptoms, some may have considered the possibility of receiving a cancer diagnosis and been frightened about the potential consequences of the disease's progression, complications and/or death. In some cases, this may have motivated medical care-seeking. For example, an older woman said that her fear of the disease and of losing her health led her to seek medical care (Participant 11, early stage). However, in other cases, fear of the impact of the diagnosis itself and its repercussions may be immobilising. For example, an older participant talked about fearing a breast cancer diagnosis in terms of being concerned about her children, her self-image, and about how she would look after surgery. This likely slowed down her seeking of medical care, and she only in fact decided to raise her concerns with her doctor after seeking care for something else (Participant 13, late stage).

7.5 Symptoms disclosure

Many women, particularly younger ones, disclosed their health concerns to significant others (usually family members) after noticing bodily changes. Some, mostly younger women again, mentioned talking about their symptoms with others who then encouraged them to seek medical care, whilst only a few women, mainly from the older group, did not tell anyone about their symptoms before they were diagnosed. For example, one younger participant that was diagnosed with breast cancer during pregnancy explained that her husband is the person she is closest to. He was worried about her when her symptoms started to worsen, and encouraged her to seek medical help (Participant 12, late stage).

After discovering their breast cancer symptoms, the participants sometimes delayed telling anyone about them. For example, an older participant waited to talk about her symptoms with her son, who immediately encouraged her to seek a medical diagnosis. She mentioned that he had expressed a wish that she had talked about her concerns earlier when she first noticed them (Participant 3, late stage). Advice from significant others is thus a very important factor, which can prompt or delay the seeking of medical help.

Many respondents reported carefully balancing the advice they received and their own opinions about seeking medical help. For example, an older woman disclosed concerns to her daughter about a lump, who promptly encouraged her to seek

medical care. However, possibly as a result of her own misconceptions, she did not follow her daughter's advice:

Yes, I talked to my daughter. She is the person closest to me. She said, "Go. Go" [to healthcare]. But I did not go immediately.

(Participant 7, late stage)

The respondents mostly reported receiving immediate support and encouragement once they had disclosed their symptoms to third parties, regardless of when they disclosed their concerns to significant others.

7.6 Healthcare, help-seeking and diagnosis

The healthcare provision that is available might influence the time it takes for women to seek medical investigations and care for breast cancer. Several participants believed that the attention and care provided by health professionals had an impact on their decisions to seek medical investigations (both in public and private medicine). A younger participant explained that free healthcare and quicker appointment times would have encouraged her to seek healthcare more promptly (Participant 10, late stage), whilst an older participant believed that having private health insurance encourages medical care-seeking because the health facilities covered by private insurance provide more attention and care than public healthcare:

I went [to the hospital] covered by the medical insurance. My sister has a medical file in the hospital and she took time and tried to go there. So this factor [medical insurance] helps a woman to seek medical care and to be confident and not worried. She will get an appointment quickly and feel cared for [by the health workers].

(Participant 4, early stage)

However, not all women can afford to pay for insurance, or are eligible for it. The majority of participants relied on public healthcare, and thus the quality of healthcare on offer could have influenced their decisions about which health facilities to visit. An older participant talked about the long waiting time for an appointment as a barrier to seeking medical care:

What led me to not seek help immediately [from the hospital] is the waiting time. [A] long waiting time, that is why I did not go quickly. I prefer to tolerate [the problem] and not to go unless it's something very severe.

(Participant 7, late stage)

Seeking medical care is only the beginning of the patient's journey in breast cancer investigations, diagnosis and treatment. After the participants sought care, they experienced important differences in their diagnoses and treatments, with health professionals' reactions to concerns varying in relation to the age of the women. For older women, an early diagnosis of breast cancer sometimes resulted from women raising concerns about breast cancer symptoms during medical appointments for something else. One older participant decided to raise concerns about a lump during a follow-up appointment for other health concerns in a hospital, and was diagnosed with breast cancer (Participant 1, early stage). The health professional responded promptly to her concern.

Conversely, whilst younger women tended to seek medical care promptly, some were misdiagnosed by healthcare professionals who believed that their conditions were benign, or ascribed their symptoms to other conditions, such as hormonal changes that occur after giving birth or breastfeeding. One younger woman who sought medical care promptly after she felt a lump was misdiagnosed by her doctor, who explained that her lump was related to her current breastfeeding. This woman reported that the doctor reassured her that she would not get breast cancer because she breastfed her baby. After eight months, the participant went to the same doctor because the lump had increased in size. The doctor was surprised and referred her to a specialist, who then diagnosed her with breast cancer (Participant 14, late stage).

Another younger woman who sought medical care after being alerted to the presence of a lump in her underarm by her husband was told by her doctor that it was not a serious health issue, and that it could not be cancer because it was too small—not even being obvious if she raised her arm. The doctor reassured her that the lump could be related to her sleeping position. Later, the woman discovered another lump in her breast. Uncomfortable with the doctor's diagnosis, she sought another physician's opinion.

I went to the doctor [the second one] in the hospital and when I met the doctor, she said "you will be referred to see what this lump is—if it is normal or abnormal".

(Participant 2, late stage)

7.7 Discussion: Late help-seeking or late diagnosis

In this study, participants were asked to report the time interval between becoming aware of their symptoms and seeking medical investigations for them. The time from self-discovery of symptoms to seeking medical investigations ranged from zero days to more than one year. The length of the period varied between participants diagnosed at early and late stages, being shorter among women diagnosed at early stages (zero days to six months) compared to those diagnosed at late stages (less than one week to more than one year).

The estimate of the length of time that it took patients to seek medical care investigations depended on the presence of breast cancer symptoms at the time the patient interpreted these symptoms as abnormal. Because this study gathered details about when participants noticed symptoms and sought medical investigations through face-to-face interviews, and considered the events during the process of medical care-seeking, this period represented a valid data source (Andersen et al., 2009).

In accordance with other studies, this study defined prompt care-seeking as that occurring within three months of the patient first noticing symptoms (Ramirez et al., 1999). Where there was a shorter period between symptoms recognition and seeking medical attention—i.e. less than three months—this did not necessarily translate to an early stage diagnosis. Nor did a delayed seeking of medical investigations (more than three months) necessarily lead to a late stage diagnosis.

Including participants with both early and late stages of breast cancer, and from different age groups in the investigation of treatment-seeking and diagnosis provided new insights into how to define late presentation. For example, there were two older women that took nearly six months before they sought medical attention, but were diagnosed at an early stage of breast cancer. In contrast, there were two younger women who sought medical help less than three months after noticing symptoms, but were diagnosed at an advanced stage of breast cancer. One of these was pregnant, and the other one had a benign breast tumour at first.

Surprisingly, one of the women from the older cohort was diagnosed with breast cancer even though she had frequent mammography screening. The length between her negative mammogram and her positive one was nine months (Participant 4, early

stage), which is less than the recommended period for performing periodic mammography screening.

Thus, there is not a straightforward relationship between the length of time after recognising symptoms to seeking medical investigations and the expected outcome (stage at diagnosis). Within the study context, tumour aggressiveness could be one mediator of this relationship, however. The role of tumour aggressiveness (or grade) was not examined in this study, but the breast cancer literature in Saudi Arabia indicates that Saudi women have a greater tendency to develop late stage tumours than Swiss women (Al-Kuraya et al., 2005). Tumour aggressiveness might explain the reason that late stage diagnoses were made after only a short period had elapsed between noticing symptoms and seeking medical investigations in this study. The criteria of 'length of time to seek medical investigations' might thus need revising for assessing late presentation in relation to Saudi women with breast cancer.

Younger women tended to seek medical investigations for breast cancer more quickly than older women in Saudi Arabia. Nevertheless, some younger women were diagnosed at a late stage. Being diagnosed at a late stage after immediately seeking medical investigations upon discovering breast cancer symptoms is something that a patient could have done nothing practicable to prevent. Such cases of rapid disease progression may be related to (i) the healthcare system—the patient was misdiagnosed at an earlier appointment; or (ii) biological factors —Saudi nationality is a risk factor for developing aggressive breast cancer (Al-Kuraya et al., 2005). When late stage diagnoses are made in younger women who have sought medical investigations quickly, they are thus more likely to be related to healthcare or biological factors.

The analysis of the older cohort of women shows that their behaviour in seeking medical care is a more dominant factor in determining the disease stage than the healthcare system itself is. For older women, late presentation or late stage diagnoses are more likely to arise from patient-related factors. This may, in part, be attributed to the fact that the older women tended to be less aware about breast cancer and held more misconceptions, such as those bodily changes are not serious if they are not painful, and thus there is no reason to seek medical investigations for them. In addition, this cohort often had comorbidities that might have led them to prioritise when to seek medical care. The period of time it took them to seek medical care was

frequently shortened by speaking to (significant) others about their symptoms, and their decisions might also be affected by their previous knowledge or experiences of others with breast cancer. Moreover, healthcare professionals reacted more positively to older women's concerns about breast cancer symptoms, and were more likely to promptly refer them to specialists or suspect the possibility of breast cancer than they were with the younger cohort.

There is thus a need to rethink the assessment of late presentation for female breast cancer in the context of Saudi Arabia, and to be more open to the role of socio-cultural factors and healthcare on the stage at diagnosis. It appears that women who take longer to seek medical care do not intend to delay, and therefore that it is unfair to either blame them or label them *as* 'late presenters'. In addition, some women who promptly seek medical care are diagnosed at late stages, thus we should also be aware of the role that healthcare may play in the phenomenon of late diagnosis.

As there is no precise way to quantify patient delay (Andersen et al., 2009), and due to the contextual and biological factors that influence breast cancer in Saudi Arabia, using 'stage at diagnosis' does however remain a valid indicator of late presentation, regardless of how long the patient has taken to seek medical investigations.

7.8 The study model

This study data shows that numerous factors influenced women's medical care-seeking behaviours. A central factor in this study is age, as Figure 14 shows. Generally, both younger and older women displayed poor knowledge about breast cancer, with some having no knowledge about it before their diagnoses were made. The knowledge they did have about breast cancer was often incomplete, and did not necessarily come from official healthcare or educational resources, or from public health campaigns. The lack of prior knowledge about breast cancer is more apparent among older women, who were often only diagnosed with cancer because they had presented for the treatment of other health problems, or because it was detected during opportunistic screening. In this context, it is understandable that women might not realise their symptoms indicate breast cancer. This incorrect interpretation of symptoms may increase for patients who have numerous misconceptions about the disease. For older patients, the misconception that any symptoms need to be painful before medical care-seeking is indicated was prominent. For the younger

participants, a lack of awareness about breast cancer did not stop them from seeking medical investigations, but it may have affected the speed at which they sought investigation. For example, they might link their symptoms to other potential problems, such as a benign breast tumour.

For some women, a fear of cancer negatively impacted upon their timely care-seeking, although this was not common in this study. Many women in the study, particularly those in the younger cohort, tended to speak about their symptoms to family members. Some of them sought opinions from women who had experience of benign or malignant breast tumours, and reported that these third parties had helped them to think about their symptoms and decide what actions to take. Most of them sought out medical investigations promptly, even though some of them had not suspected the possibility of breast cancer. Some older women, however, did not disclose their concerns immediately to others, or at all. As a result, they did not receive any encouragement to seek medical care. Nonetheless, it is possible that even if they were encouraged to seek timely medical diagnoses, they might not do so because of the misconceptions they held.

Once women came into contact with healthcare facilities, the health professionals' reactions often varied in relation to their age. Health professionals reacted positively in undertaking breast cancer investigations for older women, even when the patients did not identify breast cancer symptoms. In contrast, health professionals' reactions to younger women were not always positive, with some younger women being misdiagnosed due to the presence of other reproductive health issues that could have interfered with clinical breast examinations, and diagnostic tests such as mammogram not being used. Such misdiagnoses, together with the biological features of breast cancer among the study participants (Al-Kuraya et al., 2005), might have had negative consequences on the stage of breast cancer seen at the point of diagnosis.

Women's education is not recorded by the SNCR; therefore its main effect on late-stage at diagnosis was not examined in the quantitative analysis or used to purposively recruit participants in this study. In the literature review, it was seen that education had been found to influence late presentation, with women who promptly seek medical care tending to be better educated and more aware of breast cancer (see Chapter 4). There may be a link between being better educated and more informed

about breast cancer (and therefore more aware about its symptoms and the need to detect it at early stages). However, the qualitative analysis indicated that education is a confounding factor to age. Most women knew that the presence of a lump could indicate breast cancer, but were not aware about other breast cancer symptoms, such as underarm lumps, changes in breast colour, and inverted nipples. The women's narratives indicated that none of them had an advanced knowledge about breast cancer. Mostly, they sought medical care as a result of opportunistic factors, such as having a son diagnosed with cancer or a relative who knew about breast cancer. Younger women tended to be better educated than older ones, with main difference between them being the added misconception prevalent among the older cohort that if a symptom does not *hurt* it is not *serious* and so there is no need to visit a doctor. The figure 14 below shows the different ways in which age can impact on investigations and diagnoses for breast cancer.

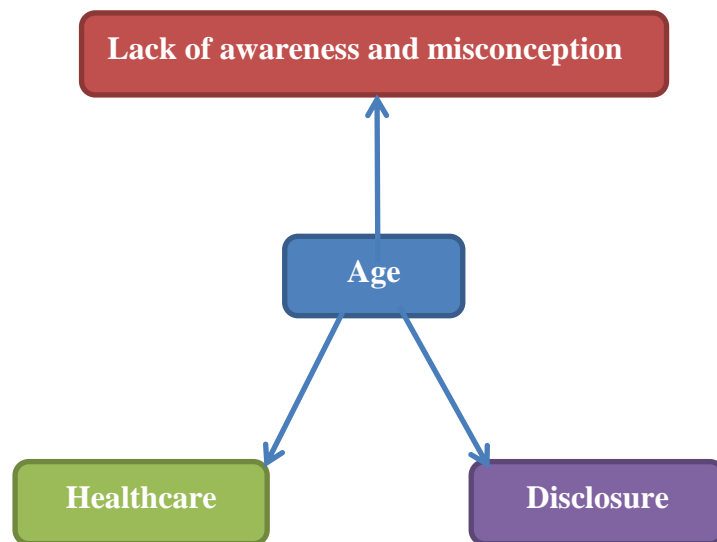


Figure 14: Factors influencing late-presentation breast cancer

7.9 Discussion of the study findings

Various models for understanding the late presentation of breast cancer have been proposed and adopted (see Chapter 3), the most recent being the Model of Pathways to Treatment (Walter et al. 2012) – a refinement of the Andersen Model of Total Patient Delay (Andersen et al., 1995) providing a theoretical approach for studying cancer diagnosis and treatment.

The Model of Pathways to Treatment (Walter et al., 2012) describes four main *time intervals* involved in seeking medical diagnosis and treatment in terms of beginning and end points. These comprise: the appraisal interval – the time between detection

of symptoms to perceiving the need for medical consultation; the help-seeking interval – the time between the patient perceiving the need for a medical consultation to his first contact with healthcare providers; the diagnosis interval – the time between the patient's first medical consultation and their receiving a diagnosis; and the pre-treatment interval – the period between the patient receiving their diagnosis and treatment commencing. This model also recognises the processes within each interval and the how the lengths of these intervals could be affected by the patients, the healthcare system or the disease itself (Walter et al., 2012).

In this study, the time taken to present was measured from the self-recognition of symptoms to first medical contact, thus considering the 'appraisal interval' and the 'help-seeking interval' (Walter et al., 2012) as a single interval.

The process of presentation for healthcare was understood to involve the recognition of symptoms as abnormal (but not necessarily related to breast cancer), the monitoring and self-management of these symptoms, talking to others, and seeking medical care. It is important to note this process did not progress in a linear or identical manner among all of the participants. The factors that influenced the participants' pathways to presenting for healthcare investigations can be split into the categories below.

(i) Patient-related factors: As shown in the study model (Figure 14), age is an important factor associated with presentation. A lack of breast cancer awareness together with misconceptions about it interfered with patients' recognitions of the seriousness of their symptoms and the possibility that they could be related to breast cancer. Talking to third parties and receiving family support might speed up the process of presenting for healthcare investigations. These factors are also identified in the literature (McEwan et al., 2014, Rastad et al., 2012, Smith et al., 2005). Married and unmarried women talked about receiving family support – including from husbands, sisters, brothers and children. Perhaps this could explain why married and unmarried women were equally likely to be at risk of having advanced stage tumours at the time of diagnosis, as the quantitative analysis showed.

(ii) Disease-related factors: It is possible that time to presentation and stage at diagnosis are influenced by tumour characteristics as there is a chance that Saudi women might experience highly aggressive tumours (Al-Kuraya et al., 2005). The biology of tumours is not a factor that is commonly addressed in qualitative research.

Future research could further investigate whether a longer presentation time – more than three months – is associated with more advanced stages of cancer at diagnosis, and if this varies according to age groups among Saudi women.

