Improving Surgical Outcomes in Low and Middle-Income Countries through Surgical Technology Innovation

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Abstract

Improving global surgical care is essential to achieve the World Health Organisation's goal of Universal Health Coverage by 2030. In 2015 the Lancet Commission on Global Surgery recognised that novel surgical technologies and innovations are key enabling factors in this aim. Globally, only 9.8% of surgical technology innovation reach clinical trial and less than 1% achieve widespread adoption. The aim of this Thesis was to investigate how surgical innovation occurs in LMICs, the barriers to innovation, strategies to increase innovation research capacity and capability, and the steps needed to increase the efficiency of clinical translation and adoption of surgical innovation for LMICs globally.

Data from two surgical trials, qualitative studies involving healthcare staff, surgeons, and researchers from within LMICs, and the presentation of a novel Global Surgical Innovation IDEAL Sub-Framework provide a compelling pathway to improve innovation evaluation and adoption in global surgery. By combining literature in the field with a comprehensive range of mixed methodologies, it can be concluded that given the significant barriers, it is important to explore context-specific evaluation approaches, with in-built researcher training and qualitative methodologies along the innovation pathway. Importantly, technology enhanced learning tools such as virtual reality appear feasible in low-resource settings and will be important in addressing the substantial human resource barrier. This work also led to a Sub-Framework that guides the evaluation and appropriate adoption of technology and innovation in global surgery and aims to be widely applicable across contexts. This can now be used to inform future work, in which the Sub-Framework itself can be tested, iterated, and validated in wider populations and contexts, to improve the subsequent dissemination of innovation in global surgery.

Abbreviations and Definitions

AKA	Above knee amputation
BKA	Below knee amputation
COMAHS	College of Medicine and Health Sciences
DALY	Disability-adjusted life year
DAC	Development Assistance Committee
EWH	Engineering World Health
FGD	Focus group discussion
FIXT	Feasibility of Ilizarov frame fiXation for closed Tibial fractures in Sierra Leone
HTA	Health Technology Assessment
HIC	High income country
ICTRP	International Clinical Trials Registry Platform
IDEAL	Idea, Development, Exploration, Assessment, Long-term study
IDEAL-D	IDEAL for devices
LMIC	Low and middle-income country
GHRG-ST	Global Health Research Group in Surgical Technologies
GILLS	Gas Insufflation Less Laparoscopic Surgery
MCQ	Multiple choice question
MRC	Medical Research Council
NIHR	National Institute for Health and Care Research
NGO	Non-governmental organisation
ODA	Official development assistance
OSAT	Objective structure assessment of technical skills
PRISMA-P	Preferred Reporting Items for Systematic Reviews and Meta-analysis Protocols
QALY	Quality-adjusted life year
RCT	Randomised controlled trial

SSI	Semi-structured interviews
THET	Tropical Health and Education Trust
UHC	Universal Health Coverage
UK	United Kingdom
US	United States (of America)
VITAL	Virtual reality technology to Improve surgical Training in SierrA Leone
VR	Virtual Reality
WBLT	Web-based learning tool
WHIG	WHO Health Innovation Group
WHO	World Health Organisation

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1 Introduction

Innovation in global surgery is a complex process that demands a range of study designs and methodologies to develop technology interventions, as well as context-specific implementation and adoption strategies. Generating evidence to inform the evaluation, adoption, and dissemination of innovation in global surgery is essential to ensure efficient uptake and adoption. There are unique and substantial barriers to evidence generation, and this leads to poor adoption of surgical technologies and innovations in low and middle-income countries (LMICs). Understanding these barriers, and exploring strategies to overcome them, may improve the surgical innovation pathway in these contexts. This Chapter describes the role technology and innovation plays in upscaling global surgical care and focuses on innovation approaches that are particularly applicable in global surgery. A commentary on current strategies to evaluate surgical innovation in both high-income countries (HICs) and LMICs is then provided. The extent of the evidence around how surgical innovation is currently evaluated in LMICs will be discussed in the context of complex interventions and the challenges of conducting global health research. Finally, the structure of this doctoral body of work will be outlined to describe a compelling pathway to improve evaluation of innovation in global surgery.

1.1 Global surgery

Surgery plays an essential role in the management of many medical conditions, reducing death and disability following trauma and complications of childbirth, treating life threatening infection and organ dysfunction, palliating chronic disease, and is central to the treatment of many cancers. Global surgery refers to a globally orientated conceptualisation of a synthesised field combining clinical surgical care with public

health and epidemiological planning, policy making, intervention delivery, data collection and advocacy (1,2). Academic global surgery aims to contribute to this field through augmenting this work via scientific research. Global surgery refers to just that, surgery across the globe, and so is not limited to exploration of the topic in LMICs. However, because the unmet surgical need and public health challenge is often greater in LMICs, much focus is placed on work in these countries. In recent years, several landmark publications and a World Health Assembly 2015 resolution have strengthened the case for global surgery as a vital component of Universal Health Coverage (UHC) (3), highlighting that nearly one-third of the global burden of disease is attributed to conditions treatable by surgery (4,5); less than 6% of all surgical operations are carried out in LMICs where over a third of the world's population live, and a huge scale up in surgical services and workforce is needed urgently (1); surgery is a cost-effective global public health strategy and the economic return on investment is substantial (5,6); and that 5 billion people lack access to safe, timely and affordable surgical care (1). These concepts are summaries for surgical care by the Lancet Commission on Global Surgery in their five key messages (1):

1. **5 billion people do not have access to safe, affordable surgical and anaesthesia care when needed felt worst by populations in LMICs.**
2. **143 million additional surgical procedures are needed in LMICs each year to save lives and prevent disability.**
3. **33 million individuals face catastrophic health expenditure due to payment for surgery and anaesthesia care each year, and the burden is felt most heavily by those in poverty.**
4. **Investing in surgical services in LMICs is affordable, saves lives, and promotes economic growth.**
5. **Surgical and anaesthesia care should be an integral component of a national health system in countries at all levels of development.**

The World Health Organisation (WHO) are coordinating efforts to achieve UHC by 2030 as a central component of the wider United Nations 2030 Agenda for Sustainable Development (7). UHC results from the entirety of the population having access to all essential healthcare services at a price they can afford. This requires the necessary workforce, technology, equipment, resources, infrastructure, and finance systems. Surgery is heavily reliant on technology and a trained workforce, and is interdependent on several other specialties including radiology, pathology, anaesthetics, obstetrics, intensive and emergency care. Targeted strengthening of surgical services may result in collateral strengthening of these specialties, including medical technologists and engineering (8). Global advocacy is required to strengthen the case for global surgery has been solidified as a public health intervention essential to achieving UHC by 2030 (1).

1.2 Surgical technologies in low-resource settings

Healthcare technologies is a broad term that includes examples ranging from automobile seatbelts to vaccinations (Figure 1). In this body of work, I will focus on technologies and medical devices aimed at improving surgical care and training in LMICs. Technology dissemination is used to describe the holistic process of ideating, developing, implementing, and adopting a technology. Technology is playing an increasing role in the delivery of healthcare with particular impact on the delivery of surgical and perioperative care (9–11). The Lancet Commission on Global Surgery recognised that novel technologies are key enabling factors in the realisation of the goal to scale up and strengthen surgical care worldwide by 2030 (1). Specifically, it identified the need to reduce costs, optimise healthcare system and resource use, and improve the delivery of surgical and anaesthesia care and training.

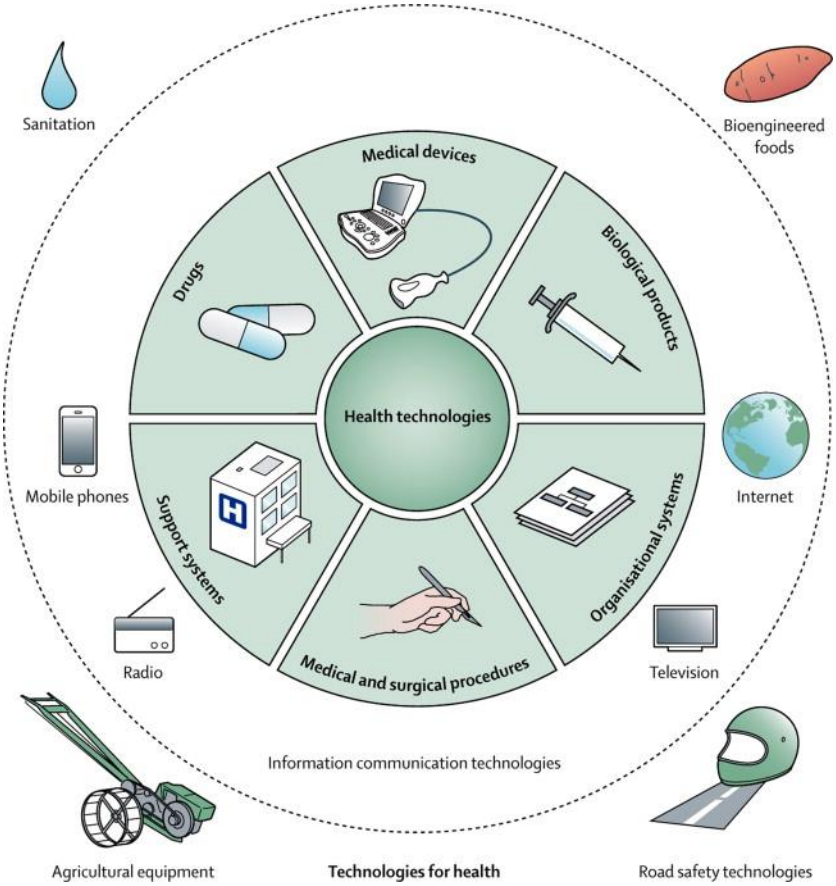


Figure 1: Overview of technologies for global health (12). Surgical technologies are those that impact directly on the provision of surgical care.