(iii) Healthcare-related factors: while women talked about issues related to quality of care, the findings revealed additional factors related to healthcare professionals themselves, not just the time taken to present to healthcare. These were linked to the ‘diagnostic interval’ – the time from first medical consultation to diagnosis (Walter et al., 2012). The results indicated that that age of women might impact on timely diagnosis, with younger women being more likely to be misdiagnosed while older women receive timely diagnoses. That is, being younger is positively associated with healthcare provider delay (Ramirez et al., 1999). Studies in the Middle East indicated that the misdiagnosis of breast cancer occurred in the Middle East, but the patient’s age was not specified in these studies (McEwan et al., 2014, Rastad et al., 2012).

The three main factors that contributed to late-presentation for breast cancer in this study – patients, the healthcare system and disease-related aspects – concur with those proposed by the Model of Pathway to Treatment.

7.10 Strengths and limitations of the study

Qualitative research is often considered to not be generalisable or context specific (Firestone, 1993). By using mixed methods, this research has attempted to ameliorate this limitation. Participants were recruited purposively—that is, they were recruited on the basis of possessing characteristics that might be associated with the stage of breast cancer at the time of diagnosis, and these characteristics were located through the quantitative study (phase II) of this research. Data was thus gathered from women with a variety of characteristics in order to enrich the analysis.

During the data collection phase, the researcher talked to women—both formal and informal participants—about their experiences with breast cancer. These discussions revealed that patients that had been diagnosed a long time before the discussion might not remember the chain of events that led them to seek treatment in detail, especially when they were older patients. In addition, such patients were likely to prefer talking about the problems they were currently facing rather than their breast cancer diagnoses. Because of this, recently diagnosed participants (within six months of diagnosis) alone were recruited. Another limitation of the study is that not all the

interviews were audio recorded, which resulted in an inconsistent presentation of the data.

The study participants were recruited from only one major hospital. It is thus possible that the sampling reflects the referral patterns of the hospital rather than the Saudi Arabian healthcare system in general. However, because the sample was based on quantitative findings, it is more likely than not that it is representative.

It is important to note that the women who were interviewed in this research were those who reached the hospital. This means that the data provides no insights into women who do not manage to receive treatment or the issues that this cohort faces.

7.11 Linking the qualitative results with the quantitative data

This study reveals the factors that influence women's late presentation for investigations into breast cancer in Saudi Arabia. It has found that there is an interaction between women's age and their timely seeking of medical care. Specifically, late presentation in older women is more likely to be related to patient factors (such as breast cancer awareness and misconceptions, disclosure of symptoms to family or peers, and the presence of comorbidities) than to issues within the healthcare system (such as medical practitioner error), which is more common feature of late presentation in younger patients.

The quantitative findings presented in Chapter 5 showed that age was significantly associated with late stages of cancer at diagnosis, but did not provide clear-cut information about the interactions between the variables and the stage at diagnosis. This inspired me to reanalyse the quantitative data in order to better understand how age interacts with other factors and affects the stage at diagnosis. The next chapter presents this analysis.

7.12 Summary

Women with poor knowledge about breast cancer, or who did not consider their symptoms to be serious or to indicate breast cancer, tended to take longer to seek medical care.

Women frequently depended on non-medical sources for information about breast cancer, including significant others or people who had undergone breast disease

investigations. Thus, since the incidence of breast cancer in Saudi Arabia is low, awareness about breast cancer is likely to be very low.

As a consequence of this lack of awareness, women with breast cancer might not seek medical care promptly, and thus increasing awareness about symptoms, early detection and screening may encourage women to seek medical care more promptly, as one older participant suggested (Participant 6, early stage). In addition, women might have misconceptions or fears that might prevent them from seeking medical care. Although the increase in breast cancer campaigns may have made women more aware about breast cancer, it is clear that there are still numerous misunderstandings and misconception, relating to risks and protective factors in particular.

The participants in this study often relied on their families for advice and support about whether to seek medical care. Those who disclosed their concerns and received proper advice were more likely to follow that advice and seek medical care immediately. This pattern was seen frequently amongst the older participants, whereas younger participants tended to seek medical care more promptly, but were more likely to have their breast cancers missed or misdiagnosed at their early stages by healthcare professionals.

Chapter 8 Phase IV: Integration of findings and discussion

8.1 Introduction

This thesis applied a mixed methods design including quantitative phase of data collection and analysis followed by a qualitative phase of data collection and analysis (See Chapter 3).

The first phase was a literature review of published research on causes of late presentation of breast cancer in the Middle East (see Chapter 4). This phase revealed the need for further study. It also helped determine which methods could be employed to explore the issues which it disclosed, primarily lack of evidence regarding late presentation of female breast cancer in Saudi Arabia and the Middle East. Consequently, the quantitative work first explored the general pattern of late presentation and the factors associated with it at the macro level. This stage of the research informed the qualitative phase, especially its framing sample which enabled the qualitative work to focus on issues of age and knowledge of breast cancer, and be less concerned about factors such as marital status.

The sequence of data collection and analysis to investigate the study problems revealed factors associated with late stages disease at diagnosis of breast cancer. Following a complete analysis of the quantitative data, qualitative data more deeply elaborated these reasons for late presentation of breast cancer, refining and explaining the quantitative results especially around age.

This chapter interprets these thesis results. Following a complete analysis of the quantitative and qualitative data separately, the investigation then restructured the data to provide a clearer picture using meta-inferences. A 'Meta-inference' refers to an interpretation drawn from both quantitative and qualitative data (Teddlie and Tashakkori, 2009).

This chapter starts with a fuller description of meta-inferences and how they have been applied. Then, it describes the data integration (section 8.3) and findings integration (discussion, section 8.4).

8.2 Meta-inference

The process of meta-interference began with a question: how can the quantitative results and qualitative results be linked to achieve the thesis aim?

Meta-inferences explore whether the addition of qualitative data provides a better understanding of the study problem than do quantitative data alone (Creswell and Plano Clark, 2011). The process of meta-inference included two steps. The first step was data integration, in which each study's results informed the other studies, as described in Chapter 3.

The second step was findings integration, combining the results of both the quantitative and qualitative analyses in the discussion section (Creswell and Plano Clark, 2011) to illustrate reasons for late presentation of female breast cancer. Findings integration has been implemented when explanatory sequential mixed methods have been used (Ivankova et al., 2006). It allows factors associated with late presentation of female breast cancer to be identified. It also helps provide further insight into how these factors might interact. Narrative interviews clarified the statistical findings. In addition, published findings, both quantitative and qualitative, on late presentation of female breast cancer in the Middle East enriched the understanding of the thesis results and the mixed methods meta-inference (see Figure 15). The following sections describe each step in the meta-inference process.

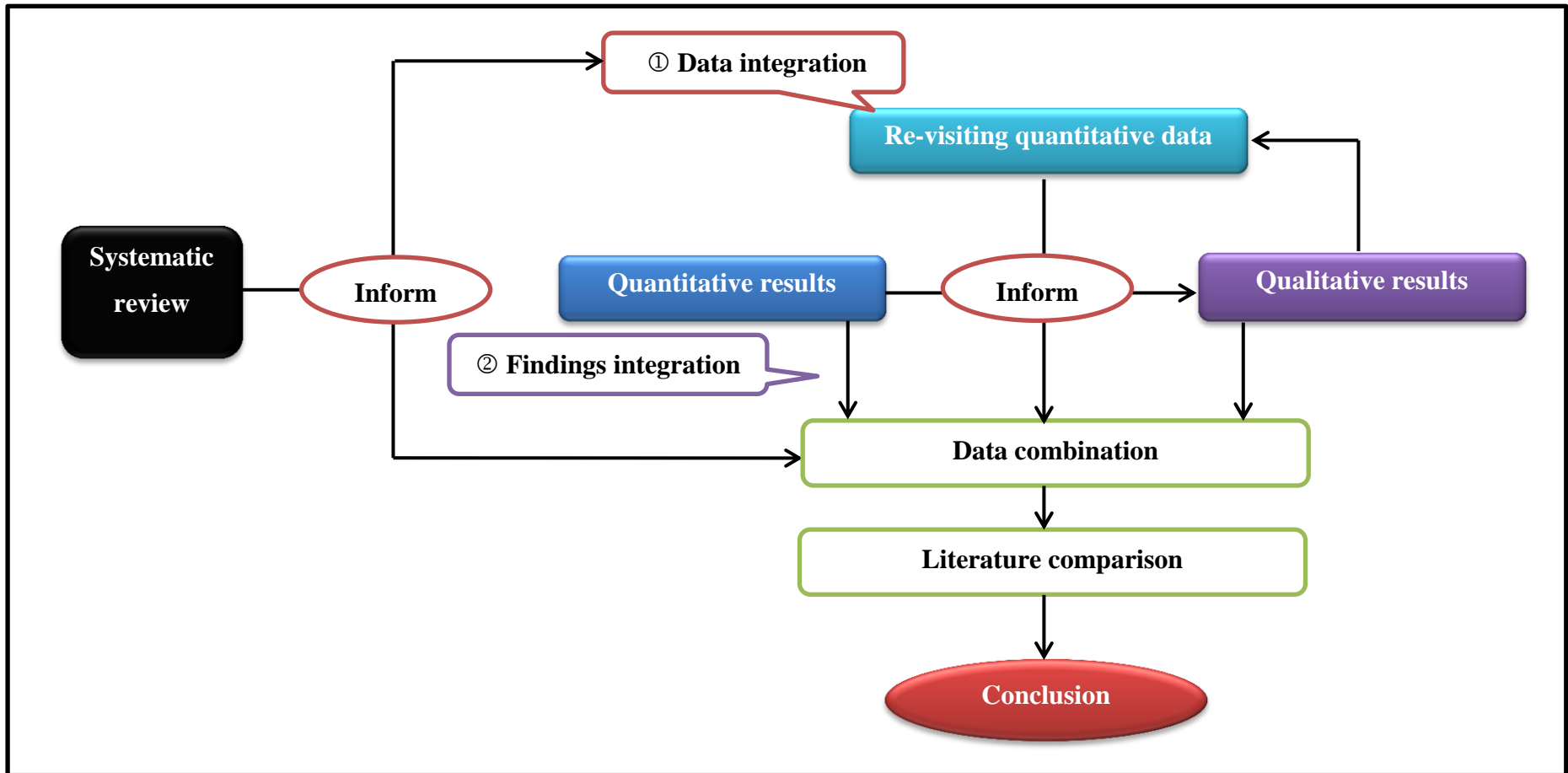


Figure 15: Process of meta-inference

8.3 Step 1: Data integration

This thesis comprises three main studies: a systematic review, a quantitative study and a qualitative study. The systematic review informed the thesis methods (see the study design section 3.4.1 in Chapter 3). The quantitative study then informed the qualitative data sampling (see Chapter 6). Findings from the qualitative data indicate potential differences in causes of late presentation for younger and older female breast cancer patients (Chapter 7). The findings benefited from the increased understanding offered by the qualitative study and the opportunity it gave to revisit the quantitative data to explore how various factors, particularly age, interact with each other by using a classification decision tree (as illustrated in Figure 15).

8.3.1 Rationale for using a classification decision tree analysis

In multivariable analysis, several variables are used to predict or explain a single variable as the outcome. A classification decision tree is a type of multivariable analysis, much like other statistical methods such as regression analysis (West, 2012). The distinctive feature of the classification decision trees is that it acknowledges interactions between factors that other methods often ignored to reduce complexity (Camp and Slattery, 2002). The qualitative results suggest that factors associated with late presentation is different. The hierarchical nature of classification trees allows further understanding of the interaction between variables (West, 2012). This structure helped in identifying subgroups with observed higher and lower risk of advanced stages at diagnosis within the total cohort (n=10,663). Additionally, the classification decision trees are flexible and can be used for continuous variables, categorical variables or a mixture of both of them (West, 2012).

Decision tree analysis creates sequential divisions of the cohort into subgroups based on the value of the independent variable for each division. The split (or division) is based on the purity of the subgroups, with the variable that produces the most pure subgroups chosen for the split. The splits end when a subgroup of the cohort becomes completely pure or when further splitting would result in branches containing less than a defined minimum number (West, 2012).

Since the qualitative data suggested that interaction between covariates might be important, especially interactions with age, this suggest to re-think about the

quantitative data and running a decision tree analysis to better understand the interactions of variables (Breiman et al., 1984) associated with the disease stage at breast cancer diagnosis. Breiman et al. (1984) explain that classification analysis is often used with the intention to provide accurate understanding and improved prediction. A good decision tree provides insight into the predictive structure. The size of the quantitative study is large (n=10,663) although to run a classification analysis with a large sample size is not as important as whether the association between the variables tested is different (Breiman et al., 1984). The complexity of late presentation of breast cancer suggests that greater richness may well be achieved from a classification analysis.

The outcome variable was stage of cancer at diagnosis, which is a categorical variable, based on disease progression: in-situ, localised, regional or distant (SEER, 2013). The decision tree analysis treated this as an ordinal variable. Table 31 describes the independent variables and how they were handled in the analysis. All variables were treated as they were in the previous quantitative analysis (see Chapter 5), except for age, which was used as a continuous variable to provide flexibility in the analysis: the classification will select more optimal cut points. Missing categories were treated as missing values. Decision trees often use the following technique: if a variable is missing for a split then the split is made using a surrogate (or proxy) variable.

Table 31: Description of independent variables

Independent variable	Measure
Age	Continuous
Nationality	Nominal (Saudi nationals and non-Saudi)
Years of diagnosis	Nominal (1994–1996, 1997–1999, 2000–2002 and 2003–2006)
Place of residence	Nominal (Regions with advanced oncology care and other regions)

8.3.2 Statistical analysis

The classification decision tree analysis used SPSS software version 20 (IBM Corp., Released 2011). The Chi-Squared Automatic Interaction Detector (CHAID) (Kass, 1980), a powerful and popular method to divide data into homogenous groups (StatSoft, 2013), partitioned data into subsets to best describe dependent variable (Kass, 1980). This method of splitting the data chooses the most significant variables rather than the most explanatory. It does not consider the nature of the variable, for example, ordinal or nominal, or the number of categories included (Kass, 1980). CHAID runs in steps to find the best partition for each dependent variable. It then compares the dependent variables and selects the best one, subdividing the data based on dependent variables (Kass, 1980).

Exhaustive CHAID, a modified CHAID algorithm, was selected for analysis (StatSoft, 2013). Other algorithms might not suit the purpose of the study as some work best for continuous outcomes or spilt the data into a binary tree (StatSoft, 2013).

Development of the decision tree included all female breast cancer patients for whom stage at diagnosis was known (n=10,663). Table 32 describes the parameters for tree development. The maximum permitted tree depth was five, which was chosen to facilitate simpler interactions and avoid over-fitting, but the fit was only four deep.

Table 32: Description of parameters used in the Exhaustive CHAID

Parameter	Value
Maximum tree depth	5
Minimum parent node	100
Minimum child node	50
Significance threshold for splitting node	0.05
Results tree depth	4

8.3.3 Results

Figure 16 reproduces the decision tree which had nine nodes besides the root node. Node 0, the root node (outcome variable), shows the number and percentage of women diagnosed with breast cancer in each cancer stage (ordinal variable). The

final row in the root node indicates the size of the entire cohort (n=10,663). The variables that tested for significance were year of diagnosis, nationality, location and age, resulting in data set split into four levels with nodes 1–9.

This decision tree revealed four predictors associated with late stages at breast cancer diagnosis: year of diagnosis (diagnosed before 2000 or in 2000 or later), nationality (Saudi or non-Saudi national) and location (living in regions with access to advanced oncology care, or living in other regions) and age (≤ 42 years, between 42–58 years or above >58 years).

The analysis yielded year of diagnosis as a predictor for the split at the root node ($P < 0.001$, $\chi^2 = 45.295$, $df = 1$). Women diagnosed with breast cancer before 2000 were at higher risk of being diagnosed at advanced stages²¹ (70.1%, n=2,767) and very advanced stages (21.8%, n=860) compared to those diagnosed in 2000 or later (68.5%, n=4,607) and (15.2%, n=1,023) respectively. This finding indicates that good progress has been achieved since 2000 in disease stage at presentation. Node 2 is a terminal node as there is no further splitting under it.

For women diagnosed between 2000 and 2006, analysis yielded their nationality as the second level predictor. Saudi nationals were at greater risk of being diagnosed at late stages (70.4%, n=3,392) and very late stages (16.2%, n=780) than were non-Saudi nationals (63.9%, n=1,215) and (12.8%, n=243) respectively ($P < 0.001$, $\chi^2 = 29.087$, $df = 1$). No further splitting among non-Saudi patients occurred. Thus, one focus of research should be to investigate the reasons for late presentation of breast cancer in the Saudi cohort.

Among Saudi women, location split the tree further. Late stage at diagnosis was less likely in regions with advanced oncology care namely Riyadh, Makkah and Eastern Saudi Arabia, compared to other regions in the Kingdom ($P < 0.001$, $\chi^2 = 21.428$, $df = 1$). In regions with advanced oncology care, the percentages of Saudi nationals diagnosed at late stages (68.6%, n=2,501) and very late stages (15.5%, n=565) were lower than in regions with less access to advanced oncology care: 76.2% (n=891) and 18.4% (n=215) respectively.

Among Saudi women diagnosed since 2000 and living in regions with advanced oncology care, age split the tree. Women over 58 were at higher risk of very late stages at presentation (21.1%, n=173) than women between 42 and 13.1% (n=199) or

²¹ Advanced stages means regional and distant stages and very advanced stages means distant stages.

younger than 42 (14.7%, n=193), ($P < 0.021$, $\chi^2 = 15.776$, $df = 2$). Additionally, women older than 58 or 42 and younger were at higher risk for late stages diagnosis (70.5%, n=578) and (69.9%, n=917) respectively, compared to those aged between 42 and 58 (66.3%, n=1,006).

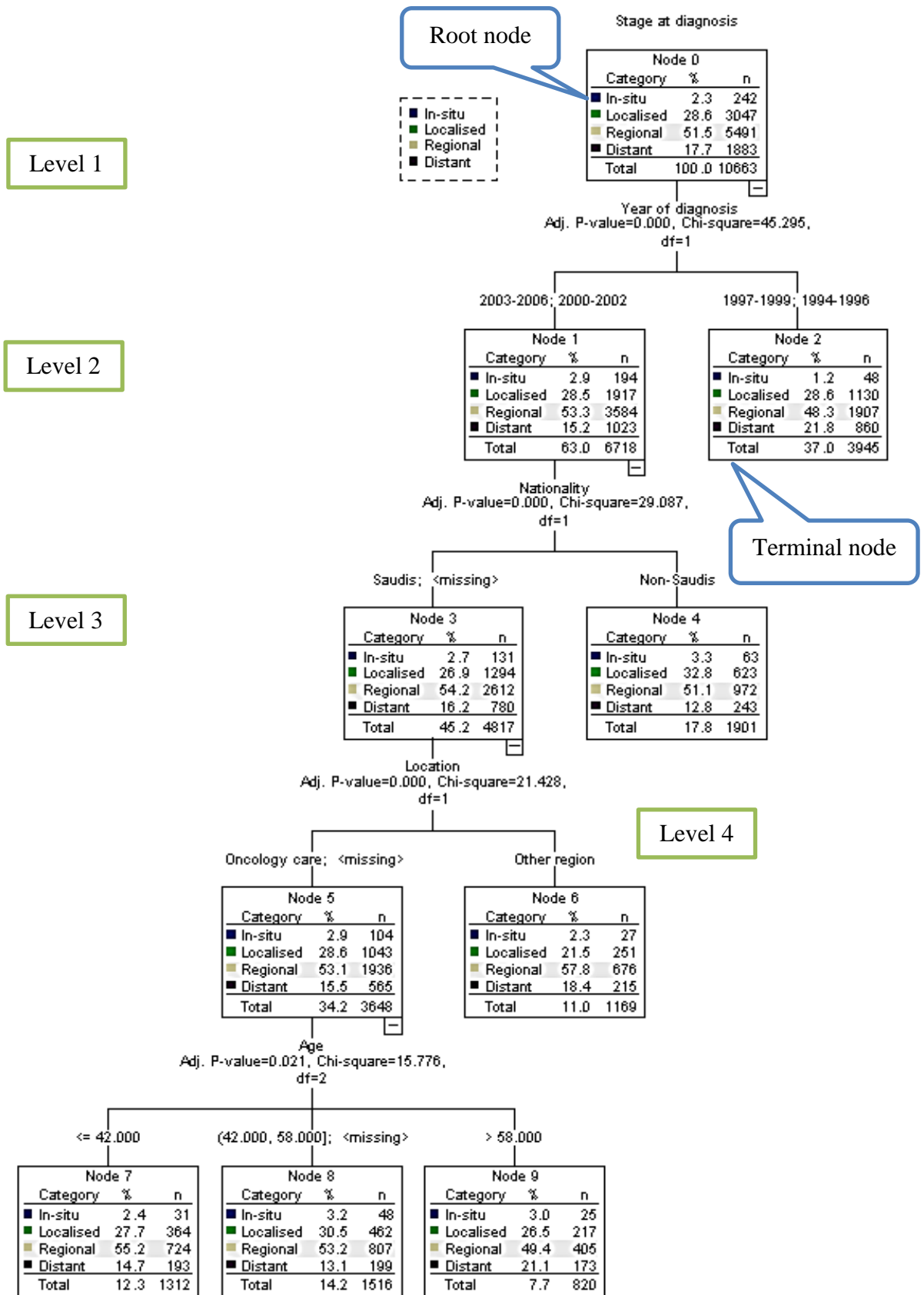


Figure 16: Classification tree of factors associated with stage at diagnosis (1994–2006).

Table 33: Description of terminal nodes associated with advanced stages at diagnosis of female breast cancer (1994-2006)

Level	Node number	Percentage of cohort	Sample size	Description
Higher risk of advanced stages at diagnosis				
1	2	37%	3945	Women diagnosed before 2000 had a higher risk of late stages at diagnosis.
3	6	11%	1169	Saudis women diagnosed with breast cancer in 2000 or later <i>and</i> who did not live in Riyadh, Makkah or Eastern regions that have advanced oncology had a higher risk of late stages at diagnosis.
4	7	12.3%	1312	Saudis women diagnosed with breast cancer in 2000 or later, who live in regions with advanced oncology care (namely Riyadh, Makkah or Eastern regions) and ≤ 42 years old had a higher risk of late stages at diagnosis.
4	9	7.7%	820	Saudis women diagnosed with breast cancer in 2000 or later; living in Riyadh, Makkah or Eastern regions; and >58 years old had a higher risk of very late stages at diagnosis.
Lower risk of late stages at diagnosis				
2	4	17.8	1901	Non-Saudi nationals diagnosed with breast cancer in 2000 or later had lower risk of late stage at diagnosis.
4	8	14.2	1516	Saudi women diagnosed in 2000 or later, living in regions with advanced oncology care and aged 42-58 years had a lower risk of late stage at diagnosis.

8.3.4 Discussion of the classification decision tree

From a public health perspective, identifying the groups with a high risk of late presentation²² of breast cancer is vital to reduce advanced stage at diagnosis of breast cancer in Saudi Arabia. The decision tree analysis helps identify characteristics of subgroups of women at higher or lower risk of advanced stages of breast cancer at diagnosis during 1994–2006 (see Table 33) who are those living in regions with less advanced oncology care, women aged 42 years or younger and those aged 58 years or more. The decision tree is a valuable statistical tool to assist medical decisions (Podgorelec et al., 2002) and identify at-risk groups (Lemon et al., 2003). In cancer-related research, this method has been used effectively to examine the interaction of risk factors for colon cancer (Camp and Slattery, 2002) and to identify target groups for colorectal screening (Ishikawa et al., 2013).

Generally, as expected, the decision tree analysis yielded results consistent with evidence from the quantitative study (as described in Chapter 5). It identified the same explanatory factors, but there were also *interactions*. The classification tree was used as a complementary (rather than a confirmatory) tool to the regression analysis in the quantitative study. It aided further understanding about the interaction of main effects variables associated with advanced stages at diagnosis.

Regression models are widely used to examine the association between dependent and independent variables. Lemon et al. (2003) suggest that the lack of wide application of the classification decision tree to identify high-risk groups for specific intervention can be ascribed to lack of awareness of the method's utility and uncertainties of its statistical properties.

Some anticipate that the results from logistic regressions and classification decision trees could vary because they work in different ways. Regression models allow for investigating the main effects—the association between dependent and the independent variable—while holding the confounder effect (Lemon et al., 2003). In addition, such models can test the interaction between variables, though interpreting results can be difficult, especially if three or more variables are included (Lemon et al., 2003).

²² At higher risk of advanced stages at diagnosis if breast cancer symptoms recognised compared to the general public.

A strength of the classification decision tree is its visual presentation of the subgroups of women, which could assist clinicians in identifying target groups at risk of advanced stages at diagnosis. The decision tree splits data based on homogeneity between groups. The root node sample will be larger than subsequent node samples. This issue should be considered during the interpretation of findings (Camp and Slattery, 2002).

The current limited evidence in Saudi Arabia about characteristics of women with higher risk of late presentation demands innovative methods to generate evidence. This thesis is exploratory in nature; however, the consistency of results across the various types of statistical methods may reflect the internal validity of the research.

8.4 Step 2: Findings integration

This thesis applied an explanatory mixed methods approach to explore potential factors associated with late presentation of breast cancer in Saudi Arabia.

Phase I was a systematic review that identified the gap in existing knowledge in some parts of the world, such as the Gulf states (see Chapter 4), and then identified variables of interest at first naïve, the quantitative study in Phase II looked at the breast cancer data and found the main effect of age, year of diagnosis, place of residence, nationality and marital status (see Chapter 5). Phase III a qualitative study, provided further understanding of the contextual factors. It showed the complexity of the problem and the possibility of interaction between variables. Age was an important characteristic that helped elaborate differences in participants' stage at diagnosis. Older participants were different from younger one in reasons of late presentation (see Chapter 7). Phase IV began its evidence integration by revisiting the quantitative data to examine the interaction between variables and stage at diagnosis using classification decision tree analysis. The results of the tree analysis showed that women with breast cancer were diagnosed at different stages and did not form homogenous groups: the factors influencing the different subgroups varied. The qualitative study also shows this heterogeneity. The next step in making meta-inferences is findings integration and discussion. This section presents the main results from this mixed-methods thesis and their contribution to the exiting literature. A discussion of methodological considerations and implications follow, before the chapter concludes with recommendations for future research and practice.

8.4.1 Contextualising the concept of late presentation of female breast cancer

The definition of breast cancer delay introduced by Pack and Gallo (1938) has been widely adopted in the delay literature. It focuses on the time between first recognition of symptoms and first medical contact. This definition has been widely used to explore factors associated with delay both in breast cancer studies using quantitative methods (Ramirez et al., 1999) and those using qualitative methods to further understand how these factors interact (Smith et al., 2005). Andersen (2011) argued that the term ‘‘delay’’ is inappropriate to describe retrospectively the process of patients seeking help because it implies poor behaviour if the patient took a long time was taken to seek medical attention. The complexity of the process of recognising breast cancer symptoms and seeking medical care may not acknowledge the social aspect in seeking health care (Andersen, 2011).

Breast cancer is a complex, heterogeneous disease and certain types of breast cancer may present differently from others (Li et al., 2005). The variation in defining delay or late presentation (as discussed previously in section 1.5, Chapter 1) indicates the complexity of measuring and examining factors associated with these constructs. It could be defined according to delay avoidance, time delay, sources of delay and stage at diagnosis. The time delay, the one above, is the most widely used.

This thesis did not use the variable of time to seek medical care. Instead, analysis used stage at diagnosis which brings new questions about how late presentation could be reasonably defined in the study context of Saudi Arabia. It is not that the role of time in seeking medical care for cancer prognoses or for the breast cancer patient’s life after the experience of bodily changes is not recognised as important or relevant in this thesis. Saudi women are different in their presentation of breast cancer. Their younger age at diagnosis and the biological characteristics of their breast cancer raise questions about using time to seek medical care as an indicator for better breast cancer outcomes.

Patients must have clear clinical criteria to know when to seek medical care. For example, a month, two months or three months from noticing any changes in the breast and first medical contact for investigation. With such criteria, a woman who experiences breast cancer symptoms will know better when to seek medical care to avoid late presentation. The lack of consensus in Middle Eastern studies in defining

late presentation, as section 4.5, Chapter 4 illustrates does not indicate the presence of such clear criteria yet.

In a clinical perspective, tumour progression can be assessed biologically by evaluating tumour aggressiveness. In the study context, tumour aggressiveness requires attention as Saudi women are more likely to develop an aggressive tumour than women in the West (Al-Kuraya et al., 2005). Thus, when defining late presentation, rate of tumour growth *must* be considered to avoid labelling a woman who sought medical care promptly, but was diagnosed at late stage as a ‘late presenter’: in this case, advanced stage diagnosis was out of the woman’s control.

This thesis used “stage at diagnosis” to define late presentation (as described in section 1.5.5) in the quantitative analyses as a proxy to time seek medical care. It assumed that women who were diagnosed at early stages were more likely to have sought medical care promptly.

The lack of consensus in defining late presentation between Middle Eastern studies, which Chapter 4 describes, made comparisons between the studies difficult. Using stage at diagnosis to define late presentation would enable better comparison between studies from the Middle East and the world.

Furthermore, using the stage at diagnosis overcomes the SNCR’s lack of recorded time to seek medical care and controls for the effect of tumour growth by making stage at diagnosis an outcome of both seeking medical care and the speed of tumour growth. Stage at diagnosis is a valid and widely used indicator to assess cancer prognosis and guide cancer care (Coleman et al., 2011). In this thesis, this variable helps demonstrate the characteristics of women with breast cancer who were diagnosed at various stages and predict which women are at risk of advanced stages at the time of diagnosis or presentation. Thus, using the stage at diagnosis may provide better evidence to guide future breast cancer care and help set priorities, especially if national mammography screening is enacted.

The use of time to seek medical care was problematic as breast cancer tumours sometimes progress so quickly. This problem also appears in the qualitative study. In-depth analysis of the qualitative data provided further understanding about the concept of late presentation. Analysing the length of time to seek medical help and stage at diagnosis revealed that longer time to seek care (more than three months) does not necessarily mean that the patient will be diagnosed at a late stage,

particularly among older women. In contrast, seeking medical help within fewer than three months does not necessarily guarantee an early stage at diagnosis, especially among younger women. Although this finding was based on only 19 breast cancer patients, it is in line with study conducted in Saudi Arabia that found no association between delay in seeking investigation and breast cancer prognosis (Ibrahim, 1990) and studies compared between pregnant and non-pregnant women with breast cancer (Ezzat et al., 1996, Ibrahim et al., 2000).

Integrating time to seek diagnosis and treatment into future research on late presentation in a large cohort will help confirm this issue and provide an estimate of the appropriate period of time before seeking care for the study context. With this knowledge, health professionals and education campaigns can better inform women about the risk of advanced stages at diagnosis and how soon they should seek help for symptoms.

8.4.2 Discussion of factors associated with late presentation of female breast cancer

Late presentation of breast cancer is an under researched area in Saudi Arabia and the Middle Eastern countries when compared to international literature. The systematic review illustrated that such literature in this part of the world is limited and is a new area for research, as investigations began in the 1980s (see Chapter 4). The review found no such studies conducted in Saudi Arabia and indicated that late-presentation breast cancer is a complex health problem with multiple associated factors.

This section discusses the findings integration from this mixed methods study. As Chapter 3 discusses, the study was designed to address multiple objectives from a variety of perspectives. A mixed methods approach can increase and enhance understanding more than when a single research approach is used. Teddlie and Tashakkori (2009) explain that this increase is possible by integrating the results from quantitative and qualitative studies and by exploring possible agreement or disagreement between study results.

This mixed methods study addressed a gap in the breast cancer literature. It also provides strong evidence to help understand the associations and interactions between year of diagnosis, nationality, place of residence, age and marital status, as

well as their effect on stage at diagnosis using a quantitative approach; this thesis also explored the contextual factors underlying this interaction qualitatively.

A “mixed methods matrix” that can display evidence from both quantitative and qualitative data was used to triangulate²³ the results (O’Cathain et al., 2010), as Table 34 shows. The left column demonstrates factors examined by the classification decision tree. The rest of the columns describe whether findings from decision tree analysis and thematic analysis were in agreement, offered complementary explanations, or contradicted each other. In addition, there is a comment column which offers more explanation on certain issues.

Key results from the decision trees analysis helped develop the meta-inferences, as informed by the qualitative results. These results emphasised the interaction between stage at diagnosis and several variables. Moreover, contextual data from the qualitative analysis expanded understanding about the interaction of these factors, which was further enriched by the findings from the wider literature.

Yet, making direct comparison between the findings from a quantitative classification decision tree and the qualitative data can be misleading without acknowledging differences in perspectives between data. The quantitative data represent factors associated with late stages at diagnosis from the perspective of the healthcare system. The qualitative data, however, represent the patients’ perspective. The meta-inference attempts to produce a clearer picture of factors associated with late presentation of female breast cancer. This facilitates both interpretation of the findings and making recommendations. The following sections discuss each factor separately.

²³ The term ‘triangulation’ here is used to describe the data integration which means results have been used to draw a complete picture of the study problem. O’cathain, A., Murphy, E. & Nicholl, J. 2010. Three techniques for integrating data in mixed methods studies. *BMJ*, 341, c4587.

Table 34: Mixed methods meta-inferences matrix

Factors	Findings integration of factors associated with late stages at diagnosis			
	Findings agree (convergence)	Findings offer complementary information	Findings appear to contradict	Comment
Year of diagnosis	✓ Quantitatively			Not applicable qualitatively
Nationality	✓ Quantitatively			Not applicable qualitatively because the target population is Saudi nationals only
Place of residence by region	✓ Quantitatively		✓ Qualitatively	These findings appear to be contradictory because the time gap between conducting the two studies
Age	✓ Quantitatively ✓ Qualitatively	✓ Qualitatively		Both show that age associated with late presentation. The qualitative offers further details about this difference.
Marital status	× Quantitatively	× Qualitatively		It is about family support

8.4.2.1 Year of diagnosis

The decision tree analysis shows there was improvement in stage at diagnosis over time (1994–2006). The tree first splits women with breast cancer into two groups, based on the year of their diagnosis; those diagnosed in 1994–1999 and those diagnosed in 2000–2006. Those diagnosed from 2000–2006 had a better stage at diagnosis profile than those diagnosed in earlier years. Furthermore, the decision tree found no further splits for those diagnosed between 1994 and 1999. This means that women were equally likely to receive a late-stage diagnosis during 1994–1999, regardless of their other characteristics.