Innovation is also a broad term, bearing different connotations depending on the context. The WHO Health Innovation Group (WHIG) adopts a comprehensive working definition of health innovation and does not limit innovation to purely the development of technologies (13):

> ***HEALTH INNOVATION IS TO DEVELOP NEW OR IMPROVED HEALTH POLICIES, SYSTEMS, PRODUCTS AND TECHNOLOGIES, AND SERVICES AND DELIVERY METHODS THAT IMPROVE PEOPLE'S HEALTH, WITH A SPECIAL FOCUS ON THE NEEDS OF VULNERABLE POPULATIONS.***
>
> - ***WHO ENGAGES IN HEALTH INNOVATION IN THE CONTEXT OF UNIVERSAL HEALTH COVERAGE***
> - ***HEALTH INNOVATION ADDS VALUE IN THE FORM OF IMPROVED EFFICIENCY, EFFECTIVENESS, QUALITY, SAFETY AND/OR AFFORDABILITY***
> - ***HEALTH INNOVATION CAN BE IN PREVENTIVE, PROMOTIVE, THERAPEUTIC, REHABILITATIVE AND/OR ASSISTIVE CARE***

The WHIG advocates an 'integrated innovation' approach which is the coordinated application of scientific/technological, social and business innovation to develop solutions to complex challenges (Figure 2) (13). The group especially highlight specific innovation methodologies as being accelerating strategies in global health innovation, such as reverse innovation which refers to the recognition that innovations emerge from anywhere and learning from best practice wherever it arises harnesses the potential of the global flow of innovation. These methodologies will be expanded upon and explored later in this Chapter and elsewhere. In this body of work, I will use the term innovation to capture the use of technology or processes within the context of this complex interaction between accompanying processes.

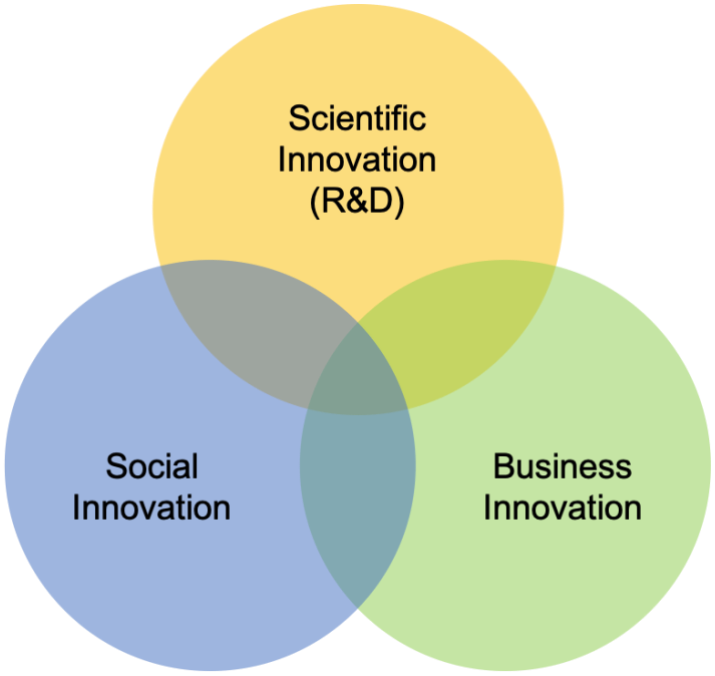


Figure 2: WHO Health Innovation Group's approach to innovation (13)

Healthcare in LMICs suffers from a lack of technological development and adoption, which needs to be addressed if UHC is to be realised (1,3,14,15). Technology dissemination is a complex process involving need assessment, conception, innovative research and development, evaluation, and wider implementation and adoption (12). Many challenges in surgical innovation evaluation are universal, but more pronounced in least developed countries, including a lack of human resource, infrastructure, and finances. Additionally, country-specific healthcare system factors, regulatory factors and local environmental factors all make technology dissemination more difficult. Understanding the specific clinical and healthcare system needs and generating an evidence base to address these is essential to inform wider dissemination and adoption. In addition, the appropriate system and process infrastructure is required to ensure effective implementation.

1.2.1 Factors that drive global surgical technology dissemination

Key driving factors of technology innovation and dissemination in global surgery include (Figure 3) (16)[1]:

1. Understanding local contexts, systems and environments ensuring complimentary process and system innovations accompany technology.
2. Rigorous, appropriate, and timely evaluation and evidence synthesis to inform embedded, sustainable adoption and implementation.
3. Effective interdisciplinary collaboration with local and international industry, policymakers, healthcare professionals and patients, and academic institutes.
4. Employing ethical principles, responsible and frugal innovation at every stage, respecting cultures, and contexts across different countries.
5. Investing in local human resources to build research, technology and equipment capacity and capability locally to enhance global workforces.

[1] A review of some of the literature in this chapter is published in the British Journal of Surgery: Bolton WS, Aruparayil N, Quyn A, Scott J, Wood A, Bundu I, et al. Disseminating technology in global surgery. BJS. 2019;34–43.

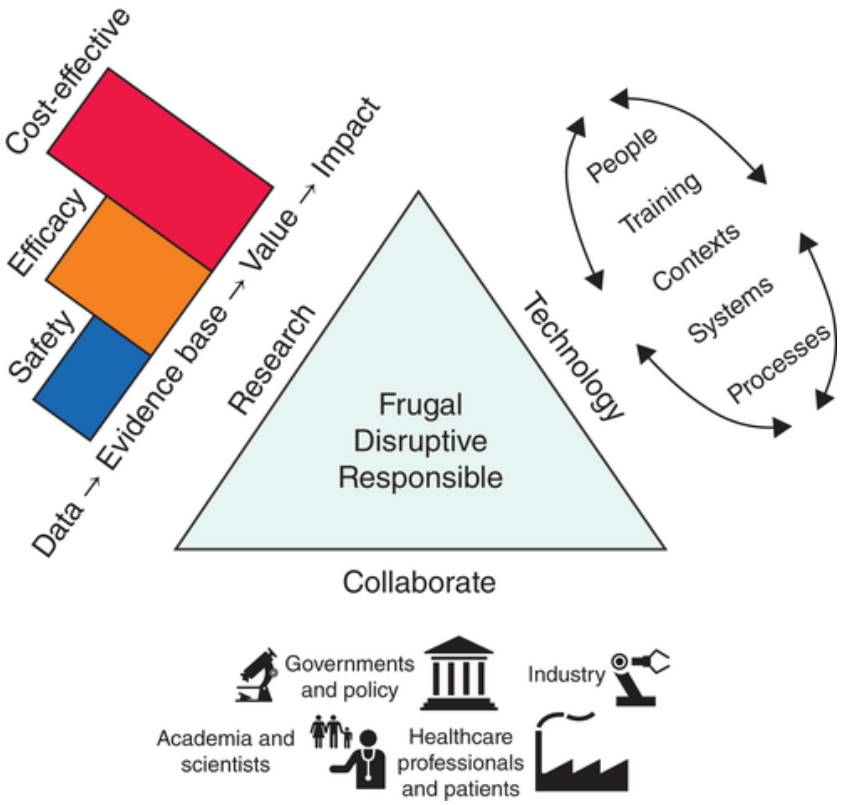


Figure 3: Key factors driving technology innovation and dissemination in global surgery (Reproduced from Bolton et al[1]).

1.2.2 Barriers to technology dissemination in global health

Howitt *et al* identified 3 key barriers to technology dissemination in global health (12):

Barrier 1 – The necessary technologies do not exist

Barrier 2 – Technology exists, but is not accessible

Barrier 3 – Technology is accessible, but is not adopted

Some elements are limited by the pace of scientific discovery, which could be expedited by increased research and development funding. If the technology exists but is not accessible, this could be due to high costs, lack of human resources and

infrastructure. Accessibility challenges should be considered at every stage of technology development, evaluation, and implementation. Finally, a lack of wider adoption could be due to lack of key stakeholder buy-in, such as early involvement of patients, local healthcare professionals and policymakers, or due to a lack of wider system and process considerations.

Malkin *et al*, along with researchers from Engineering World Health (EWH), highlighted three principle design-related barriers to health care technology dissemination: cost, spare parts, and consumables (17,18). Context-specific design for low-resource settings should attempt to minimise the reliance on consumables and the need for maintenance and repair. Collaboration with in-country distributers and industry is important to ensure successful dissemination (19). Importantly, the lack of technically trained staff is a significant barrier to technology development and adoption. This is often attributed to a ‘brain drain’ where technical skills developed to disseminate a technology are lost as people move out of the areas of need to more attractive environments (17,20). One strategy to overcome this challenge is to develop bi-lateral, international training partnerships, which has been highly effective in building biomedical engineering capacity (21).

1.3 Current practices in global surgical innovation

It is critical to understand why some current innovation practices in global surgery are inefficient or even harmful. Of particular importance is the subject of medical technology donation from HICs to LMICs. This process is often counter-productive and ignores many of the principles of participatory design, development and evaluation discussed in this Chapter. Donation of HIC technology with little situational and contextual awareness can have a negative impact on global surgical innovation (22). It is estimated that around 40% of donated medical equipment in LMICs is out of service (23). However, a subsequent survey has found that the majority of broken instruments

could be repaired cost-effectively, without the need to import spare parts, by investing in human resource capability (24). The WHO and Tropical Health and Education Trust (THET) provide guidance on responsible and ethical practices in equipment donations to LMICs (25,26).

A lack of adoption often results from attempting to apply technologies designed for different contexts without any stakeholder consultation or context specific adaptation. As well as this adaptation, for new technologies the initial genesis of innovation should bear in mind contextual factors and involve LMIC partners from the outset in accordance with participatory design principles. This process is informed by innovation approaches discussed in this Chapter, and often leads to more appropriate and efficient development and adoption of technology.

Globally advocating for improved innovation practices is essential to demonstrate the value of low-cost technologies, influence industry, and lobby global organisations. Organisations such as the G4 Alliance for Surgical, Obstetric, Trauma, and Anaesthesia Care, and the International Federation of Surgical Colleges, play a valuable role in showcasing successes to government organisations and policy-makers, disseminating information to wider audiences, and ensuring that appropriate technology research and innovation in global surgery remains high on the international healthcare agenda (27,28).

1.4 Innovation approaches valuable in global surgery

Innovation of surgical technology spans the identification of unmet clinical needs, innovation design and manufacture, through to evaluation, implementation, and adoption. Within the low resource setting, utilising appropriate innovation methodologies is essential to derive high-value, context specific and efficiently adopted technologies.

1.4.1 Frugal innovation

Frugal innovation refers to the concept of doing better with less. By concentrating on user-centred design, focusing on core functionalities, reducing cost and waste, frugal innovation can produce elegant, context-specific solutions to complex problems (12,29). An example of this is MittiCool, a low-cost, environmentally friendly refrigerator made from locally available materials including clay, which requires no electricity and elegantly addresses the unmet public health need of keeping precious food fresh in low-resource environments (30).

In English, the term ‘frugal’ can evoke the idea of cheapness, scantiness, or insufficiency. These are not the qualities that the process of frugal innovation aims for and perhaps a more helpful notion comes from a single Hindi word often used to capture the attributes of frugal innovation: ‘Jugaad’. Jugaad innovation is synonymous with frugal innovation. In their 2012 book *Jugaad Innovation*, authors Navi Radjou, Jaideep Prahbhu and Simone Ahuja explain that Jugaad means an innovative fix; an improvised solution born from ingenuity and cleverness; resourceful and elegant; highlighting qualities that the method advocates include a flexible approach to problem-solving that maximises the use of limited resources in an innovative way (29). There are six core principles to frugal innovation:

PRINCIPLE ONE: SEEK OPPORTUNITY IN ADVERSITY

PRINCIPLE TWO: DO MORE WITH LESS

PRINCIPLE THREE: THINK AND ACT FLEXIBLY

PRINCIPLE FOUR: KEEP IT SIMPLE

PRINCIPLE FIVE: INCLUDE THE MARGIN

PRINCIPLE SIX: FOLLOW YOUR HEART

Principle one captures the concept that adversity and constraints often force lateral thinking and a sense of urgency that often results in an upsurge of innovative activity. Periods of intense adversity, such as world wars, economic recessions and global pandemics are often associated with rapid innovation development and technological breakthroughs in several industries. Principle two forces the innovator to think creatively, focusing on leveraging existing concepts and ruthless extraction of value from the resources available. Principle three expresses the need to have adaptability and improvisation at the heart of the innovation process. Principle four is not about creating simplistic solutions. Frugal innovations are simple because they focus on core functionalities mapped against a set of minimum requirements that have been derived from early and continuous assessments of stakeholder needs. Principle five instructs frugal innovators not to ignore marginal user groups, economies, societies, and contexts. An inclusive approach with consideration of this margin facilitates and catalyses additional innovation methods such as reverse innovation, access to growing emerging markets and servicing a wider user base. Finally, principle six highlights that connection to people, creation of interdisciplinary teams and innovating responsibly are holistic and facilitating strategies. The book focuses on how businesses can adopt frugal innovation methodologies into their working practice to improve growth, and these principles are immediately relevant to the development of surgical technology both in HICs and LMICs (31).

1.4.2 Responsible innovation

To compliment fugal innovation, responsible innovation focuses on working sustainably and ethically, embedding innovation and research within the society, environment and context locally (32,33). Responsible innovation in medical device sectors has helped foster effective partnerships between industry, clinicians, researchers and policy

makers and this may be especially important for improving innovation in LMIC contexts (34–37).

Ethical practices are essential in healthcare and these should be employed throughout the processes of technology dissemination in global surgery (38,39). Development and evaluation of technologies in global surgery should be held to the same ethical standards globally with rigorous alignment to international and local regulatorily frameworks. It is essential that the innovation process and stage of development is transparent to both surgical colleagues and patients. This facilitates informed consent about receiving an innovative treatment and also fosters trust and enhanced adoption by other professionals (40). Timely, consistent and open reporting of outcomes during the evaluation pathway is advocated by the WHO Global Model Regulatory Framework for Medical Devices (41).

Many of the principles of frugal innovation focus on the need to ensure that everyone benefits from the innovation. Responsible innovation captures the moral obligation to ensure innovation is targeted towards the areas of greatest unmet need. Aside from the compelling ethical argument, there is an increasingly realised economic argument in addition. Whilst global industries have been reluctant to target LMICs in the past, this might change in the future, driven by the potential market size and rapidly growing markets in emerging countries. In the United Kingdom (UK), academic involvement in technological development in LMICs has been recently fuelled by large funding programmes from national organisations such as the National Institute for Health Research (NIHR) and Research Councils UK (42,43). Fundamentally, there is a significant scientific argument to innovate in this way as reverse innovation teaches us that often, impactful innovation comes from LMICs that may be useful for patients across the globe.

1.4.3 Reverse innovation

Reverse innovation often refers to the flow of innovations from low to high-income countries and several technologies have impacted healthcare systems across the world in this way (44,45). One striking example of this process is the use of mosquito netting in place of commercially produced mesh for abdominal wall hernia repair(46). The success of this innovation has been demonstrated in rigorously conducted safety and efficacy studies, which combined with a significant reduction in costs has resulted in the technology having a powerful disruptive potential (46,47). The term reverse innovation implies unilateral flow of ideas from LMICs to HICs and perhaps a more helpful notion is that of sharing innovation globally and adopting best practice wherever it originates.

Multi-lateral partnerships between LMICs and HICs is essential for this global flow of innovation. Generating centralised, international technology repositories such as the WHO Compendium of Innovative Health Technologies for Low-resource Settings will facilitate the sharing of best practice (48). Increasingly, technologies developed for low-resource settings using frugal design will be used to improve health and help stem the rising costs of healthcare world-wide.

1.4.4 Disruptive innovation

Frugal innovation often results in disruptive technologies. These are technologies which fundamentally alter existing systems providing a much higher value often delivered via frugal thinking (49,50). An important example of disruptive innovation making an impact in global surgery is in the field of mHealth, an abbreviation for mobile health. The WHO defines mHealth as the "use of mobile and wireless technologies to support the achievement of health objectives." In 2019, there were 5.11 billion unique mobile phone users and 4.39 billion internet users worldwide, representing a penetration of 67% and 57% respectively (51). Importantly, in LMICs mobile phone

penetration is over 90% and the mobile internet connectivity is around 40% (51). By leveraging existing technologies like these, devices such as mobile phones and wearable technologies are assisting with clinical data collection, health promotion, detection of disease and post-operative complications, and in management of chronic illness in LMIC settings (52,53).