The massive improvement in healthcare in Saudi Arabia in recent years may explain the improvement in early stage at diagnosis since 2000 in the 2000–2006 cohort. Differences according to diagnosis year were not observed in the qualitative study as all of the qualitative participants were diagnosed in the same year. However, one woman interviewed explained that healthcare quality is improving. She was talking about quick referral for one of her children, who had cancer, to oncology specialist compared to the past (Participant 16, late stage).

Al-Rikabi and Husain (2012) suggest an increase in mammography screening due to greater awareness of breast cancer may explain the increase in diagnosis of benign tumours since 2007 compared to 2000–2007. Screening facilities and breast cancer awareness activities are increasing (Abulkhair et al., 2010b, Akhtar et al., 2010) and this is in line with the strategic plan of the Ministry of Health (Ministry of Health, 2012a). However, the qualitative study did not support the assumption that the awareness about breast cancer is improving as will be discussed in section 8.4.2.4.

8.4.2.2 Nationality

The second factor that showed significant association with late-stage diagnosis in the classification decision tree was nationality. The tree splits women based on their nationality (Saudi vs. non-Saudi) for those diagnosed since 2000. Non-Saudi women had lower percentage of later-stage, and distant stage diagnoses compared to their Saudi counterparts. Furthermore, the tree identified different characteristics among Saudi and non-Saudi women in stage at diagnosis.

Quantitative literature in this area has pointed out differences in late presentation by ethnicity (Ramirez et al., 1999). Because this thesis focuses on breast cancer

outcomes in Saudi Arabia, non-Saudi nationals were not the primary population of concern in this study. Nevertheless, the difference identified between these groups raises further concerns about late presentation among the Saudi population and questions about the reasons for such differences between Saudi and non-Saudi women.

The difference could be biological, socio-cultural, related to healthcare or an interaction of all of these (Lyrtatzopoulos et al., 2012). The biological factor could explain the reasons of late-stage diagnosis as non-Saudi nationals are diverse however; its association with late-stage diagnosis was not examined in this study. Participants in the qualitative study were Saudi nationals. They revealed sociocultural factors that interact with seeking treatment and a diagnosis of breast cancer. It would be interesting to conduct future research to examine the potential differences and similarities between different nationalities living in Saudi Arabia.

The following sections, however, explain other factors related to late-presentation female breast cancer among Saudi nationals. Section 8.4.2.3 explain the association between place of residence and late presentation, section 8.4.2.4 explain the role of age and other factors and section 8.4.2.5 explain the reasons that marital status is not predictor of late stage diagnosis among female breast cancer.

8.4.2.3 Place of residence

For Saudi women diagnosed with breast cancer since 2000, the tree split further based on their place of residence. Women who lived in regions with less available oncology care, regardless of age, had higher percentages of later stages at diagnosis compared to those who lived in regions where advanced oncology care was available.

The majority of advanced oncology services are located in three regions: Riyadh, Makkah and Eastern regions. Other regions have health services which provide cancer diagnosis and care (Al-Eid and Garcia, 2012, Al-Eid and Manalo, 2011, Ibrahim and Ezzat, 2010), however, quality may vary (Ibrahim and Ezzat, 2010).

Alghamdi et al. (2013) conducted an observational study estimating the ASIR on the Kingdom based on data from the SNCR for breast cancer patients diagnosed between 2001 and 2008. They found that the Eastern, Makkah and Riyadh regions had the highest ASIRs and they are the regions where advanced oncology services are

located. The variation in access to cancer care across the Kingdom may be linked to the variation in the incidence of breast cancer. Regions with lower incidence of breast cancer such as Jazan region, with ASIR of 4.8 (Alghamdi et al., 2013) may be less likely to have advanced breast cancer care.

The qualitative data analysis found no notable differences between women's experiences based on where they live. The qualitative absence of a relationship between place of residence, seeking help and diagnosis does not necessarily imply contradiction between the quantitative and qualitative findings. This difference could be due to differences in the times in data collection between the qualitative and quantitative studies. With continuing improvement in healthcare in Saudi Arabia, the observed differences according to place of residence may have become considerably less pronounced. Repetition of the quantitative analysis using more recent breast cancer data from the SNCR could confirm this explanation.

Ideally, PHC access should be equal through the Kingdom, so if a woman wants a doctor to investigate and diagnose suspicious breast symptoms, PHC should be available. However, the autonomous nature of healthcare across the regions may lead to variation in health needs and quality of healthcare.

As discussed in Chapter 6, the interviewed participants were recruited from a single oncology centre. Although breast cancer patients are referred from all regions in the Kingdom, the data represents the experiences of those women who sought healthcare at this specific facility. Perhaps those women who sought treatment at local facilities due to convenience may have had other experiences in seeking healthcare. Future research using qualitative methods should recruit participants from all regions to explore if location is an important predictor of later stages at diagnosis.

8.4.2.4 Age

As highlighted in the systematic review in Chapter 4, previous studies in the Middle East have shown the effect of older age on late presentation of breast cancer (Abdel-Fattah et al., 1999, El-Zawawy, 1991, Elzawawy, 1999, Ermiah et al., 2012). This agrees with findings from the rest of the world (Ramirez et al., 1999) However, the review presented in Chapter 4 did not uncover more detailed explanations about which age groups are at higher risk or estimates of the effect.

The classification decision tree analysis showed that age is one of the important factors associated with late-stage breast cancer diagnosis. This is in contrast to some studies from the Middle East, based on a sample of 1,232 women diagnosed with breast cancer, that age was not associated with late diagnosis of breast cancer (Abdel-Fattah et al., 1999, Al Saad and Alsayed, 2012, Mousa et al., 2011, Stapleton et al., 2011).

The quantitative study assessed the association between age and tumour stage based on the SEER staging. The Middle Eastern studies used different criteria and methods to assess the association between age and late presentation and late diagnosis (as described in section 4.5.1). The classification tree offers a more sophisticated tool for exploring the issue of age than the first analysis run in Chapter 5.

The relationship between age and stage at diagnosis was not linear; it was more complex than merely looking at binary categories of younger vs. older women. The decision tree splits age into three groups (age 42 years or younger, between age 42 and 58 and over 58). The risk of being diagnosed at a later stage, especially at the distant stage, was higher among women older than 58. These age groups were more varied than those either in the previous quantitative (Chapter 5) or qualitative (Chapter 7) analyses. Both show that age is an important predictor of late-stage diagnosis although the definition of the age groups differs slightly. This last detail is less important than the identification of older women and younger women as high risk groups. The notion that age interacts with other factors, which the qualitative study found strengthened in the decision tree analyses. This demonstrates the value of data integration.

Furthermore, the tree shows that middle aged women (between 42 and 58) had the least risk of later stages at diagnosis. Women younger than 42 were at higher risk of later-stage diagnoses compared to middle aged ones.

The literature offers a strong support to the thesis findings of an association between older age and late presentation of breast cancer (Ramirez et al., 1999). Partridge et al. (2012) evaluated the relationship between age, time to presentation for diagnosis and stage at diagnosis for 21,818 women diagnosed with breast cancer, in the US. They found that being younger (less than or equal to 40) was not an independent predictor of a delay of diagnosis of more than 60 days. Younger age can only modestly more likely to associate with a later stage at diagnosis (Partridge et al., 2012). They also

found that women diagnosed based on their symptoms identification—not based on screening—were more likely to delay, both women younger than 40 (OR, 3.31; 95% CI, 3.08–3.56) and older women (OR, 4.31; 95% CI 4.05–4.58), compared to those diagnosed through screening.

Elkum et al. (2007) compared the clinical characteristics and outcomes of women in Saudi Arabia with breast cancer aged 40 years or younger with those older women. Based on 867 subjects, they found that younger women have a worse prognosis than older ones. They suggested researching the interaction between the genetic and environmental factors to improve treatment for Saudi women.

The qualitative study was conducted before the classification decision tree analysis. As such, the women's interviews were not analysed based on the three age groups (≤ 42 , 42-58 and >58 years old). The analysis divided subjects into those aged 50 and older and younger than 50 on early and late stage and the analysis and showed consistent difference between younger and older women.

While age is associated with stage at diagnosis, its effects shown in the classification tree— appears among Saudi national women, diagnosed with breast cancer since 2000, who were living in regions with advanced oncology care. Women at risk of later stage diagnoses, with the risk being greater among older ones— as shown quantitatively— however; the qualitative study shows that the mechanisms vary.

Many studies conducted in Saudi Arabia show that public awareness about cancer and breast cancer is poor (Alam, 2006, Amin et al., 2009, Dandash and Al-Mohaimed, 2007, Ibrahim et al., 1991b, Jahan et al., 2006, Mahfouz et al., 2013, Ravichandran et al., 2010, Sait et al., 2010). Two studies from the Middle East found an association between lack knowledge about breast cancer and delay (Corbex, 2009, Harirchi et al., 2005).

The qualitative study confirms a lack of awareness among women with breast cancer and the presence of some misconceptions that may interfere with seeking medical examination quickly. The misconceptions were different for older and younger subjects. Among older women, who often have other comorbidity, the misconception that if a symptom (a lump) is not painful, it is not serious and if the changes are not serious, seeking medical care is not necessary, was strongly present. Thus, older women frequently did not recognise the initial symptoms as serious enough to seek medical care which consequently resulted in delay in presentation for investigation.

Furthermore, older women's other health concerns might also decrease their attention to the presence of seriousness of breast cancer symptoms. In addition, older women were more likely to wait and tolerate pain than to express their concerns about abnormality immediately to someone else who might direct them to medical attention.

Younger women recognise breast symptoms—not necessarily related to breast cancer—and because of their interpretation that these symptoms are abnormal they are more likely to be proactively seeking medical care promptly. However, the lack of awareness and misconceptions they had such that once a woman breastfed her children, she will not get breast cancer together with the presence of reproductive health issues lessen the recognition that these symptoms are serious and could be related breast cancer. Misdiagnosis among younger women when they sought healthcare promptly could be a reason for late stage diagnosis.

Literature from the Middle East suggests that lower education levels are associated with late presentation of breast cancer (Abdel-Fattah et al., 1999, Ermiah et al., 2012, Harirchi et al., 2005, Montazeri et al., 2003). However, the heterogeneity in defining late presentation and education categories hindered conclusions about what level of education is associated with increased risk of late presentation. The quantitative analysis did not examine the association between education and stage at diagnosis because the SNCR does not recorded level of education. Therefore, the main effect remains unclear in the study context. The qualitative study gives more insights into the association between age, education and late presentation; with education possibly confounding age, awareness and misconceptions play a fundamental role in late presentation. If level of education influences late presentation, then it is expected that those who are educated will be more aware about breast cancer from credible sources therefore, they will be informed what to do if they detect symptoms. However, this was not always the case in the qualitative data. The difference between women is the difference in their interpretation that the symptoms are serious and need medical consultation. This might explain why Mousa et al. (2011) did not find an association between education attainment less than a bachelor's degree and late presentation, while other studies, which included illiteracy found an association between education and late presentation (Abdel-Fattah et al., 1999, Ermiah et al., 2012, Harirchi et al., 2005, Montazeri et al., 2003).

Younger women consider the presence of breast cancer symptoms to be abnormal and, therefore, may seek medical help promptly. But due to a lack of awareness and the presence of reproductive health issues, they do not necessarily link these symptoms to the possibility of breast cancer.

Frequently, the late stage at diagnosis among younger women could also result from misdiagnosis by clinicians. The younger age is one of the risk factors for provider delay in breast cancer (Ramirez et al., 1999). Misdiagnosis is an issue that has been reported in qualitative studies across the Middle East but it was not clear if this an issue among younger, older women or both (McEwan et al., 2014, Rastad et al., 2012). It is not surprising that health workers may lack sufficient knowledge about breast cancer's burden in Saudi Arabia as the majority are expatriates.

A recent study in the UK indicated low awareness of the risks associated with age effect on presentation time and high perceived barriers to symptomatic presentation. This was not the case in Denmark, also a developed country (Forbes et al., 2013). In the qualitative data, lack of awareness was a fundamental issue, both among older and younger women. This finding is supported by several studies which suggested the low breast cancer awareness among women (Al-Mulhim, 2001, Alam, 2006, Amin et al., 2009), men (Al-Amoudi and Abduljabbar, 2012) and health workers in Saudi Arabia (Al-Amoudi et al., 2010).

Greater effort should be given to raising awareness about breast cancer and the value of early stage diagnosis. Moreover, specific attention needs to be given to address the misconceptions found in this thesis found. Even though more focus should be on women such awareness campaigns should target everyone in the Kingdom, but with more emphasis on women. Because this research demonstrates that (significant) others, including men, have an important role in directing a woman to seek medical help. It is therefore important that the population is aware of breast cancer, its symptoms and importance of seeking early help. Additionally, more effort is needed to increase awareness among health professionals of the epidemiology of breast cancer and how to assess symptom severity. The differences in the biological nature of breast cancer among older and younger women should also be considered. Older women are at greater risk of developing breast cancer (US Preventive Services Task Force, 2009) while younger women are at greater risk of developing larger tumours (Zabicki et al., 2006). This study did not explore the role of cancer grade. More

research is needed to explore the role of tumour grade, adjusted for age, to determine its effect on late presentation.

Additionally, research into genetic mutation might provide greater understanding of what groups are more at risk of developing the disease and should receive special attention when they raise concerns about breast abnormalities. Also, if there is a specific mutation(s) (like BRCA1 and BRCA2 which is more likely to affect women of a particular, Middle Eastern descent). Family history is a vital characteristic, especially among older patients that could be integrated into patients' care and referral (Vig et al., 2013). Interventions could target increasing awareness of genetic the susceptibility to breast cancer. Amin et al. (2012) pointed out the potential impact such research could have as women in Saudi Arabia are interested in genetic testing despite having poor knowledge about the association between genetic factors and breast cancer (Amin et al., 2012).

Health workers need to be aware of potential communication barriers with older patients, as well as unfamiliarity with cancer signs among younger ones, to avoid multiple medical consultations before referring patients to a hospital for cancer. Even when a woman presents with a symptom like breast lump, a GP's first contemplated diagnosis may not be breast cancer. In the UK for example, a GP may only diagnose one patient with breast cancer each year. Malignancy may not be the first thing a GP consider (Hamilton, 2009), especially for patients with less risk of cancer such as younger women. With no checklist or guidelines for referral at the GP level, this problem become worse, especially in the absence of national screening.

Another feature that might be associated with late presentation and could differ with age is disclosure of the symptoms. Older women were more likely not to tell someone else about the symptoms. Symptoms disclosure is one of the key theme in qualitative research in this area (Smith et al., 2005). Discussing breast cancer symptoms with someone else may encourage seeking medical care for breast cancer diagnosis and help women to make connections between the symptoms they have, possibility of illness and the need to see a doctor.

8.4.2.5 Marital status

Quantitatively, marital status was not associated with advanced stage at diagnosis. Previous studies also illustrated that being unmarried was not associated with late

presentation (Ramirez et al., 1999). In the Middle East, marital status is more likely not be associated with late presentation (Abdel-Fattah et al., 1999, El-Zawawy, 1991, Elzawawy, 1999, Ermiah et al., 2012) as Chapter 4 explains.

There was no attempt to include marital status in the recruitment strategy of the qualitative study as the quantitative part did not identify it as an important factor. Explanations from the qualitative results confirm quantitative findings and demonstrated that marital status was not as important as receiving proper support in seeking medical care promptly once a woman disclosed her health concerns to significant others.

The discussion of findings from this study helps to understand the problem of late-presentation breast cancer; the following section discusses the application of methods in relation to making the inference.

8.4.3 Adopting mixed methods approach in this study

The process of meta-inference follows a course from the beginning of research ideas; through data collection, analysis and results; to inference generation and interpretation. The thesis adopted a mixed methods approach, which is very *organic* and shows an integrated relationship between the thesis phases. The results from one method informed, enrich and strengthen the evidence generation of the other and thereby enhance the integration and generalisability of the thesis findings.

In mixed methods ‘‘Legitimation’’ (Onwuegbuzie and Johnson, 2006) is a term used to denote validity. The inference validity and rigor in this thesis has been given consideration.

The mixed methods approached followed a sequence of phases started inductively by the systematic review (phase I) without predetermined models to explain the problem. Because of the lack of models applied in contexts similar to Saudi Arabia (see section 3.4.1, Chapter 3). The systematic review did not help in prioritising the variables to be examined or in estimating their effect, even when the studies were current. Rather, the review gave an indication of which factors might be involved in late presentation of breast cancer in Saudi Arabia.

The nature of this review encouraged the *inductive* generation of evidence. This was grounded in quantitative data assessed in phase II, which was based on a large cohort of 10,663 patients representing the intended population—Saudi females. Such a large cohort enhances the power of the study (as explained in section 5.4.6). This study

uses secondary data and, as such, there was no control over the type and process of data collection. Data collected by the SNCR informs cancer control in the Kingdom. It focuses on specific clinically based useful information. Ideally, a greater depth of information is required to understand quantitatively the research problem in more detail.