1.4.5 Interdisciplinary and collaborative innovation

Developing context specific technologies, through interdisciplinary collaboration and employing the principles of frugal, responsible and disruptive innovation is a fundamental starting point in the dissemination of technology solutions in global surgery (16). However, the vast majority of technologies are not widely adopted, particularly in LMIC settings (12).

Central to the tenant of interdisciplinary innovation is the need for user-centred design, which might involve patients and public, local surgeons, allied healthcare professionals, industry, academics, engineers, scientists, governments and ministries of health (54,55). Ensuring all key stakeholders provide critical feedback throughout the evolution of a technology is essential for its ultimate acceptance and wider adoption. It is only through the well-planned execution of interdisciplinary collaboration between HIC and LMIC partners that context specific solutions emerge and are successfully adopted. Moreover, breaking down barriers between disciplines and geographies in this way fosters a collaborative culture that will benefit patients and innovators worldwide.

1.4.6 Environmental impact of surgical innovation

The provision of surgical care and the development of surgical technology represents a significant contribution to emissions from healthcare sectors (56). With governments across the world signing up to the Paris Agreement under the United Nations

Framework Convention on Climate Change, methodologies from frugal, responsible, reverse, and disruptive innovation are likely to gain traction as they appeal to maximising the use of resources and limiting waste in a social, ethical, and sustainable manner. In this way, the terms ‘global surgery’ and ‘green surgery’ may become closely related through innovating for a future that is both frugal and sustainable. There is increasing evidence that through these innovation approaches, growth can be maintained in a more environmentally conscious way (57). It will be interesting to examine if these methodologies reduce the environmental impact of delivering surgical care on a global scale. Indeed, the political and scientific pressure to address climate change may act as a catalyst for the use and development of these innovation approaches.

1.5 Examples of good practice in global surgical innovation

1.5.1 Fracture management

One striking example of successful technology development for global surgical comes from the orthopaedic management of fractures and injury. Injury accounts for 5.8 million deaths each year world-wide, more than tuberculosis, malaria and human immunodeficiency virus combined (58). Operative fixation of long bone fractures can reduce hospital stay, provide a quicker return to work, improve fracture healing, and limit disability (59,60). Padhi and Pulate *et al* demonstrated the safe and cost-effective application of external fixation technology in LMICs, including India, highlighting the importance of locally sourcing materials, local industry engagement, and reducing waste by re-sterilisation and re-use where safe and feasible (61,62). A further example of technology innovation for fracture fixation in LMICs is the ‘Joshi external stabilization system’ (JESS), again from India (Figure 4) (63,64). This external fixation device was designed to be locally manufactured, versatile and re-usable, with many orthopaedic applications spanning age ranges, anatomical areas and mechanisms of injury (65,66).

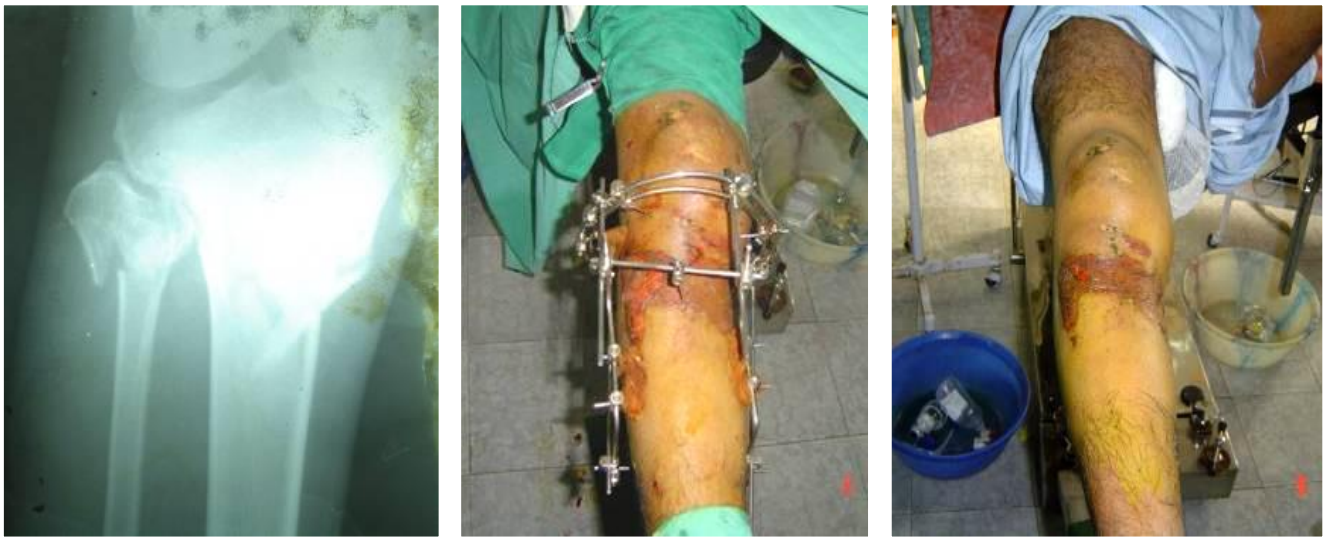


Figure 4: Joshi's External Stabilization System (JESS) stabilising a tibial fracture. Reproduced with permission from Dr J Gnanaraj, photograph credit to Dr Ram Prabhoo.

1.5.2 Safe Anaesthesia

The safe delivery of anaesthetic and perioperative care is of paramount importance to improving surgical outcomes. The WHO Safe Surgery Saves Lives programme introduced the WHO Surgical Safety Checklist which has had an impact on surgical safety across the world (67–69). One of the mandated items on the checklist is the use of pulse oximetry, which is the only piece of equipment required. Funk *et al* highlighted the global lack of pulse oximetry as a significant unmet global health need(70). This need was met by the non-governmental organisation (NGO) Lifebox (https://www.lifebox.org), an international group who developed a novel pulse oximeter designed specifically for the needs of low-resource settings (71,72) (see Figure 5). The Lifebox pulse oximeter project has disseminated over 15,000 pulse oximeters to hospitals across 100 countries (73). Its success is attributed to careful consideration of the design specification, focusing on minimal standards and core functionalities, and

building in affordable cost, durability, and low-resource environmental factors, such as limited power supply and distribution challenges (74). Other key disseminating strategies included LMIC user-centred design, effective industry and local partner engagement, and importantly, rigorous clinical evaluation (75–77).

Figure 5: LifeBox Pulse Oximeter being used in a theatre in India. Reproduced with permission from LifeBox, photograph credit to Ritesh Uttamchandani.

1.5.3 Laparoscopic surgery

Laparoscopic surgery is the preferred technique for many general surgical and gynaecological conditions due to improved short-term clinical outcomes (78,79). These benefits are even more pronounced in LMICs where access to follow-up care is limited and there is a greater urgency to return to work to prevent spiralling poverty (80). Laparoscopy also provides a cost-effective diagnostic tool where radiological facilities are limited and may reduce high negative laparotomy rates (81,82). Laparoscopic surgery requires advanced equipment and infrastructure, including laparoscopes, laparoscopic instruments, and piped carbon dioxide (CO_2), and trained surgical

providers. It is usually performed under general anaesthesia, requiring the presence of a trained anaesthetist with appropriate equipment and drugs.

Although these are formidable challenges, laparoscopic surgery has been successfully implemented in low-resource settings with similar complication rates to HICs (83). In a recent systematic review, Chao *et al* described several adaptive strategies to enhance the adoption of laparoscopic surgery in LMICs (80). These included infrastructure and system innovations, such as soft drink companies providing CO_2, sunlight as a light source, and low-cost box trainers for surgical training (84–86). Price *et al* successfully introduced laparoscopic surgery in Mongolia by building high-volume, bilateral training teams and adapting to local community needs to build sustainable laparoscopic services (85). The availability of low-cost, high-quality equipment, with minimal maintenance requirements, is key to successful implementation. An example is the Xenoscope, a laparoscope that provides high resolution images at an affordable cost (87) (Figure 6). To avoid the need for CO_2 insufflation, abdominal wall lift devices have been developed to facilitate GILLS (Gas Insufflation Less Laparoscopic Surgeries). Using this technique, a range of laparoscopic abdominal and gynaecological procedures can be safely performed under spinal anaesthesia, which is readily available through trained healthcare workers even in the most remote environments (88) (see Figure 7). GILLS also negates the need for specialist laparoscopic instruments and trocars, where modified open instruments can be used to perform single incision surgery for patients in rural settings (88,89).

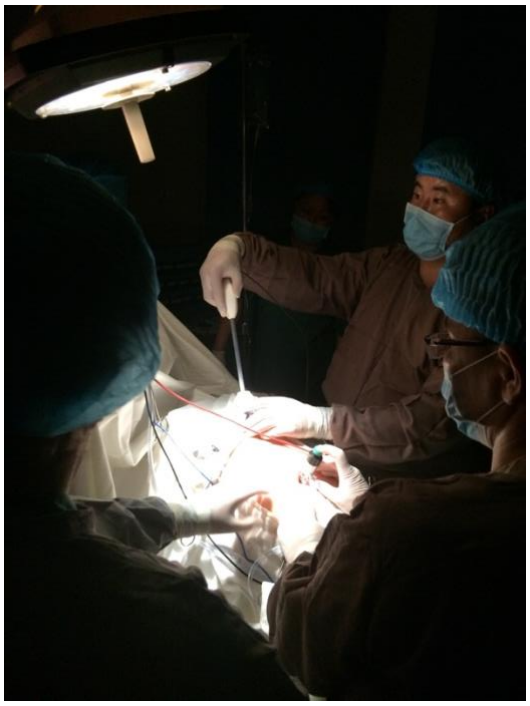


Figure 6: The Xenoscope being used to perform laparoscopic surgery in rural areas of Mongolia. Reproduced with permission from Xenocor Ltd. (Salt Lake City, USA).

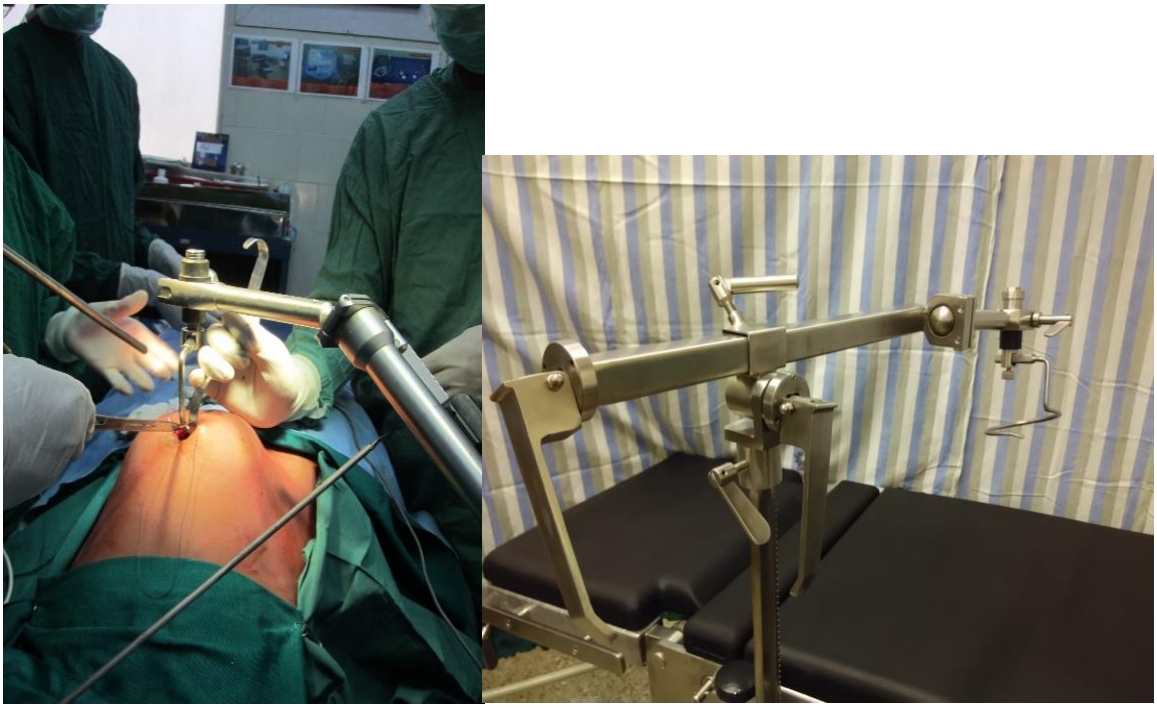


Figure 7: Gas Insufflation Less Laparoscopic Surgery (GILLS) abdominal wall lift device facilitating laparoscopic surgery in low-resource settings. Reproduced with permission of Dr J Gnanaraj.

1.6 Evaluating innovation

Globally, only 9.8% of surgical technology innovation reach clinical trial and less than 1% achieve widespread adoption (90). Generating the necessary evidence to inform adoption through scientifically robust, clinical, system and health-economic evaluations poses a significant barrier to the widespread adoption of technologies (12,16). The barriers to generating this evidence, which is required to persuade surgeons and policy makers to adopt technology, is one of the most significant factors contributing to this statistic. The evaluation of surgical innovation, as with all complex interventions, is methodologically challenging even in HICs, involving many inter-related variables including the surgical setting and quality of care (91). Obtaining data on safety, clinical and cost effectiveness in LMIC settings is no less important, but much more challenging given resource restraints (16).

1.6.1 Surgical innovation evaluation in HICs

Surgical innovations are almost always complex interventions. The evaluation process for complex interventions is often considered less established than the well adopted development and evaluation pathway for pharmaceuticals. In the UK, the Medical Research Council (MRC) defines a complex intervention as one that contains several interacting components (92). The MRC guidance for evaluating complex interventions recommends focusing on four phases: development, feasibility/piloting, evaluation, and implementation. This guidance was updated in 2021 and included a greater focus on flexibility in intervention delivery as well as interaction between the intervention and its context, highlighting that the act of innovation can be described as the intervention as an event in a system/context (93). In the US, the Institute of Medicine describes six domains that should guide the evaluation of healthcare interventions: safety, effectiveness, timeliness, equity, patient-centredness and efficiency (94).

In 2009, the IDEAL Framework (Idea, Development, Exploration, Assessment, Long-term Follow-up) was conceived to facilitate the evaluation specifically of surgical technologies and innovations through a structured framework that lends itself to scientific evaluation (91,95–97). This includes the rigorous collection of safety, feasibility, and efficacy data via a range of study designs to inform the technology's wider adoption. The Framework has been developed for and employed in HIC settings (98).

1.6.1.1 The IDEAL Stages of Surgical Innovation

IDEAL consists of 4 stages (Figure 8). Stage 1 focuses on a small number of participants and the evaluation usually takes the form of structured case reports where the main outcomes are proof of concept related. Stage 2 is split into 2a and 2b. 2a includes still a small number of selected participants in a single group design and aims to document the evolving procedure or technology development. 2b builds on this and evaluations often take the form of exploratory or feasibility randomised controlled trials (RCTs) with main outcomes including feasibility and short-term clinical safety outcomes. Stage 3 expands and takes the form of multicentre RCTs with longer follow-up time points, focusing on clinical and cost effectiveness. Finally, stage 4 takes the form of long-term surveillance studies, including registries and routine databases. Here the focus is on ensuring and maintaining standards through real world evidence.

	1 Idea	2a Development	2b Exploration	3 Assessment	4 Long-term study
Purpose	Proof of concept	Development	Learning	Assessment	Surveillance
Number and types of patients	Single digit; highly selected	Few; selected	Many; may expand to mixed; broadening indication	Many; expanded indications (well defined)	All eligible
Number and types of surgeons	Very few; innovators	Few; innovators and some early adopters	Many; innovators, early adopters, early majority	Many; early majority	All eligible
Output	Description	Description	Measurement; comparison	Comparison; complete information for non-RCT participants	Description; audit, regional variation; quality assurance; risk adjustment
Intervention	Evolving; procedure inception	Evolving; procedure development	Evolving; procedure refinement; community learning	Stable	Stable
Method	Structured case reports	Prospective development studies	Research database; explanatory or feasibility RCT (efficacy trial); diseased based (diagnostic)	RCT with or without additions/ modifications; alternative designs	Registry; routine database (eg, SCOAP, STS, NSQIP); rare-case reports
Outcomes	Proof of concept; technical achievement; disasters; dramatic successes	Mainly safety; technical and procedural success	Safety; clinical outcomes (specific and graded); short-term outcomes; patient-centred (reported) outcomes; feasibility outcomes	Clinical outcomes (specific and graded); middle-term and long-term outcomes; patient-centred (reported) outcomes; cost-effectiveness	Rare events; long-term outcomes; quality assurance
Ethical approval	Sometimes	Yes	Yes	Yes	No
Examples	NOTES video[6]	Tissue engineered vessels[7]	Italian D2 gastrectomy study[8]	Swedish obese patients study[9]	UK national adult cardiac surgical database[10]

RCT=randomised controlled trial. SCOAP=Surgical Clinical Outcomes Assessment Programme. STS=Society of Thoracic Surgeons. NSQIP=National Surgical Quality Improvement Program. NOTES=natural orifice translumenal endoscopic surgery.

Table: **Stages of surgical innovation**

Figure 8: The IDEAL Framework summary (91)

The IDEAL Collaboration offers a range of recommendations throughout their Framework to guide researchers at each stage of the innovation process. These recommendations are often methodological considerations and delivery strategies that help overcome barriers to evaluation. Almost exclusively, these recommendations have been made with HIC surgical researchers and HIC contexts in mind, and therefore some of the guidance may not be applicable to LMIC settings. Finally, given the unique challenges associated with evaluations in LMICs, many context-specific recommendations and strategies may be missing from the current version of the Framework.