The more in-depth understanding could be achieved using qualitative methods. Phase III takes advantage of qualitative methods to understand the variation in time to presentation for healthcare and diagnosis among Saudi women with breast cancer. To better comprehend the reasons for late presentation, Phase III included findings from the quantitative analysis into sampling of women with breast cancer based on factors that appeared clinically relevant.

The data gathered qualitatively in Phase III through interviews are individually based. They thus provide detailed information about women's experiences with symptom recognition and medical help-seeking. The sampling of the qualitative study was guided by generalisable findings from the quantitative study. Often, qualitative studies are context specific, with reliability is given less attention than validity because these studies don't aim to replicate findings and because unstructured strategies are used in data collection (Guest et al., 2012). This thesis attempted to enhance reliability (Chapter 6), as well as the consistency in findings between the qualitative study (Chapter 7) with other qualitative studies in the Middle East (McEwan et al., 2014, Rastad et al., 2012). Despite use of different interview guides, the indications that reliability can be maintained in qualitative research.

In qualitative research, establishing good relationship with the participants is crucial to facilitating open discussions (Patton, 2002). The researcher tried to establish a good relationship with participants while conducting interviews that discussed difficult issues related to their diagnosis with breast cancer (As described in Chapter 6). Narratives from 19 women with breast cancer enlarged the context of data on the presentation time to healthcare facility and stage at diagnosis. Great understanding the context-specific factors revealed the complexity of late presentation and a notion of the interaction between factors that may shape late presentation. Qualitative analysis pointed out that age might be an important factor which interacts with healthcare, awareness and misconceptions and symptoms disclosure. Thus, further quantitative analysis explored this interaction in Phase IV.

A potential problem in mixed method studies is that the inference can be different if the order of the quantitative and qualitative investigations reversed (Onwuegbuzie and Johnson, 2006). This thesis minimised that legitimisation threat by revisiting the quantitative data. The sequence of evidence was quantitative → qualitative → quantitative, which yields consistent results.

Furthermore, the inference generated two balanced views. The quantitative analyses represent the outsiders' views while the qualitative analysis represents an insider view (Onwuegbuzie and Johnson, 2006). Thus, this mixed methods study provides a balanced perspective. Discussion with the thesis supervision team, who have extensive experience in quantitative, qualitative and mixed methods research, has helped maintain this balanced view.

Implementing the thesis design (Figure 7) involved learning and applying different research methods and skills, as well as, creative thinking focused on the thesis's aim. The thesis phases were carried out sequence, with each phase conducted, reported and summarised alone and in relation to the broader thesis aim before beginning the next phase. The inference in this thesis was generated by combining, comparing and contrasting evidence from each phase and explaining the differences, limitations and strengths.

At a phase level, the thesis discussed the strengths and limitations of each study separately. Chapter 4, section 4.7 discussed the systematic review, Chapter 5, section 5.8 discussed the quantitative study and Chapter 6, section 7.10 discussed the qualitative study strengths and limitations.

At the thesis inference level, the inference (conclusion) was drawn from these studies effectively to answer the research questions. The components of the thesis design are consistent in terms of methods and sequence. Inference rigor is strengthened as the results from each study proved consistent with each other (Onwuegbuzie and Johnson, 2006). In general, the inference is in line with scholars' conclusions in this area, but the thesis inference offers a more detailed and sophisticated exploration of the issue.

Transferability means the extent to which a conclusion applies in other contexts, time, settings or groups (Teddlie and Tashakkori, 2009). The systematic review concludes that there is a need to investigate the problem of late presentation of female breast cancer in Saudi Arabia. The quantitative analysis concludes that year

of diagnosis, age, nationality and place of residence significantly associated with late-stage of diagnosis. The qualitative analysis goes beyond the systematic review and the quantitative findings and demonstrates that there were other issues might influence late presentation. The meta-inference from the three studies offers a more generalisable and meaningful findings than those that could be afforded by each study alone.

In terms of policy and practice recommendations, the more similar the setting and context to the study population the more likely that the inference is transferable (Teddlie and Tashakkori, 2009). The inference drawn by the thesis was limited to available and accessible evidence in the literature and the cancer registry data. Additionally, qualitative results reflected issues related to late presentation from only one health institution. It is possible that other factors might interact with late presentation and lead to different inference. Additionally, with the rapid changes in Saudi Arabia in terms of population density, lifestyle and healthcare, it is possible that the inference might not remain valid for long. Continuous research could help identify differences in late presentation overtime.

8.4.3.1 Reflections on conducting a mixed methods study

Prior to conducting this thesis, I had quantitative research experience but having clinical experience as a health educator stressed the importance of understanding patients' behaviour in order to help them achieve better health outcomes.

This study had multiple objectives, which required diverse methods. A mixed methods study was an ideal research approach to supply that diversity. However, the challenge in implementing this approach was to learn and conduct the various methods from multiple perspectives. This required training in research methods, reading about conducting different types of research, conducting study phases in sequence, and surveying late-presentation literature, together with supervisory meetings assisted me learning how to conduct mixed methods research.

Prior to data collection, I gained insights from the process of applying for ethical approval of the research by thinking about the benefits of the research and its risks for me and the participants.

One question that raised my interest during this study was what are the factors associated with late presentation? The quantitative study uses secondary data from

the SNCR, a valid and useful source for generating powerful results. The systematic literature search shows that the SNCR data have not been used before to assess the problem of late-presentation. The analysis was conducted and validated by using various regression methods. However, interpreting the results was not simple. Discussions with my supervisor and reading the literature helped me to overcome these difficulties. The results successfully answered part of the question above.

I acknowledge the value of using qualitative research to uncover issues that are not examined quantitatively. During the planning of the qualitative study, I thought about how to purposively sample women. There were many ways to do so, and discussions with my supervisors highlighted the risks and benefits of each, but ultimately I faced the challenge of deciding which to use. By reading the mixed methods literature, I realised that I needed to carefully choose participants to ensure rigor in the mixed methods inference. Therefore, I thought about linking the general picture with representative voices by applying the findings from the quantitative study into a sample of the qualitative work.

When I interviewed the participants, I realised the need to incorporate their views into the research. However, analysing their narratives was challenging and time consuming. By doing the analysis systematically, based on standards of qualitative data analysis and with the support and guidance of my supervisors, I was able to overcome the challenge in analysing and writing up qualitative findings.

The qualitative study had two outcomes. The first was a model of factors influencing late presentation among Saudi females with breast cancer. The second was becoming a mature researcher, looking at the problem from different perspectives and research approaches. My thoughts on the research problem evolved by performing quantitative and qualitative sections in sequence. I viewed each section as a puzzle. However, there still seemed to be a few pieces missing in the picture.

To understand why late presentation occurred, I needed to reevaluate how I viewed the quantitative data. Because every behaviour is a result of the interaction of multiple factors, I asked myself, what factors are associated with late presentation and how do they interact? The flexibility of mixed methods and the richness of the data collected allowed me to revisit the quantitative data to investigate this interaction.

The decision tree clearly illustrates several characteristics of women who were at higher and lower risk of late-stage diagnosis. The consistency between the findings of the two quantitative analyses methods—logistic regression and the classification decision tree— enhances the validity of the quantitative results. As described in Chapter 3, the analysis was an ongoing process. Each phase undertook a series of analysis steps in which both the data and the analysis methods were investigated to ensure validity. Furthermore, the consistency between quantitative and qualitative findings enhances inference rigor.

The inference generation that combined the results of the systematic review, the quantitative and qualitative work was challenging because of the difference in perspectives each approach has. As I focused on the thesis aim and objectives, I was able to synthesise the evidence. Writing up the findings integration increased my ability to view the wider picture, allowing me to complete the puzzle and draw the conclusions. The journey of conducting this mixed methods thesis was enjoyable and rich in teaching me research skills that I would never have gained using a single research alone.

8.5 Thesis implications

The “pluralism of perspectives” has great value in helping to answer mixed-methods enquiry and suggesting practical solutions (Onwuegbuzie and Johnson, 2006). This pluralism could be related to research approaches as described in Chapter 3, or to the nature of data collected. In this mixed methods study, the data presents two perspectives: the medical perspective of the cancer registry data and the patient perspective in the interviews regarding patients’ experiences in seeking healthcare. Understanding the problem from both perspectives is necessary because medical services are offered to people, their views and opinions are needed to build evidence to improve breast cancer service delivery.

This study could be the start of achieving a better understanding of late-presentation female breast cancer in Saudi Arabia and more appropriate, customised services to be offered. The thesis findings indicated two areas for recommendations to improve the early presentation of female breast cancer: healthcare and research.

8.5.1 Recommendations for healthcare

The focus of this study was to reduce the time before presentation to healthcare and late-stage diagnosis for women who are alerted by breast cancer symptoms. Healthcare policymakers and professionals need to be aware of the characteristics of women who are at higher risk of late-stage diagnosis to act positively toward early detection of breast cancer. The high risk groups are those who are living in regions with less advanced oncology services, women aged 42 or less, and greater than 58 years.

In the literature, evidence is limited about interventions that effectively increase the early presentation of cancer (Austoker et al., 2009). Although there is moderate evidence in the literature indicates that individual-based interventions to promote awareness are effective for a short time, their effectiveness on early presentation is unclear (Austoker et al., 2009).

The lack of awareness and misconceptions found in this study indicate the need for more generic parts, aimed at raising awareness about breast cancer among all women and incorporate messages about breast cancer, symptoms, risk factors and the effectiveness of early detection. In addition, messages need to be tailored to overcome misconceptions detected depending on age.

Older women need to be more aware that it is not necessary that serious symptoms are painful and that they should visit a doctor, painless lump might be serious and thus, needs immediate medical investigation. For younger women, they need to know that breast cancer could be a diagnosis for a lump even during pregnancy, breastfeeding or postpartum therefore. Consequently, they should investigate the lump soon after recognition. Because the family has an important role in seeking medical care, breast cancer awareness programmes should also target all family members, both male and female.

Channels and venues to disseminate breast cancer messages need to target older and younger women. For example, younger women can be reached in malls and older women can be reached in Qur'an learning and memorising circles.

The variation between healthcare professionals and the public in health literacy may create a gap in understanding messages about breast cancer (Manning and Dickens, 2006). More effort is needed to ensure that breast cancer messages in public health campaigns can be understood by laypeople. For example, the concept of a risk factor

should be better explained to public, such as the association between HTR, breastfeeding and breast cancer. Because the qualitative data showed that women understood the effect of breastfeeding as absolute, not as probability, same occurred with the HTR.

The gap between health professionals and laypeople in understanding the principle of a risk factor needs to be considered in developing future breast cancer awareness programmes. Such a gap has been identified in the UK, with possible solutions being inclusion of dialogue and debate about the risk of breast cancer (Chiu et al., 2009).

Mansell et al. (2011) reviewed 22 studies on interventions to reduce cancer delay in referral from PHC to secondary care and none of them assess the effect of intervention on referral delay reduction. They found limited evidence on interventions regarding education, audit and feedback, diagnostic and assessment tools, specific skills training were found in specific outcomes.

Healthcare professionals especially, those working in the PHCs need to be aware about breast cancer epidemiology in Saudi Arabia, including the younger age seen at diagnosis and the risk of late stages at diagnosis. More attention is needed in regions with less advanced oncology facilities. Establishing a breast cancer risk assessment tool and diagnostic algorithms can be used at the PHC level could assist in clinical-decision making to facilitate timely diagnosis of breast cancer.

These guidelines need to be adapted to the needs and epidemiology of Saudi female breast cancer. For example, these guidelines can set time limits in referral from PHC and appointments in breast clinic for diagnosis. Training in how to implement the guidelines with guidance on health facilities which offer diagnostics services may explained to GPs who may not familiar with location of breast cancer services.

8.5.2 Recommendations for research

The thesis suggests many areas for future research to improve our understanding about what might contribute to late presentation. Its studies focused on patient-related factors and the role of the health professional. Future research needs to focus on factors related to the healthcare system related factors and delve further into the diagnosis and treatment. Additionally, it should explore tumour aggressiveness, a biological factor, on the time to seek medical care and diagnosis.

For each breast cancer patient, health professionals could record the time intervals from symptoms recognition to seeking medical care to diagnosis and finally to

treatment (if appropriate). This would help to establish the magnitude of the problem concerning delays in presentation, diagnosis and treatment, and to identify areas in which improvements in cancer care could be made. More analysis of late presentation and survival also needs to be undertaken in future research. For instance, it would be in the interests of both the public and stakeholders to know how many deaths might be avoided if late presentations or diagnoses were to be reduced.

It would also be beneficial for health promoters to address the lack of breast cancer awareness among the public. This could be achieved by assessing levels of public awareness about breast cancer, together with the wide distribution of misconceptions that exist, especially those addressed in this thesis. Researchers in the field of health promotion could use a validated tool such as the Cancer Awareness Measure (Stubbings et al., 2009) to assess public levels of awareness about breast cancer and evaluate the impact of awareness campaigns.

For healthcare professionals – who are in direct contact with potential breast cancer patients – research needs to uncover the extent of, and reasons for, late diagnosis. Failure of the doctors to recognise breast cancer among younger women during the first medical consultation is reported in this thesis. Future research could investigate the association between breast cancer symptoms, age and the accuracy of diagnosis. Auditing cases of late diagnosis by GPs and late referrals from PHCs could be used as an indicator to improve breast cancer care. Future research could investigate the variation in the quality of cancer care across regions of Saudi Arabia and its impact on late presentation and diagnosis.

The experience and knowledge of specialists involved in breast cancer might guide the implementation of cancer care policies. Focus groups could provide a useful tool for collating the knowledge of GPs, health promoters and specialists on current good practices and their opinions on areas that require improvement in late presentation, diagnosis and treatment.

The growth of contextual understanding is important as the explanatory, quantitative data. This thesis uncovered the important role of factors beyond demographics. Future research could test the distribution of factors shown in the qualitative study and their main effect on late presentation. Such research is vital due to the rapid changes in healthcare services and population demography.

Future research should focus on the age group, 42 or younger, between 42 and 58 and greater than 58, which was identified in classification tree.

In addition, differences between Saudi and non-Saudi female breast cancer patients need to be explored to guide future policies for breast cancer care.

Given the complexity of the research problem, future research needs to search for the best methods for understanding late presentation and diagnosis. Findings from the qualitative study indicated that stage at diagnosis is an effective and practical parameter that should be used in future research in Saudi Arabia. Future research could use the same parameter and investigate the interaction of other factors on late presentation of female breast cancer.

The quantitative data indicated positive changes in stages at diagnosis from 19994 to 2006. Future research needs could assess whether this trend has continued in recent years and if there are differences in late-stage diagnosis across regions.

This thesis focused on female breast cancer. Future research could investigate late-presentation of other types of cancer or male breast cancer and then compare them to female breast cancer. Such research would benefit from mixed methods research to generate evidence.

8.6 Thesis strengths and limitations

The strengths and limitations of the individual studies are described in Chapters 4 (systematic review), Chapter 5 (quantitative study), and Chapter 7 (qualitative study). This section describes the strengths and limitations of the overall thesis

One of the major strengths of this thesis was its use of a mixed methods design to understand late presentation of female breast cancer from multiple perspectives using different research strategies. Using systematic review to examine the extent to which the problem has been studied was powerful in guiding further steps in this research. It helped in assessing the research needs and choosing methods appropriate and applicable methods to the study context. As described in Chapter 3, section 3.4, the application of an explanatory sequential study design was able to meet the thesis objectives. It assisted in answering the thesis questions and confirmed the results in a chronological order.

The quantitative data from SNCR were able to provide insights into the associations and interactions with advanced stage at diagnosis on a national level. Using data for

breast cancer patients diagnosed during 1994–2006 enhanced the generalisability of the findings. In addition, the qualitative study in this thesis provided an in-depth understanding of contextual factors related to late presentation. It gave a complementary and context-specific understanding that, though not generalisable alone, when triangulated with the quantitative results makes all the results more likely to be generalisable.

Findings from the qualitative work aided in the interpretation of the quantitative results and raised questions about the interaction effect on stage at diagnosis. This led to re-analysis of the quantitative data to enhance evidence integration. The process by which the evidence on risk factors for late presentation of female breast cancer was developed is a platform for innovative investigations, with each phase drawing inference from previous ones and, thereby, more likely to reflect reality, especially when there is consistency in the results.

However, there are some limitations. Data gathered for the quantitative and qualitative work were different in samples and periods. Participants recruited in the qualitative study were different from those in quantitative study. This could raise an issue in the validity of the findings (Creswell and Plano Clark, 2011). However, both samples represent the same population, female breast cancer patients in Saudi Arabia. Moreover, there is a gap of five years between the quantitative data (1994–2006) and the qualitative data (2011). A better picture could have been drawn if both studies had been conducted during the same period.

8.7 Conclusion

This study provides an understanding of factors associated with late presentation of female breast cancer among Saudi nationals. A mixed methods research design was used by implementing a series of phases; systematic review, quantitative study, qualitative study, revisit of the quantitative data and evidence integration.