1.6.2 Surgical innovation evaluation in LMICs

In recognition of the unique challenges associated with conducting evaluations in LMICs, the WHO Medical Device Technical Series provides researchers and

technologists with guidelines for each stage of development and evaluation, including device regulations, needs assessment, human resources, procurement, and maintenance. In addition, WHO Health Technology Assessment (HTA) of Medical Devices guidelines provide practical advice around adaptive global healthcare considerations (99,100). Within the LMIC setting, a priority HTA strategy is the use of health economics evaluation using cost-effectiveness and quality-adjusted life years (QALYs) or disability-adjusted life years (DALYs) to inform wider adoption and healthcare budgets (5,6). Cost-effectiveness analyses are critical in every healthcare system, but these may be uniquely conducted and especially helpful in extremely resource constrained environments with LMIC healthcare systems. The use of the DALY as a measure gives a more complete picture of the burden of disease as one DALY represents the loss of the equivalent of one year of full health, rather than a cruder measure like mortality. This is particularly useful when deriving meaningful comparisons between different disease entities across different geographies and contexts.

Identifying barriers to evaluation is an essential first step in developing solutions. A priority setting study undertaken by Rosala-Hallas *et al* identified appropriate outcome measures and training of research staff as the most important issues in conducting clinical evaluations in LMICs (101). Researcher training is critical to conducting high quality research and in-building research capacity and capability within LMICs. The Special Programme for Research and Training in Tropical Diseases and the Global Health Network have developed the Global Competency Framework for Clinical Research which describes the core competencies for a research team in LMICs (102). It provides a range of e-learning materials to help researchers achieve these competencies (103). Of equal importance is the global lack of surgical workforce and up-scaling of surgical training and task shifting is urgently required to realise UHC by 2030.

An important step to improving technology adoption in global surgery will be the effective utilisation of low-resource specific surgical innovation evaluation guidelines that address the key elements of the IDEAL/MRC frameworks, focusing on guiding the generation of evidence required to inform policy makers and wider adoption. Existing literature is often not suited to practical use for surgical technology evaluation in low-resource environments because it fails to address context-specific challenges and is often prohibitively and unnecessarily complex. Versatile, context-specific, and practical guidance for surgeons working in LMICs is required to allow them to contribute to the evidence generation for surgical innovation. Shelton offers twenty criteria to consider when disseminating interventions and technologies in LMICs, including user-centred design, scalability and sustainability, which should be reflected in future research efforts (104). Keown *et al* offer lessons on disseminating innovation in healthcare from eight countries, highlighting the need to foster an organisational culture of innovation and adoption in health systems (105). Moreover, Howitt *et al* offer recommendations to different organisations such as Ministries of Health, industry, academic institutes and healthcare organisations and such guidelines should aim to facilitate inter-organisation collaboration (12).

There is a global lack of surgical trials, and while all stages of evaluation are essential to ensure safety and efficacy, it is surgical trials, particularly large RCTs, that are often required to convince policy makers and regulators to widely adopt innovation and technologies (106). Large surgical RCTs are complex and challenging evaluation studies to conduct, even with the resources available in HICs. It has been shown that early stage use of the IDEAL Framework to guide evaluation studies improves the generation of the prerequisite evidence needed to successfully design, fund and deliver later stage multicentre RCTs and inform technology adoption (98).

While the IDEAL Framework has been robustly developed and evaluated in HIC settings, there may be significant barriers to applying the current Framework in many

LMIC contexts. The IDEAL Framework has undergone adaptations to improve the applicability of the guidance to other areas of evaluation. For example, the Framework has been applied to the evaluation of other complex interventions such as physical therapy in the form of the IDEAL-Physio Framework (107). In a similar way, the IDEAL-D Framework focuses on the development and iterative evaluation of medical devices (108). This was adapted using an iterative modified Delphi approach and consensus methodology with expert participants (108,109). In particular, the IDEAL-D Framework incorporates a new IDEAL Stage 0 that provides recommendations for the pre-clinical development before the device is first used in humans. This is where a large proportion of the modifications to the innovation occur, and these heavily impact subsequent evaluation and implementation. The innovation methodologies of frugal, responsible, reverse, and disruptive innovation may be especially important when considering IDEAL Stage 0 evaluations in global surgical innovation given the need for context-specific interventions.

It is not currently known where the barriers and facilitators lie in the effective application of the current IDEAL Framework in LMIC settings. The IDEAL Framework was designed with the evaluation of *novel interventions* in mind and therefore researchers should progress from IDEAL Stage 1 to 2a, 2b, 3 and finally Stage 4. What often happens in global surgery is the attempted application of technologies that are 'established' in HICs for use in LMICs. For example, it is unclear if an established technology in one context needs to begin from IDEAL stage 1 and move systematically through to stage 4 simply because it has been applied in a *novel context*. Moreover, are there other evaluation techniques and processes that could be employed to get the necessary evidence and make the whole process more efficient and context specific. In many LMIC settings it simply may be impossible to go from stage 2 to stage 3 without adaptive strategies such as enhancing the human resources or equipment supply.

Stage 3 of the IDEAL Framework describes RCTs as the gold-standard when evaluating the efficacy of a surgical technology innovation. While RCTs may give evidence of intervention efficacy during the trial, these benefits are often not generalisable to clinical practice outside the trial, although pragmatic RCT designs may help mitigate this effect (110). Conducting a randomised study may not be possible due to a lack of equipoise among LMIC surgeons through ethical, logistical, or technical considerations depending on the context and technology. An established technology in routine clinical practice in HIC settings, having undergone RCT evaluation, may not require the same RCT evaluations to be repeated in each LMIC setting (and indeed the *vice versa* effect may apply as demonstrated by the principle of reverse innovation). In this case, the clinical effectiveness is already determined elsewhere, in a different context. Applying the intervention to a new context does not make the intervention itself novel, and this non-novel intervention may not, therefore, require further Stage 3 studies. However, researchers cannot be certain that a certain intervention will have the same success or consequence profile in different contexts. Alternative processes to assess this circumstance and evaluate the impact will be discussed in later chapters.

RCTs often compare existing, standard of surgical care with a novel intervention that researchers hope is either more clinically or cost-effective and at least as safe as the standard care. In many LMIC settings there is simply a lack of intervention, particularly in surgery, so dissemination of technology and evaluation require alternative strategies such as novel design methods for RCTs and phased evaluation-implementation-evaluation cycles seen in implementation evaluation techniques (110,111). As well as identifying which intervention or technologies are non-inferior or superior, particularly in global surgery contexts, often the most essential research questions to answer include how the intervention/technology works and how the system functions (110). It is not possible to assume that RCT research findings can be immediately implemented to improved outcomes without engaging in the scientific study of how the intervention will perform in the system across variable contexts (112). This is the case in any discipline,

but in multi-national global surgical trials, where systems, workforce and contexts may vary widely, understanding this is essential.

Increasingly, principles and techniques from the field of implementation science are being utilised to develop and evaluate innovations and technology solutions, particularly in global health (110,112). According to Weiser *et al*, 'Innovative solutions to problems in healthcare, particularly global health, require new evaluation techniques', and implementation research provides the scientific methodology to promote the systematic, sustainable uptake of research findings and evidence-based interventions into routine practice (110,113,114). In particular, this includes the study of influences on healthcare professional, healthcare system and organisational behaviour; factors which are even more important in global surgery contexts (113). However, implementation science is not well utilised among global surgical research programmes and, indeed, is not well reflected within current frameworks such as IDEAL (110).

Innovations and technologies in surgical care are often complex, interdependent interventions, particularly across different countries, cultures, and systems. The WHO described five key elements essential for successful implementation of a complex intervention in global health: the resources (human, equipment and system) needed to make changes; the training and education required to close knowledge and skill gaps; the ongoing evaluation essential for measuring effectiveness and sustainability; the communication strategies for promoting and maintaining improvements across different settings; and the cultural changes and considerations fundamental for sustaining an ethos of responsible innovation and collaboration (115). This need to adapt and consider wider contexts, processes, and systems, means a versatile and practical context-specific framework for innovation stakeholders in global surgical technologies needs to be developed. To be successful, such a framework also needs to be adaptive and dynamic, something which is not offered by existing frameworks such as IDEAL. The framework will need to take the most applicable components of evaluation

methodologies outlined in IDEAL and adapt them, or add to them, to increase their utility for LMIC surgeons and researchers. The directing aim of this framework should be to ensure standardised, efficient, and appropriate evaluation of innovations and technologies are widely adopted in global surgery to improve outcomes for patients in LMICs.