The thesis results support the idea that late presentation is a complex issue and has multi factors. The inference drawn from this study shows characteristics of women at high risk of late presentation resulted from the integration of quantitative and qualitative data. These characteristics include living in areas with less oncology services, being older than 58 or 42 years or younger as shown in the classification tree analysis. Furthermore, contextual understating of the reasons of late presentation

was gained from the qualitative study especially in relation to the variation between younger and older women. The lack of awareness among women and the presence of misconceptions interfere with timely seeking medical care. But, talking to some else speed the seeking process. In addition, the qualitative study elaborated the role of healthcare in supporting early stage at diagnosis.

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Appendix A: Systematic review searching

Searching data bases

Database: BIOSIS Previews <1969 to 2014 Week 26>

Search Strategy:

-
- 1 "breast cancer*".m_titl. (104589)
 - 2 limit 1 to human (99398)
 - 3 breast carcinoma*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (26307)
 - 4 breast neoplasm*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (131168)
 - 5 breast tum?r*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (14997)
 - 6 2 or 3 or 4 or 5 (186328)
 - 7 Middle East*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (7085)
 - 8 Eastern Mediterranean*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (3645)

9 Saudi*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (11309)

10 Kuwait*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (3114)

11 Qatar*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (838)

12 Bahrain*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (627)

13 Oman*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (2804)

14 Emirate*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (1253)

15 Egypt*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (22191)

16 Sudan*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases,

geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (10655)

17 Algeria*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (5728)

18 Morocco*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (9216)

19 Tunis*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (9906)

20 Libya*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (2033)

21 Palenstin*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (0)

22 Leban*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (3795)

23 Iraq*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods &

equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (5246)

24 Syria*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (17241)

25 Yemen*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (2333)

26 Iran*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (27533)

27 Jordan*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (7485)

28 7 or 8 or 9 or 11 or 12 or 13 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 (136740)

29 delay*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (288932)

30 Late present*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (758)

31 ealry present*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods &

equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (0)

32 postpon*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (4549)

33 wait*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (17186)

34 hesitat*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (777)

35 defer*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (20456)

36 early stage*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (86201)

37 late stage*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (19434)

38 advance* stage*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (17382)

- 39 late action*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (24)
- 40 early action*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (0)
- 41 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 (442273)
- 42 Help seeking behavior*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (332)
- 43 Waiting time*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (2370)
- 44 motivation*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (48845)
- 45 Priority*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (43421)
- 46 consultation*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (16434)

47 health service* use*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (661)

48 access to care*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (1541)

49 symptom* attribution*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (48)

50 Symptom* duration*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (1353)

51 sick role*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (112)

52 seek* advice*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (165)

53 barrier*.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (136643)

54 time factor.mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases,

geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (907)

55 (Seek* or ask* or Look* near care or attention or assist* or help*).mp. [mp=abstract, biosystematic codes, original language book title (non-english), book title (english), chemicals & biochemicals, concept codes, diseases, geopolitical locations, gene name, major concepts, miscellaneous descriptors, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, title, time, taxa notes] (703258)

56 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 (925227)

57 41 or 56 (1332017)

58 6 and 28 and 57 (107)

Database: Embase <1996 to 2014 Week 21>

Search Strategy:

1 breast cancer.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (248897)

2 breast carcinoma*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (41238)

3 breast neoplasm*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (6512)

4 breast tum?r*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (51761)

5 1 or 2 or 3 or 4 (285270)

6 Middle East.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (8240)

7 Eastern Mediterranean*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (1271)

- 8 Saudi*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (11786)
- 9 Kuwait*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (3052)
- 10 Qatar*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (1253)
- 11 Bahrain*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (1020)
- 12 Oman*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (1791)
- 13 Emirate*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (2216)
- 14 Egypt*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (3)
- 15 Sudan*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (5003)
- 16 Algeria*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (2415)
- 17 Morocco*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (4454)
- 18 Tunis*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (7380)
- 19 Libya*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (1082)
- 20 Palenstin*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (0)
- 21 Leban*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (3489)
- 22 Iraq*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (6607)
- 23 Syria*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (6558)
- 24 Yemen*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (1345)

- 25 Iran*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (33139)
- 26 Jordan*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (5283)
- 27 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 (98947)
- 28 delay*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (310656)
- 29 Late present*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (2352)
- 30 Early Present*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (890)
- 31 postpon*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (6677)
- 32 wait*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (41846)
- 33 hesitat*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (1728)
- 34 defer*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (21112)
- 35 early stage*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (94413)
- 36 late stage*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (19288)
- 37 advance* stage*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (27809)
- 38 early action*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (195)
- 39 late action*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (19)

- 40 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 (506244)
- 41 Help seeking behavior.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (4810)
- 42 Waiting time*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (7528)
- 43 motivat*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (95229)
- 44 Priorit*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (5718189)
- 45 Consult*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (111699)
- 46 health service* use*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (2284)
- 47 access to care*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (6961)
- 48 symptom* attribution*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (116)
- 49 Symptom* duration*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (2723)
- 50 sick role.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (209)
- 51 seek* advice*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (614)
- 52 barrier*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (170625)

53 (Seek* or ask* or Look* near care or attention or assist* or help*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (1596341)

54 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 (6968090)

55 40 or 54 (7208273)

56 5 and 27 and 55 (710)

Database: Global Health <1910 to 2014 Week 20>

Search Strategy:

-
- 1 breast cancer.m_titl. (9904)
 - 2 breast carcinoma*.mp. [mp=abstract, title, original title, broad terms, heading words] (999)
 - 3 breast neoplasm*.mp. [mp=abstract, title, original title, broad terms, heading words] (433)
 - 4 breast tum?r*.mp. [mp=abstract, title, original title, broad terms, heading words] (475)
 - 5 1 or 2 or 3 or 4 (11033)
 - 6 Middle East.mp. [mp=abstract, title, original title, broad terms, heading words] (64402)
 - 7 Eastern Mediterranean*.mp. [mp=abstract, title, original title, broad terms, heading words] (718)
 - 8 Saudi*.mp. [mp=abstract, title, original title, broad terms, heading words] (6529)
 - 9 Kuwait*.mp. [mp=abstract, title, original title, broad terms, heading words] (1538)
 - 10 Qatar*.mp. [mp=abstract, title, original title, broad terms, heading words] (453)
 - 11 Bahrain*.mp. [mp=abstract, title, original title, broad terms, heading words] (400)
 - 12 Oman*.mp. [mp=abstract, title, original title, broad terms, heading words] (901)
 - 13 Emirate*.mp. [mp=abstract, title, original title, broad terms, heading words] (934)
 - 14 Eygpt*.mp. [mp=abstract, title, original title, broad terms, heading words] (5)
 - 15 Sudan*.mp. [mp=abstract, title, original title, broad terms, heading words] (7907)
 - 16 Algeria*.mp. [mp=abstract, title, original title, broad terms, heading words] (3629)
 - 17 Morocco*.mp. [mp=abstract, title, original title, broad terms, heading words] (4318)
 - 18 Tunis*.mp. [mp=abstract, title, original title, broad terms, heading words] (5026)
 - 19 Libya*.mp. [mp=abstract, title, original title, broad terms, heading words] (1174)

- 20 Palenstin*.mp. [mp=abstract, title, original title, broad terms, heading words] (0)
- 21 Leban*.mp. [mp=abstract, title, original title, broad terms, heading words] (1907)
- 22 Iraq*.mp. [mp=abstract, title, original title, broad terms, heading words] (3654)
- 23 Syria*.mp. [mp=abstract, title, original title, broad terms, heading words] (2685)
- 24 Yemen*.mp. [mp=abstract, title, original title, broad terms, heading words] (1481)
- 25 Iran*.mp. [mp=abstract, title, original title, broad terms, heading words] (24826)
- 26 Jordan*.mp. [mp=abstract, title, original title, broad terms, heading words] (2998)
- 27 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 (88802)
- 28 delay*.mp. [mp=abstract, title, original title, broad terms, heading words] (43482)
- 29 Late present*.mp. [mp=abstract, title, original title, broad terms, heading words] (381)
- 30 Early Present*.mp. [mp=abstract, title, original title, broad terms, heading words] (125)
- 31 postpon*.mp. [mp=abstract, title, original title, broad terms, heading words] (1325)
- 32 wait*.mp. [mp=abstract, title, original title, broad terms, heading words] (4494)
- 33 hesitat*.mp. [mp=abstract, title, original title, broad terms, heading words] (541)
- 34 defer*.mp. [mp=abstract, title, original title, broad terms, heading words] (2679)
- 35 early stage*.mp. [mp=abstract, title, original title, broad terms, heading words] (12436)
- 36 late stage*.mp. [mp=abstract, title, original title, broad terms, heading words] (2892)
- 37 advance* stage*.mp. [mp=abstract, title, original title, broad terms, heading words] (2517)
- 38 late action*.mp. [mp=abstract, title, original title, broad terms, heading words] (3)
- 39 early action*.mp. [mp=abstract, title, original title, broad terms, heading words] (39)
- 40 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 (68460)
- 41 Help seeking behavi?r.mp. [mp=abstract, title, original title, broad terms, heading words] (31)
- 42 Waiting time*.mp. [mp=abstract, title, original title, broad terms, heading words] (711)
- 43 motivat*.mp. [mp=abstract, title, original title, broad terms, heading words] (11078)
- 44 Priorit*.mp. [mp=abstract, title, original title, broad terms, heading words] (17766)
- 45 Consult*.mp. [mp=abstract, title, original title, broad terms, heading words] (17483)
- 46 health service* use*.mp. [mp=abstract, title, original title, broad terms, heading words] (471)

- 47 access to care*.mp. [mp=abstract, title, original title, broad terms, heading words] (1334)
- 48 symptom* attribution*.mp. [mp=abstract, title, original title, broad terms, heading words] (4)
- 49 Symptom* duration*.mp. [mp=abstract, title, original title, broad terms, heading words] (212)
- 50 sick role*.mp. [mp=abstract, title, original title, broad terms, heading words] (25)
- 51 seek* advice*.mp. [mp=abstract, title, original title, broad terms, heading words] (173)
- 52 barrier*.mp. [mp=abstract, title, original title, broad terms, heading words] (24371)
- 53 time factor*.mp. [mp=abstract, title, original title, broad terms, heading words] (252)
- 54 (Seek* or ask* or Look* near care or attention or assist* or help*).mp. [mp=abstract, title, original title, broad terms, heading words] (171344)
- 55 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 (227148)
- 56 40 or 55 (285843)
- 57 5 and 27 and 56 (81)

Database: Ovid MEDLINE(R) <1946 to May Week 3 2014>

Search Strategy:

-
- 1 breast cancer.m_titl. (101334)
 - 2 limit 1 to humans (98510)
 - 3 breast carcinoma*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (23605)
 - 4 breast tum?r*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (12767)
 - 5 breast neoplasm*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (215891)
 - 6 2 or 4 or 5 (218966)

- 7 Middle East.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (8255)
- 8 Eastern Mediterranean*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (999)
- 9 Saudi*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (9935)
- 10 Kuwait*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (2965)
- 11 Qatar*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (663)
- 12 Bahrain*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (609)
- 13 Oman*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1313)
- 14 Emirate*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1555)
- 15 Egypt*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1)
- 16 Sudan*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (7151)
- 17 Algeria*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (2917)
- 18 Morocco*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (4660)

- 19 Tunisia*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (7365)
- 20 Libya*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1190)
- 21 Palenstin*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (0)
- 22 Leban*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (3691)
- 23 Iraq*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (6538)
- 24 Syria*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (9581)
- 25 Yemen*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1502)
- 26 Iran*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (16773)
- 27 Jo.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1058)
- 28 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 (82258)
- 29 delay*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (365094)
- 30 Late present*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1754)

- 31 early present*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (0)
- 32 postpone*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (6731)
- 33 wait*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (36029)
- 34 hesitate*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1575)
- 35 defer*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (24623)
- 36 early stage*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (88824)
- 37 late stage*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (18725)
- 38 advance* stage*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (22584)
- 39 late action*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (23)
- 40 early action*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (0)
- 41 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 (548897)
- 42 Help seeking behavior*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (376)

- 43 Waiting time*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (5635)
- 44 motivat*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (101189)
- 45 Priorit*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (62183)
- 46 Consult*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (121298)
- 47 health service* use*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1945)
- 48 access to care*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (5492)
- 49 symptom* attribution*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (94)
- 50 Symptom* duration*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1768)
- 51 sick role*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (11286)
- 52 seek* advice*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (495)
- 53 barrier*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (153257)
- 54 time factor*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1001384)

55 (Seek* or ask* or Look* near care or attention or assist* or help*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1263475)

56 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 (2553808)

57 41 or 56 (2970886)

58 6 and 28 and 57 (203)

Database: PsycINFO <1806 to May Week 4 2014>

Search Strategy:

1 breast cancer.m_titl. (4953)

2 breast carcinoma*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (80)

3 breast neoplasm*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (6871)

4 breast tum?r*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (72)

5 1 or 2 or 3 or 4 (7039)

6 Middle East.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (1581)

7 Eastern Mediterranean*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (75)

8 Saudi*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (1119)

9 Kuwait*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (757)

10 Qatar*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (183)

11 Bahrain*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (176)

12 Oman*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (252)

- 13 Emirate*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (475)
- 14 Egypt*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (2)
- 15 Sudan*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (544)
- 16 Algeria*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (393)
- 17 Morocco*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (502)
- 18 Tunis*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (436)
- 19 Libya*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (146)
- 20 Palenstin*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (0)
- 21 Leban*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (1306)
- 22 Iraq*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (3122)
- 23 Syria*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (919)
- 24 Yemen*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (205)
- 25 Iran*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (3077)
- 26 Jordan*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (2186)
- 27 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 (15752)
- 28 delay*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (60941)
- 29 Late present*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (55)

- 30 Early Present*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (78)
- 31 postpon*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (1741)
- 32 wait*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (12151)
- 33 hesitat*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (1469)
- 34 defer*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (2766)
- 35 early stage*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (10569)
- 36 late stage*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (1497)
- 37 advance* stage*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (1037)
- 38 late action*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (2)
- 39 early action*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (68)
- 40 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 (89959)
- 41 Help seeking behavi?r.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (4327)
- 42 Waiting time*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (832)
- 43 motivat*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (128634)
- 44 Priorit*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (22380)
- 45 Consult*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (40257)
- 46 health service* use*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (1912)

- 47 access to care*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (1848)
- 48 symptom* attribution*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (130)
- 49 Symptom* duration*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (264)
- 50 sick role*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (452)
- 51 seeking advice*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (115)
- 52 barrier*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (41162)
- 53 time factor*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (444)
- 54 (Seek* or ask* or Look* near care or attention or assist* or help*).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (618557)
- 55 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 (788802)
- 56 40 or 55 (856477)
- 57 5 and 27 and 56 (23)

Recent queries in pubmed

Search	Query	Items found
#19	Search (((((((((((((((delay) OR late present*) OR early present*) OR postpon*) OR wait*) OR hesitat*) OR defer*) OR early stage*) OR late satge*) OR advance* stage*) OR late action) OR early action)) OR (((((((((((((((help seeking behavior) OR waiting time) OR motivat*) OR priorit*) OR consult*) OR health service use) OR access to care) OR symptom* attribution*) OR symptom* duration*) OR sick role) OR seek* advice*) OR barrier*) OR time factor) OR (seek OR ask OR look near care OR attention OR help OR assistance)))) AND (((((((((((((((((((Middle East) OR Eastern Mediterranean) OR Saudi*) OR Kuwait*) OR Qatar*) OR Baharain*) OR Oman*) OR Emirate*) OR Egypt*) OR Sudan*) OR Algeria*) OR Morocco*) OR Tunis*) OR Libya*) OR Palestin*) OR Leban*) OR Iraq*) OR Syria*) OR Yemen*) OR Iran*) OR Jordan*)) AND (((breast cancer) OR breast neoplasm) OR breast carcinoma) OR breast tumor)	1121
#18	Search (((((((((((((((delay) OR late present*) OR early present*) OR postpon*) OR wait*) OR hesitat*) OR defer*) OR early stage*) OR late satge*) OR advance* stage*) OR late action) OR early action)) OR (((((((((((((((help seeking behavior) OR waiting time) OR motivat*) OR priorit*) OR	2294224

	consult*) OR health service use) OR access to care) OR symptom* attribution*) OR symptom* duration*) OR sick role) OR seek* advice*) OR barrier*) OR time factor) OR (seek OR ask OR look near care OR attention OR help OR assistance))	
#16	Search (((((((((((delay) OR late present*) OR early present*) OR postpon*) OR wait*) OR hesitat*) OR defer*) OR ealry stage*) OR late satge*) OR advance* stage*) OR late action) OR ealry action	96558
#15	Search (((((((((((help seeking behavior) OR waiting time) OR motivat*) OR priorit*) OR consult*) OR health service use) OR access to care) OR symptom* attribution*) OR symptom* duration*) OR sick role) OR seek* advice*) OR barrier*) OR time factor) OR (seek or ask or look near care or attention or help or assistance)	2124387
#5	Search (((((((((((((((Middle East) OR Eastern Mediterranean) OR Saudi*) OR Kuwait*) OR Qatar*) OR Baharain*) OR Oman*) OR Emirate*) OR Egypt*) OR Sudan*) OR Algeria*) OR Morocco*) OR Tunis*) OR Libya*) OR Palestin*) OR Leban*) OR Iraq*) OR Syria*) OR Yemen*) OR Iran*) OR Jordan*	330563
#4	Search (((breast cancer) OR breast neoplasm) OR breast carcinoma) OR breast tumor	285057