1.7 The ethics of global surgical innovation evaluation

When the original IDEAL recommendations were published to guide surgical innovation, ethical issues around innovating with, or 'on', living humans were raised. Indeed, it is essential that ethical principles are incorporated into any framework that guides healthcare intervention development and evaluation. For this, innovators have drawn on the accepted principles of non-maleficence, beneficence, justice and respect for patient autonomy to help guide the evaluation of their innovations (116). The main directing principle is the paramount need to limit any potential patient harm (non-maleficence). In many instances along the innovation journey, the risks may be wholly unknown, and here the precautionary principle is highly relevant (117). In view of these factors, the IDEAL Framework advocates rigorous prospective studies with appropriate study designs that are large enough to identify any unexpected safety risks and harm signals as early as possible. Next, beneficence relates to the need to ensure benefits outweigh any risks, such that if there were no therapeutic benefits at all, then even unrealised risks would be ethically insupportable.

The principle of justice in global surgical innovation is particularly difficult to navigate as it requires more nuanced judgement than the other principles. There are two important applications of justice in this context. The first arises from the fair distribution of scarce resources (distributive justice), and hence health economics evaluations and cost-effectiveness analyses are particularly important to make decisions. The second application is that justice dictates that evaluation of innovation should not unreasonably

increase costs or delay adoption, because harm is also done by reducing patient access to new treatments and suppressing the innovation process. As such, evaluation frameworks directed by justice need find a balance between the two theoretical extremes of evaluating and re-evaluating until all potential harm is eliminated (thereby *never* reaching adoption), and of adopting all innovation immediately without any prior assessment.

There remains a clear ethical obligation to swiftly adopt safe innovation and disseminate this globally to save lives and improve care (Figure 9). Any prerequisite evaluation should therefore be as simple and cost-efficient as possible, utilising agreed minimum evidence requirements (118). Decisions on the sufficiency of the evidence required to achieve this balance fall between realising the potential benefits of swift innovation adoption versus minimising the risks of missing potential harm through under-evaluation. These decisions should be made in collaboration with regulators, innovators, surgeons, and patients themselves. This is where the final principle of respect for autonomy is helpful. All surgical innovators must ensure that their patients have full information about both the risks and benefits, including a two way discussion about what remains unknown, such that the patient can make a free, informed decision (119).

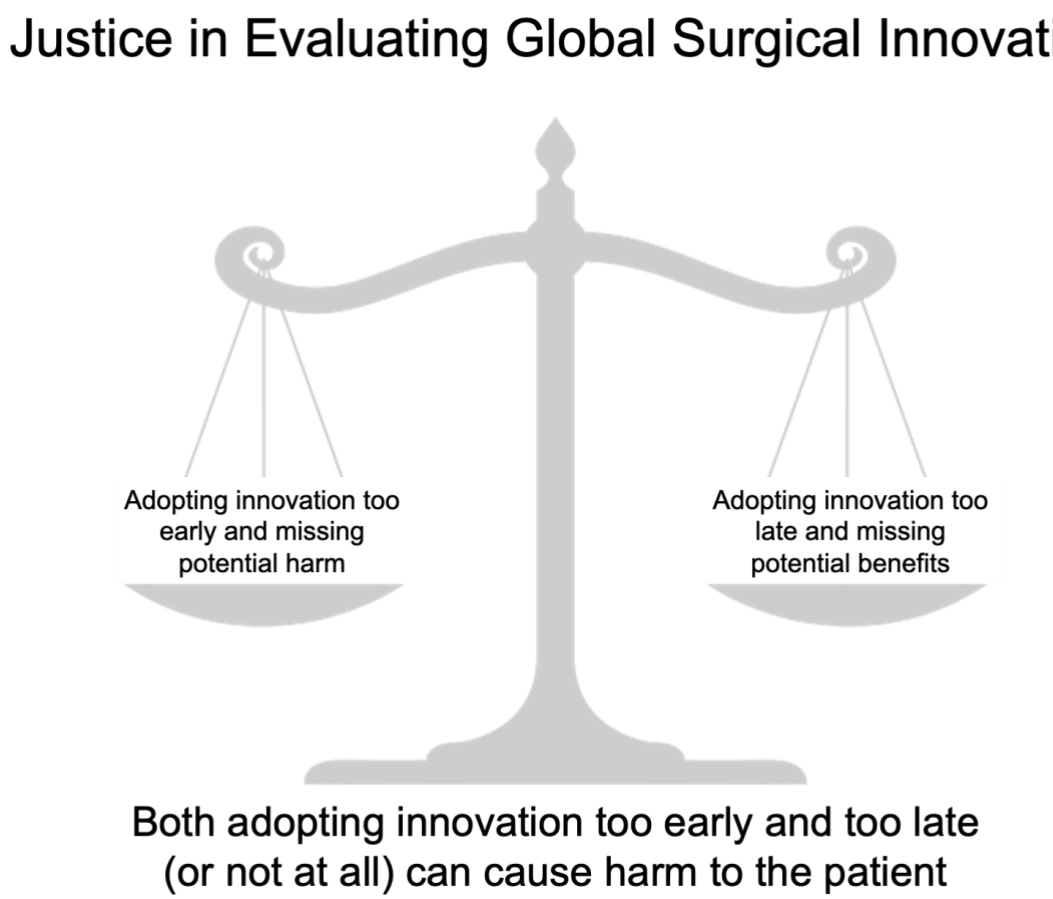


Figure 9: Justice in evaluating global surgical innovation.

This body of work in no way advocates ‘cutting corners’ along the surgical innovation evaluation pathway. Instead, it aims to put evidence behind potential solutions to the inescapable fact that real urgency to adopt innovation continues to grow and this urgency applies pressure on front-line surgeons working in LMICs. These surgeons may benefit from a framework that helps them make decisions about what evaluation is required, if any, and when it is more ethically acceptable to adopt as soon as possible to benefit their patients. As previously mentioned, these surgeons very often aren’t expecting to adopt wholly novel technologies, rather they are trying to apply established interventions to the context they find themselves in.

1.8 Surgery in Sierra Leone

Much of the field work that contributed to the data in this Thesis has come from projects in Sierra Leone, a West African country, classified as a Development Assistance Committee (DAC) 'least developed' country, with a population of approximately seven million people and one of the most constrained surgical services in the world.

An overview of the country context us useful here. Over recent decades, Sierra Leone has suffered a range of man-made and natural disasters that have caused thousands of deaths, political instability, slow economic recovery and growth, and a weakened healthcare system. These include the Sierra Leone Civil War (1991–2002), Ebola Outbreak (2014-2016), and more recently the COVID-19 Pandemic (2020-2021). The country suffers from varying natural disasters including drought, flooding, and landslides. Because of these challenges, high poverty levels, food insecurity issues and a struggling healthcare service leave much of the population vulnerable to future health crises and disasters and make improving healthcare delivery even more challenging.

1.8.1 The state of the health system

There are many possible metrics that indicate the strength of a healthcare system. Key metrics employed by the WHO include life expectancy and maternal and child mortality. The life expectancy in Sierra Leone is 45 years and maternal and child mortality is one of the highest of all countries at 156 per 1000 live births (120). The strength of the national economy correlates with the strength of the health system because more spending can be allocated and investment in improving services can become a higher priority for governments. Spending on the healthcare system in Sierra Leone is approximately $95 per capita (UK approximately $2700 per capita) (121,122). This may

improve with time as before the COVID-19 Pandemic, Sierra Leone had one of the fastest growing economies in Africa. The health system in Sierra Leone is comprised of a combination of governmental public, private, charity and non-governmental organisations and operates at three levels via peripheral health units, district hospitals and reference hospitals. Surgical care is provided mainly in hospital facilities with a mixture of private and public services (123).

A key barrier to improving access to healthcare in the country is a chronic shortage of trained healthcare workers compounded by underfunding, geographic, climate and political issues, and a heavy disease burden. The unmet surgical disease burden in Sierra Leone is enormous with only 7.8% on the need being met, leading to an estimated unmet surgical need resulting in 766 606 DALYs forgone: 606 981 DALYs lost due to mortality and 159 625 due to morbidity; and correspondingly significant loss of economic output for the country (124). Setting priorities to upscale and invest in surgical services on national health agendas is a key strategy to improve access to care. Setting political priorities for surgical care can result in targeted strengthening and investment, and this is often what is required to overcome the range of complex barriers that limit access (125)

1.8.2 The state of surgery and the surgical workforce

Delivering healthcare is reliant on trained healthcare workers. Sierra Leone suffers from one of the poorest healthcare workforce densities in the world, with estimates indicating that there are as little as 0.05 per 1000 of the population in rural populations (126). For surgical care, the unmet need for providers is even greater (123). There is limited postgraduate surgical training, which poses a significant challenge for achieving safe and effective surgical care in Sierra Leone due to the lack of a trained surgical workforce. The surgical workforce is augmented by non-specialist provers and 52.8% of all surgeries are performed by non-specialists (127). There a many barriers that limit

surgical training opportunities, but data suggests significant motivation for professional development opportunities and careers in surgery in-country (128). Overall, across all surgical providers, the mean individual productivity is approximately 2.8 operations week (127). A range of initiatives including task-sharing training programmes to upskill non-specialist further have demonstrated effectiveness and safety, and these initiatives may improve the provision of surgical care across the country (129). As well as these initiatives, improving staff morale through appropriate recognition and planning career trajectory and development opportunities may improve retention of staff and the surgical service delivery (130).