Description of studies selection

No.	Study	possible	Title and abstract	Full article/study	Eligibility	Inclusion	Included
1	(Abdel-Fattah et al., 1999)	1	Perhaps	Yes	Yes	Included	1
2	(Abdelhadi, 2008)	2	Perhaps	Yes	No	Did not examine the factors associated with late-presentation breast cancer	
3	(Aboserea et al., 2011)	3	Perhaps	Yes	No		
4	(Abuidris et al., 2008)		No	No (meeting abstract)	No	Not included	
5	(Al Saad and Alsayed, 2012)	4	Perhaps	Yes	Yes	Included	2
6	(Bedwani et al., 1999)		No	No (meeting abstract)	No		
7	(Taha et al., 2013)		No				
8	(Corbex, 2009)	5	Perhaps	Yes	Yes	Included	3
9	(Corbex and McEwan, 2010)	6	Perhaps	None retrievable			
10	(Doumit et al., 2010)		No				
11	(Weber et al., 2012)		No				
12	(Elzawawy, 1999)	7	Perhaps	Yes	Yes	Included	4
13	(El-Zawawy, 1991)	8	Perhaps	Yes	Yes	Included	5

14	(Elzawawy, 1987)	9	Perhaps	None retrievable			
15	(Elzawawy et al., 2008)	10	Perhaps	Yes	No	No uni or multivariate analysis	
16	(Ermiah et al., 2012)	11	Perhaps	Yes	Yes	Included	6
17	(Fakhro et al., 1999)		No				
18	(Fink et al., 2010)		No				
19	(Landolsi et al., 2010)	12	Perhaps	Yes	No	No evidence of univariate or multivariate analysis	
20	(Lannin et al., 1998)		No				
21	(Maamri, 2012)		No				
22	(McEwan et al., 2014)	13	Perhaps	Yes	Yes	Included	7
23	(Montazeri et al., 2010)		Perhaps	Yes	Yes	Included	8
24	(Montazeri et al., 2010)		No	Conference abstract			
25	(Mousa et al., 2011)	14	Perhaps	Yes	Yes	Included	9
26	(Omar et al., 2003)		No				
27	(Otieno et al., 2010)		No				
28	(Otieno et al., 2010)		No				
29	(Rastad et al., 2012)	15	Perhaps	Yes	Yes	Included	10
30	(Robinson et al., 1986)		No				
31	(Shaheen et al., 2011)		No				
32	(Spenser et al., 1989)		No				
33	(Taha et al., 2012)		No				

34	(Ahmad, 2004)	16	Perhaps	Yes	No	No evidence of univariate or multivariate analysis	
35	(Harirchi et al., 2005)	17	Perhaps	Yes	Yes	Included	11
36	(Stapleton et al., 2011)	18	Perhaps	Yes	Yes	Included	12
37	(Ismail et al., 2013)		Perhaps	No	No	No evidence of univariate or multivariate analysis	

Appendix B: The University of Leeds Ethical review

Faculty of Medicine and Health
Research Office

Room 10.110, Level 10
Worsley Building
Clarendon Way
Leeds LS2 9NL

T (General Enquiries) +44 (0) 113 343 4361
F +44 (0) 113 343 4373



UNIVERSITY OF LEEDS

Sultana Alhurishi
c/o Dr Jennifer Lim
Leeds Institute of Health Sciences
University of Leeds
Charles Thakrah Building
101 Clarendon Road
LEEDS LS2 9LJ

21 April 2011

Dear Sultana

Re ref no: HSLTLM/10/015

Title: Understanding female breast cancer late presentation in Riyadh, Saudi Arabia

I am pleased to inform you that the above research application has been reviewed by the Leeds Institute of Health Sciences and Leeds Institute of Genetics, Health and Therapeutics and Leeds Institute of Molecular Medicine (LIHS/LIGHT/LIMM) joint ethics committee and following receipt of the amendments requested, I can confirm a favourable ethical opinion on the basis described in the application form, protocol and supporting documentation as submitted at date of this letter.

Please notify the committee if you intend to make any amendments to the original research as submitted at date of this approval. This includes recruitment methodology and all changes must be ethically approved prior to implementation. Please contact the Faculty Research Ethics and Governance Administrator for further information (r.e.desouza@leeds.ac.uk)

Ethical approval does not infer you have the right of access to any member of staff or student or documents and the premises of the University of Leeds. Nor does it imply any right of access to the premises of any other organisation, including clinical areas. The committee takes no responsibility for you gaining access to staff, students and/or premises prior to, during or following your research activities.

Please note: You are expected to keep a record of all your approved documentation, as well as documents such as sample consent forms, and other documents relating to the study. This should be kept in your study file, which should be readily available for audit purposes. You will be given a two week notice period if your project is to be audited.

It is our policy to remind everyone that it is your responsibility to comply with Health and Safety, Data Protection and any other legal and/or professional guidelines there may be.

I wish you every success with the project.

Yours sincerely

A handwritten signature in cursive script that reads "Laura Stroud".

**Professor Alastair Hay/Mrs Laura Stroud/Dr David Jayne
Chairs, LIHS/LIGHT/LIMM REC**

Appendix C: SNCR acceptance for the study

KINGDOM OF SAUDI ARABIA
MINISTRY OF HEALTH
SAUDI CANCER REGISTRY



المملكة العربية السعودية
وزارة الصحة
السجل السعودي للأورام

Sulfana Alhurishi
PhD Student
Leeds Institute of Health Sciences

27 February 2011
Ref: SCR 067/32

Dear Dr. Al Hurishi

With reference to your data request dated January 29, 2011, regarding your research project; an epidemiological study of factors influencing breast cancer stage at diagnosis in Riyadh, Saudi Arabia. Please, find attached our data on breast cancer cases diagnosed in the Kingdom of Saudi Arabia from the years 1994 through 2006.

Should you require any further information or assistance, please do not hesitate to contact our office at 442-3929 or 442-3430.

Sincerely,


Dr. Shouki Bazarbashi
Chairman
Saudi Cancer Registry

Copy to: Chronofile
Data request log
HE/mm

Appendix D: POM of factors associated with advanced breast cancer stages at diagnosis for 10663 female breast cancer patients.

Factors	Adjusted ordinal regression	
	<i>P</i>	POR, (95% CI)
Age		
Unknown	0.131	0.487, (0.191–1.123)
18-39	0.060	0.91, (0.838–1.003)
40-49	0.002	0.870, (0.797–0.948)
50+	1 (Reference)	
Year of diagnosis		
1994-1996	0.000	1.615, (1.371–1.901)
1997-1999	0.000	1.310, (1.180–1.454)
2000-2002	0.249	1.057, (0.961–1.163)
2003-2006	1 (Reference)	
Place of residence		
Unknown	0.017	1.233, (1.038–1.464)
Other regions	0.000	1.21, (1.102–1.329)
Regions with advanced oncology care	1 (Reference)	
Nationality		
Unknown	0.952	0.989, (0.702–1.393)
Non-Saudi	0.000	0.855, (0.783–0.932)
Saudi	1 (Reference)	
Marital status		
Unknown	0.000	0.788, (0.692–0.896)
Unmarried	0.621	1.030, (0.913–1.162)
Married	1 (Reference)	
Test for parallel lines: Chi-Square=324.647, df=24 & P=0.000		
Pseudo R²: Cox and Snell=0.010, Nagelkerke=0.011 & McFadden=0.005		

Appendix E: Interview guide

Before the interview started

The researcher will introduce herself. I am Sultana Alhurishi, a PhD student at the University of Leeds. She will introduce the study " Understanding female breast cancer late presentation in Riyadh, Saudi Arabia, the role of interviewer, the confidentiality and options of tape recording will be also mentioned. After that the consent form will be obtained.

Firstly, the participant will be asked about her:

- Age
- Marital status
- No. of children.....
- Educational level
- Employment status
- Family history of breast cancer/cancer

Secondly, she will be asked about the key themes to explore. Key themes are:

(1) Experience and perceptions of body change(s)

- Describe the nature of first symptom(s) noticed?
- How did you discover the body changes? E.g. discover it yourself when you take a shower.
- What did you think when you discovered these changes?
 - Probes: these symptoms were not serious, can go, are cancer, or require medical attention.

(2) Knowledge and symptoms recognition

- What do you think about breast cancer?
- What did you know about breast cancer what you did not before you notice body changes?
 - Probes: Types of BC symptoms: lump or thickening, discharges from nipple, changes in breast size or shape of the breast, dimpling of the skin ,changes in the nipple shape, rash on the nipple or surrounding area, swelling or lump in the armpit.
- What were the sources of you knowledge?

(3) Health seeking behaviour

- Who was the first medical person consulted? And why?
- What encouraged you to seem medical care?
 - Probes: e.g. pain, symptoms become worse, others recommendation
- What do you think the facilitators to go for medical services?
 - Probes: what motivate you/help you to visit the doctor? E.g. treatment availability.
- What do you think barriers to go for health services immediately when notice symptoms change?

- Probes: e.g. of the barriers: competing priorities, fear of the diagnosis, fatalism of the disease

(4) Social network

- Did you share your symptom(s) or take about it with others? If yes,
 - Probes: talking with family or friends.
- Who were they?
- What were their advices?
- What support they provided?
- Do they help you to go for medical treatment

(5) Symptoms management:

- How did you manage these symptoms and deal with it?
 - Probes: what did you to manage these symptoms e.g. deny it/ignore it, use alternative medicine, or try to search for information about it.

(6) Time line of seeking medical care (Estimation of the seeking health care period although the recall bias is expected)

- When did you notice first body change?
- When did you think that body change (s) is illness?
- When did you decide to consult someone?
- When did you contact health care?

(7) Health care services

- How do you think the health care services affect your decision to seek medical care?
 - Probes: Are they available, accessible, and acceptable at the time when you feel about body change.
- Do you usually seek medical care when you notice body change?

(8) Health promotion and education

- What do you think is missing and could be done to improve the early presentation of breast cancer?
- What are your suggestions for health education and promotional interventions to improve early presentation of breast cancer?

Last question

- Is there any think you want to add?

Thanks for your time, and participation.

Duration of the interview (start at: _____ finish at: _____)

دليل المقابلة

عنوان الدراسة: فهم العرض المتأخر لسرطان الثدي للنساء في الرياض بالمملكة العربية السعودية: دراسة نوعية.

مقدمة

هذا النموذج للأسئلة التي سوف تطرح في المقابلات للمشاركات في الدراسة النوعية: فهم العرض المتأخر لسرطان الثدي للنساء في الرياض بالمملكة العربية السعودية، تقوم فيه الباحثة بطرح الأسئلة شفهيًا على المشاركات مع إمكانية إعادة صياغة السؤال لتوضيح المعنى ودمج الأسئلة عند الحاجة أو تغيير ترتيبها. و قبل البدء بالمقابلة سوف تعرّف الباحثة بنفسها، عنوان الدراسة ، دور الباحثة، سرية المقابلة، و خيار التسجيل الصوتي. بعد ذلك سوف تؤخذ الموافقة الخطية من المشاركة.

❖ معلومات شخصية

العمر	5
الحالة الاجتماعية	6
عدد الأطفال	7
المستوى التعليمي	8
الوظيفة	9

❖ وجود تاريخ عائلي للسرطان و سرطان الثدي

2

❖ بعد ذلك سوف يتم سؤالها عن المواضيع التالية:

الخبرة و ادراك تغييرات الجسم

- في بداية التغييرات في الثدي صفني أول عرض لاحظته؟
- كيف اكتشفت هذا العرض؟ مثلًا أثناء الاستحمام
- ما هي الفكرة التي خطررت ببالك عندما اكتشفت هذا العرض (أو الاعراض)؟ مثلًا: هذه الاعراض مرض شيء عارض، من الممكن أن تذهب، شيء طبيعي، هي سرطان، أو أعراض تحتاج للرعاية الطبية.

المعارف و تمييز الأعراض

- ما الفكرة التي لديك عن سرطان الثدي؟
- ما المعلومات التي كانت لديك عن سرطان الثدي و ما الذي كنت تجهلينه؟ مثلًا الأعراض
- ما هي مصادر المعلومات لديك و من أين حصلت عليها؟ مثلًا محاضرة، كتاب، صديقة، انترنت، أو طبيب.

3

طلب الرعاية الصحية

4

- هل من عادتتك طلب الرعاية الصحية عند ملاحظة أي تغيير في جسمك؟
- عند ملاحظتك لأول عرض، من هو أول طبيب (أو مختص طبي) طلبت استشارته؟ و لماذا تم اختياره بالذات؟ مثلًا الطبيب العام في المركز الصحي.
- ما الأسباب التي شجعتك لطلب الرعاية الصحية؟ مثلًا الألم، الأعراض تزداد سوء، أو توصية الآخرين.
- باعتقادك ما هي العوامل المساعدة على الذهاب للمرافق الصحية مباشرة عند ملاحظة أي أعراض ؟ مثلًا توفر العلاج
- ما العوامل التي تعيقك من الذهاب فورًا إلى المرافق الصحية عند ملاحظة أي أعراض؟ مثلًا تحديد الأولويات ، الخوف من المرض أو اكتشافه.

الشبكة الاجتماعية

5

- عندما لاحظت الأعراض هل تحدثت مع شخص آخر غير المختص الطبي عن هذه الأعراض؟ مثلًا أحد أفراد العائلة أو الأصدقاء. إذا كانت الإجابة بنعم
- مع من تكلمت؟ مثلًا أول شخص ، ثاني شخص و هكذا.
- بماذا نصحك؟مثلًا ماذا قال لك الشخص الأول، الثاني و هكذا.
- هل قدم لك مساعدة للذهاب للعلاج؟ و كيف ساعدك؟

التحكم في الأعراض

- كيف تعاملت مع تغييرات الثدي منذ ملاحظتك للأعراض و حتى أول استشارة طبية قمت بها؟ مثلا حاولت تجاهلها، استخدمت علاجات الطب البديل، حاولت البحث عن معلومات عن هذه الأعراض.

الجدول الزمني لطلب الرعاية الصحية

- منذ متى لاحظت الأعراض ؟
- متى أحسست أنها مشكلة صحية؟
- متى استشرت الفريق الطبي؟
- متى قررت استشارة أحد آخر غير الفريق الطبي؟

خدمات الرعاية الصحية

- كيف أثرت الخدمات الصحية في قرارك لطلب الرعاية الصحية من المرفق الصحي؟ مثلا: متوفرة، متاحة عندما أحسست بتغييرات في جسمك؟

التعزيز و التثقيف الصحي

- برأيك ما القصور الموجود و يمكن تحسينه لتسهيل الاكتشاف المبكر لسرطان الثدي؟ مثلا نقص المعارف عن المرض
- ما هي مقترحاتك لتدخلات التثقيف و تعزيز الصحة لتحسين الاكتشاف المبكر لسرطان الثدي؟

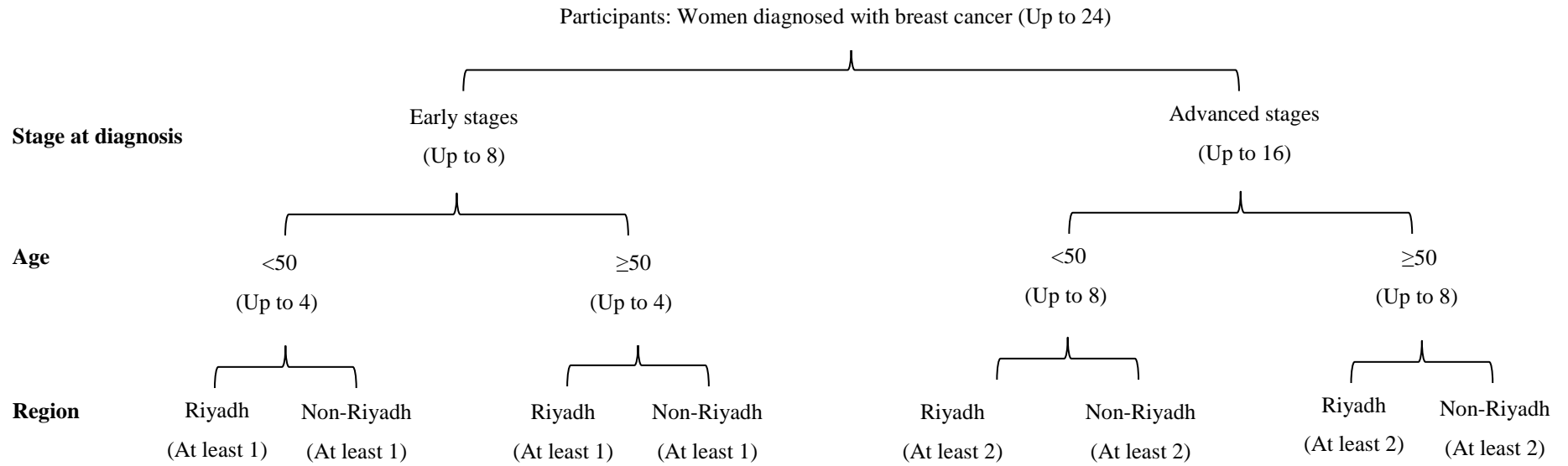
آخر سؤال

- هل ترغبين في إضافة أي شيء آخر؟

شكرا على وقتك و مشاركتك.

مدة المقابلة: (بدأت : _____ انتهت: _____)

Appendix F: The planned sampling frame



Appendix G: Information sheet

Date 29 April 2011
Version 3



Participant Information Sheet

Research title: Understanding female breast cancer late presentation in Riyadh, Saudi Arabia: a qualitative study

Dear Participant,

You are invited to participate in a Ph.D. research project. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask the researcher if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this information. If you decide to participate, you will be given a copy of this information sheet.

Background

Breast cancer is the commonest female cancer in Saudi Arabia and often diagnosed at advanced stages. It is not entirely known why some women are presenting their symptoms late while others early to the doctors. This study is attempting to investigate the factors affecting patients presenting themselves to the doctors after they discovered a breast lump or other symptoms.

What is the purpose of this study?

This study aims to understand the factors leading to breast cancer late presentation after self-recognition of breast cancer symptoms in Riyadh, with the intention to design health promotion intervention(s) to improve the early presentation of breast cancer.

We will be carrying out face to face interviews with breast cancer patients who were recently diagnosed with the disease.

Why I have been chosen?

You have been chosen because of your diagnosis and your experience which might help us to understand how to improve the health services provided and plan health promotion interventions.

Do I have to take part in this study?

It is up to you to decide whether or not to take part. If you do decide to take part, you will be asked to sign a consent form. You can still withdraw at any time without this affecting your present or future care. You do not have to give a reason for your withdrawal.

What will happen to me if I take part?

If you decide to participate in the study you will be asked to be interviewed only once. The interview will be in a private place in the hospital during your hospital visit. Once you agreed to participate in this study, we will arrange a convenient time with you to conduct the

interview. We will obtain your consent to take part in this study before the start of the interview. The interview may last up to 90 minutes. During the interview you will be asked questions about when and how you discovered your breast cancer. You will also be asked about your experience from self-discovery of your illness until you first contacted your doctor.

It is expected that you will help to agree on the date of the interview, and answer the questions about your experience of your illness. You have a right to refuse to answer any question or stop the interview at any time you decide.

What are benefits from participating in this study?

There is no immediate benefit for those who participated in this study. It is likely that this study will help in understanding the reasons women delay breast cancer presentation. This information is needed for designing and developing interventions to improve early presentation of breast cancer.

What will happen to the result of the research study?

The information that you give the researcher will be used to better understand the process of seeking medical care amongst breast cancer patients. The results will be written up in the form of a Ph.D. thesis and possibly published in research reports, journals or academic books. It may also be disseminated in seminars and conferences.

Will my responses be kept confidential?

All the information collected from you will be kept strictly confidential. All data collected will be anonymised and nobody will be able to identify you in any report or publication. Research data will be accessed only by the researcher and research supervisors. Paper copies will be kept in a locked file cabinet in a locked office and electronic data will be kept on encrypted and password protected computers.

Will the interview be audio recorded?

The interview can be audio recorded only with your approval. The recording is used because it eases data transcription. The recording will be destroyed immediately after all the interviews are transcribed.

You can still participate even though you refuse to be audio-recorded. In this case the researcher will be handwriting your responses in notes during the interview. In any case, if you are not able to provide written consent, your consent will be taken using the audio-tape recorder.

Who is organising this study?

This study is a part of a Ph.D. at the University of Leeds.

Who has reviewed this study?

This study has been reviewed by the Ethics Committee at the University of Leeds and your hospital. If you have any questions, concerns or complaints contact the researcher or her lead supervisor.

Researcher

Sultana Alhurishi

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Lead Supervisor

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لتاريخ 29 ابريل 2011

الإصدار: 3



UNIVERSITY OF LEEDS

المشاركة ورقة معلومات

عنوان الدراسة: فهم العرض المتأخر لسرطان الثدي للنساء في الرياض بالمملكة العربية السعودية: دراسة نوعية

عزيتي المشاركة

انت مدعوة للمشاركة في مشروع بحثي لمرحلة الدكتوراه. قبل أن تقرري، من المهم بالنسبة لك أن تفهمي لماذا أعد البحث وما الذي يشتمل عليه. يرجى أخذ الوقت الكافي لقراءة المعلومات التالية بعناية ومناقشته مع الآخرين إذا رغبت. أسألي الباحثة إذا كان هناك أي شيء غير واضح أو إذا كنت ترغبين في مزيد من المعلومات. خذي الوقت الكافي حتى تقرري ما إذا كنت ترغبين في المشاركة أو لا. شكرا لك على قراءة هذه المعلومات. إذا قررت المشاركة، سيتم إعطاؤك نسخة من هذه الورقة.

تقديم

سرطان الثدي هو أكثر أنواع السرطان لدى النساء في المملكة العربية السعودية وغالبا ما يتم تشخيصه في مراحل متقدمة. من غير المعروف تماما لماذا تعرض بعض النساء للأطباء أعراض المرض في وقت متأخر في حين أن أخريات منهن يعرضنها في وقت مبكر. هذه الدراسة هي محاولة لاستقصاء العوامل التي تؤثر على المريضات الاتي يقدمن أنفسهن للأطباء بعد اكتشاف وجود ورم في الثدي أو أعراض أخرى.

ما الهدف من هذه الدراسة ؟

تهدف هذه الدراسة إلى فهم العوامل التي تؤدي إلى عرض سرطان الثدي في وقت متأخر بعد الإدراك الذاتي له من قبل المريضة في الرياض، لغرض تصميم تدخلات لتعزيز الصحة تهدف لتحسين العرض المبكر لسرطان الثدي. وستجرى مقابلات وجها لوجه مع مريضات سرطان الثدي اللاتي تم تشخيص المرض لديهن مؤخرا.

لماذا تم اختياري؟

تم اختيارك بسبب التشخيص وخبرتك التي قد تساعدنا على فهم كيفية تحسين الخدمات الصحية المقدمة وتصميم تدخلات لتعزيز الصحة.

هل يجب علي المشاركة في البحث؟

الأمر متروك لك لتقرري ما إذا رغبت بالمشاركة أو لا. إذا قررت المشاركة سوف يطلب منك التوقيع على استمارة الموافقة. يمكنك الانسحاب في أي وقت دون أن يؤثر هذا على الرعاية المقدمة لك في الحاضر أو المستقبل. ولا يجب عليك إعطاء سبب للانسحاب.

ماذا سيحدث لي إذا شاركت في البحث؟

إذا قررت المشاركة في هذه الدراسة سوف يطلب منك إجراء مقابلة مرة واحدة فقط. وسوف تكون المقابلة في مكان خاص في المستشفى أثناء زيارتك لها. عندما توافقين على المشاركة في هذه الدراسة، سوف يتم ترتيب وقت مناسب معك لهذه المقابلة. سوف نحصل على موافقتك على المشاركة في هذه الدراسة قبل بدء المقابلة. المقابلة قد تستغرق وقتاً ربما يصل إلى 90 دقيقة. خلال المقابلة سوف يتم سؤالك حول متى وكيف اكتشفت سرطان الثدي وعن تجربتك منذ ان اكتشفت المرض بشكل ذاتي حتى أول اتصال لك بالطبيب. وسيتم على الأحرى، الاتفاق معك على موعد المقابلة، والإجابة على الأسئلة حول تجربتك مع المرض. كما ان لك الحق في رفض الإجابة عن أي سؤال أو التوقف عن المقابلة في أي وقت شئت.

ماالمنفعة من مشاركتي في هذا البحث؟

لا يوجد منفعة مباشرة لمن يشارك في هذه الدراسة. من المحتمل أن تساعد هذه الدراسة في فهم الاسباب المؤدية لتأخر عرض المريضات بسرطان الثدي انفسهن على الأطباء. وهذه المعلومات نحتاجها لتصميم تدخلات لتحسين العرض المبكر لسرطان الثدي.

ماذا سيحدث لنتيجة البحث؟

المعلومات التي سوف تدلين بها للباحثة سوف تساعد على فهم عملية طلب مريضات سرطان الثدي للرعاية الصحية. سوف نكتب نتائج البحث في رسالة دكتوراه، كما أنه من المحتمل أن تنشر في تقارير بحثية أو مجلات أو كتب علمية. ومن الممكن أيضاً أن تنشر في مؤتمرات و حلقات المناقشة العلمية.

هل ستحفظ استجاباتي بشكل سري؟

جميع البيانات التي سوف تجمع سوف تحفظ بسرية تامة. وسوف تكون مجهولة الهوية و لا يستطيع أحد التعرف على هويتك في أي تقرير أو اصدار. بيانات البحث سوف تطلع عليها الباحثة و المشرفين عليها فقط. سيتم الاحتفاظ بالنسخ الورقية في درج مقفل في مكتب مقفل و البيانات الالكترونية سوف يحتفظ بها في حاسبات آلية مزودة ببرنامج حماية و كلمة سر.

هل ستسجل المقابلة صوتياً؟

في حال موافقتك سيتم تسجيل المقابلة صوتياً. الغرض من التسجيل الصوتي هو تسهيل عملية تفرغ البيانات. وهذا التسجيل سوف يتم التخلص منه مباشرة بعد تفرغ كل المقابلات. وممن الممكن أن تشاركي في البحث حتى لو لم ترغبي في أن يتم تسجيل مقابلتك صوتياً وفي هذه الحالة سوف تقوم الباحثة بكتابة استجاباتك في مذكرات خلال المقابلة. وفي حال عدم مقدرتك على اعطاء موافقة خطيه لأي سبب سوف يتم تسجيل موافقتك صوتياً.

من ينظم هذه الدراسة؟

هذه الدراسة جزء من رسالة لنيل درجة الدكتوراة في جامعة ليدز

من قام بمراجعة هذه الدراسة؟

روجعت هذه الدراسة من قبل لجنة اخلاقيات البحث في جامعة ليدز والمستشفى الذي تراجعين بها. وفي حال كان لديك أي اسئلة او استفسارات او شكاوى يمكنك الإتصال بالباحثة او المشرف الرئيس.

الباحثة

سلطانة الحريشي

طالبة دكتوراة في جامعة ليدز
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Appendix H: Consent form

Consent Form

نموذج الموافقة على المشاركة في البحث

Dated 29 April 2011
Version: 3



UNIVERSITY OF LEEDS

التاريخ 29 ابريل 2011
الاصدار: 3

Research title: Understanding female breast cancer late presentation in Riyadh, Saudi Arabia: a qualitative study.

عنوان الدراسة: فهم العرض المتأخر لسرطان الثدي للنساء في الرياض بالمملكة العربية السعودية: دراسة نوعية

Initial the box if you agree with the statement to the left

اكتب الحروف الاولى من اسمك في حالة موافقتك على العبارة المترجمة في جهة اليسار

Statement	Initial الحروف الاولية	العبارة
1- I confirm that I have read and understood the information sheet (Dated 29/4/2011, version 3), explaining the above research project and I have had the opportunity to ask questions about the study.	<input type="checkbox"/>	1- أقر بأنني قد قرأت وفهمت ورقة المعلومات (بتاريخ 29 / 4 / 2011، الاصدار 3)، التي تشرح المشروع البحثي أعلاه، واتيحت لي الفرصة لطرح الأسئلة حول الدراسة.
2- I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason and without there being any negative consequences. In addition, should I not wish to answer any particular question or questions, I am free to decline.	<input type="checkbox"/>	2- أفهم أن مشاركتي تطوعية وأن لي كامل الحرية في الانسحاب في أي وقت دون إبداء أي سبب ودون ان تكون هناك عواقب سلبية. وبالإضافة إلى ذلك، لدي كامل الحرية في عدم الرد على أي سؤال أو أسئلة معينة في حالة عدم رغبتني في ذلك.
3- I understand that my responses will be kept strictly confidential. I give permission for members of the research team to have access to my anonymised responses. I understand that	<input type="checkbox"/>	3- أعلم بأن ردودي سيتم الاحتفاظ بها بسرية تامة. وأعطي فريق البحث الإذن الكامل بالاطلاع عليها مجهولة الهوية. و أفهم أن اسمي لن يرتبط بمواد البحث و لن يشار إليه و لن يستطيع أحد التعرف على في التقرير أو التقارير التي تنتج من البحث.

my name will not be linked with the research materials, and I will not be identified or identifiable in the report or reports that result from the research.		
4- I agree for the data collected from me to be used in the PhD study which is part of a doctoral thesis.	<input type="checkbox"/>	4- أوافق على أن تستخدم البيانات التي تم جمعها مني في الدراسة البحثية التي تعد جزء من رسالة لنيل درجة الدكتوراه.
5- I agree for the interview to be audio-tape recorded.	<input type="checkbox"/>	5- أوافق على ان يتم تسجيل المقابلة صوتيا.
6- I agree to take part in the above research project.	<input type="checkbox"/>	6- أوافق على المشاركة في هذا البحث المذكور اعلاه.

Name of participant اسم المشاركة Date التاريخ Signature التوقيع

(or legal representative رسميا يمثلها رسميا)

Name of person taking consent Date التاريخ Signature التوقيع

اسم الشخص الذي أخذ هذه الموافقة

(إذا كان مختلفا عن الباحث الرئيس if different from lead researcher)

To be signed and dated in presence of the participant في بحضور المشاركة في البحث

Lead researcher الباحث الرئيس Date التاريخ Signature التوقيع

To be signed and dated in presence of the participant في بحضور المشاركة في البحث

Researcher الباحثة

Sultana Alhurishi سلطانة الحريشي

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Telephone/الهاتف : 00441133431688

Appendix I: KFSH&RC ethical approval



مستشفى الملك فيصل التخصصي ومركز الأبحاث
King Faisal Specialist Hospital & Research Centre
مؤسسة عامة - Gen. Org.

OFFICE OF RESEARCH AFFAIRS
MBC ☎ 03, Fax ☎ 27894, Ext ☎ 32933

INTERNAL MEMO

TO: Sultana Al Hurishi, PhD Student
MKO/saah@leeds.ac.uk
Leeds Institute of Health Sciences
University of Leeds

DATE: 26 Shaban 1432
27 July 2011

FROM: Muhammad M. Hammami, MD, PhD, FACP, FACE
Chairman
Research Ethics Committee

REP: ORA/0936/32

SUBJECT: Project # 2111 078
Understanding Female Breast Cancer late Presentation in Riyadh, Saudi Arabia: A
Qualitative Study

The above referenced proposal was reviewed by the Research Ethics Committee (REC) on 27 July 2011.

It is my pleasure to inform you that the Committee has recommended the proposal for approval provided the requested items (emailed to you previously) are received; and I would like to take this opportunity to congratulate you on behalf of the Research Advisory Council.

Please be informed that in conducting this proposal, the Investigators are required to abide by the rules and regulations of the Government of Saudi Arabia, KFSH&RC, and the RAC. Further, you are required to submit a Final Report by 27 June 2012 to the Office of Research Affairs (ORA); so it can be reviewed by the Committees without lapse in approval. The approval of this proposal will automatically be suspended on 27 July 2012 pending the acceptance of the Report. You also need to notify the ORA as soon as possible in the case of any amendments to the project, termination of the study and any event or new information that may affect the benefit/risk ratio of the proposal.

Please observe the following:

- 1 Personally identifying data should only be collected when necessary for research;
- 2 The data collected should only be used for this proposal;
- 3 Data should be stored securely so that only a few authorized users are permitted access to the database;
- 4 Secondary disclosures of personally identifiable data are not allowed;
- 5 Should there be a need to contact the research subjects for follow-up information, you will need to seek the authorization of the RAC prior to such contact.

We wish you every success in your research endeavours

cc: Email: Lina@leeds.ac.uk
Director, Patient Relations Department

ORA
A
C

E-mail: ora@kfsr.edu.sa

Appendix J: University of Leeds ethical research practice audit



Faculty of Medicine and Health
School of Medicine Research Ethics Committee
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Tel: +44 (0) 113 343 4361

19 February 2014

Abeer H. Al Sayed, MD
Supervisor
Office of Research Affairs (MBC 03)
King Faisal Specialist Hospital and Research Centre
PO Box 3354
Riyadh 11211
Saudi Arabia

Dear Dr Sayed

Ref no: HSLTLM/10/015

Title: Understanding female breast cancer late presentation in Riyadh, Saudi Arabia – Ms Sultana Alhurishi

Following on from your email correspondence with Ms Alhurishi, I have today personally audited the participant consent forms for the above study.

The forms are held in a locked cupboard in a locked room. I can confirm that all 19 consent forms have been correctly completed and Ms Alhurishi's transcripts of interviews have been appropriately anonymised in her PhD thesis.

I am happy that Ms Alhurishi has observed appropriate standards of confidentiality in her treatment of the consent forms, recorded interviews and transcribed data.

I trust this will satisfy your ethics committee's requirements and you will be able to accept Ms Alhurishi's progress report.

Please do not hesitate to contact me if you require any further information

Yours sincerely

A handwritten signature in black ink, appearing to read "Roger Parslow".

Dr Roger Parslow
Co-Chair, School of Medicine Research Ethics Committee, University of Leeds

cc: Professor Robert West
Dr Barbara Potrata