The workforce challenge is compounded by a number of other barriers in delivering surgical care, including lack of equipment and resources, hospital management and infrastructure, and importantly financial constraints on provision and access of surgical care (131). In a large cross sectional survey, 45%) of surveyed patients accessing surgical care were already below the poverty line, and catastrophic expenditure affected 18% of study participants (132). The high rates of poverty and catastrophic expenditure result in delays to seeking care and increased morbidity and mortality associated with this. For this and other cultural or religious reasons, many patients seek the services of traditional healers which are often more affordable and more trusted in some communities.

1.8.3 Research capacity in Sierra Leone

Many LMICs suffer from a lack of research capacity brought about by a number of barriers including a lack of human resources, data management tools and systems, regulatory deficiencies (133). Building clinical research capacity is an essential component of health system strengthening. Research capacity is even more essential when faced with disease outbreaks like during the Ebola and COVID-19 pandemics. Throughout the conduct of this PhD, challenges around administering research in low-

resource environments were explored and discussed. Many of the experiences highlighted a call for better methodological support, research funding, research skills training and robust but efficient regulatory processes. The overall aim of this thesis is outlined below but there are a number of pieces of work in this thesis that may help address this research capacity gap in low resource environments.

Sierra Leone was selected as an exemplar setting for this thesis because of the significant unmet surgical need and the potential for research and innovation to make substantial improvements to surgical care, surgical training, and research delivery. The context posed several challenges that are common across many LMICs, and this provided a productive setting to conduct this programme of work.

1.9 Summary

Global surgery has been a long-neglected area of clinical and academic advancement in global health, and there is a huge unmet need in surgical care globally, felt most acutely in LMICs. Improving surgical outcomes for patients in LMICs relies on the development, dissemination and adoption of context specific surgical technologies and innovation. Several innovation and evaluation approaches may be useful to achieve this aim, including frugal innovation, combining implementation science with traditional evaluation designs in phased evaluation-implementation-evaluation cycles, and context specific surgical IDEAL Stage studies.

One of the most significant barriers to widespread technology adoption lies in the generation of evidence for safe, cost and clinically effective implementation of these technologies. Further exploration and understanding of specific barriers to the evaluation of surgical innovation in LMICs is needed to develop strategies to overcome these challenges, as well as exploration of additional evaluation methodologies that may be more appropriate to guide adoption. There is no existing framework which

addresses many of the challenges associated with evaluating innovation within LMIC settings whilst providing surgeons and researchers with appropriate guidance. This body of work will provide comprehensive evidence for such a framework, based on:

i. A systematic review of the literature documenting the barriers and facilitators to surgical trial evaluation (IDEAL Stage 3 studies) in LMICs as a mechanism for influencing healthcare policy (Chapter 3).
ii. The design and conduct of two IDEAL Stage 2 surgical trials (Chapters 4 and 5) as exemplars of methodological evaluations to facilitate the adoption and implementation of technology.
iii. Engagement of LMIC stakeholders via a global survey and qualitative study to gauge their perspective of the global surgical innovation pathway (Chapter 6).

The work in Chapter 7 explores how the IDEAL Framework for evaluating surgical innovation might be adapted to increase its applicability and relevance in LMICs and presents the initial iteration of the Global Surgical Innovation IDEAL Sub-Framework. If the widespread development, evaluation, and adoption of context-specific surgical innovation for LMICs is achieved, patient outcomes will be improved and the chances of achieving UHC by 2030 increased.

1.10 Thesis aim

The main aim of this PhD is to investigate how surgical innovation occurs in LMICs, the barriers to innovation, strategies to increase innovation research capacity and capability, and the steps needed to increase the efficiency of clinical translation and adoption of surgical innovation for LMICs globally.

I will use different methodologies, including systematic reviews, clinical feasibility studies, and qualitative research, to gain as broad a perspective of surgical innovation in LMICs, considering the views of the main stakeholders. I will use this information to construct a framework to streamline the translation of surgical innovation within the context of low-resource settings.

1.11 Thesis objectives

1) To conduct a systematic review of the literature to identify how surgical technology is evaluated in LMICs and the barriers and facilitating strategies to evaluation.
2) To conduct a research training exercise in Sierra Leone and evaluate a new training methodology to increase research capacity and capability.
3) To conduct a feasibility study in Sierra Leone investigating the use of virtual reality technology to enhance clinical training and improve the uptake and outcomes from surgical interventions.
4) To develop a Framework to increase the efficiency of clinical evaluation studies of surgical technologies in LMICs.

2 The global lack of surgical trials (IDEAL Stage 3 studies) and strategies to overcome barriers: A systematic review and narrative meta-synthesis

Clinical trials are required to generate valid and unbiased clinical effectiveness data that is often needed to persuade policy makers to adopt new interventions. In global surgery, there is a lack of surgical trials conducted in LMICs which often precludes the adoption of new innovation. Understanding barriers to evaluation of new interventions and identifying facilitators may increase the quantity and quality of LMIC surgical trials. In this chapter, I determine the number of registered surgical trials globally and identify barriers and facilitators to surgical trial evaluation in LMICs, through a systematic search of the literature. A narrative meta-synthesis is conducted using inductively generated themes via thematic analysis to present a cohesive understanding of the topic. The output from this Chapter should help to inform future study design and lines of scientific enquiry that are relevant to the LMIC context, as well as inform considerations for early stages of the development of the evaluation framework.

2.1 Background

Clinical trials, particularly randomised controlled trials (RCTs), are the accepted gold standard method to generate clinical effectiveness data. For surgical innovation, such studies are embodied within IDEAL Stage 3. Surgical trials almost always involve a complex intervention, and present challenges for surgical researchers, including standardising the intervention across surgeons and settings, learning curve effects, and access to the necessary technology (134–138). These challenges are common to the delivery of all surgical trials, irrespective of the context in which the trial is conducted.

However, there are unique and context-specific challenges that need to be considered when conducting surgical trials in LMICs.

Surgery is a complex intervention, defined as an intervention that combines several different but often interdependent factors (139). The Medical Research Council (MRC) in the UK have issued guidance on the development, evaluation and implementation of complex interventions and the characteristics that makes an intervention complex (93).

Evaluations of complex interventions require consideration of several key development, design and implementation factors (139). These can be summarised as the design of the intervention itself, the design and delivery of the evaluation study, and the implementation of the intervention more broadly. Challenges include the need to ensure standardised design and implementation of all components of the complex intervention, appropriate outcome measurement and developing understanding of the processes via rigorous process evaluations (92,140).

Because of these challenges, there has historically been a lack of surgical trials globally with less than 1% of surgical patients enrolled into surgical trials (106). This phenomenon is more pronounced in low and middle-income countries (LMICs) (1,106). Where surgical trials are conducted in LMICs, the majority of patients are recruited from middle-income countries or urban areas that are better resourced. Participation in clinical trials research enhances the overall quality of patient care, and involving LMIC surgeons in clinical trials may be one means of driving up the quality of services overall (141). It is essential that the least developed countries are not neglected, even though the conduct of surgical trials may be more challenging.

To ensure surgical innovation and technologies are implemented appropriately, rigorous scientific evaluation is required, but this process must be practical, feasible and affordable (16,95). Once preliminary studies have been conducted to ensure the safety

and feasibility of the intervention, if the clinical effectiveness of the intervention has not been defined, a large RCT should be performed to evaluate this and inform policy (95). A recent systematic review on the barriers to clinical trial delivery in LMICs did not include any papers on surgical trials (142). Understanding the barriers to surgical trial delivery in LMICs and identifying facilitating strategies should improve the quantity and quality of surgical research.

2.2 Aims

The aim of this study was to determine the number of surgical trials registered globally and to conduct a systematic review and narrative meta-synthesis of articles reporting on barriers or facilitators to surgical trial delivery in LMICs.

2.3 Methods

2.3.1 Study design

The study was conducted according to the principles of *Preferred Reporting Items for Systematic Reviews and Meta-analysis Protocols (PRISMA-P)* and was registered prospectively on the PROSPERO database of systematic reviews (registration number: CRD42019135349) (143).

2.3.2 Search Strategy

Two independent investigators (WSB and NA; WSB was the PI on this study) performed a systematic search of the MEDLINE (via OvidSP), EMBASE (via OvidSP), and all clinical trial registries listed on Primary Registries in the World Health Organisation (WHO) Registry Network via the WHO International Clinical Trials Registry Platform

(ICTRP) (https://www.who.int/ictrp/network/primary/en/). The ICTRP was used as it allows access to all primary registries meeting the WHO International Standards for Clinical Trial Registries and the requirements of the International Committee of Medical Journal Editors. The search strategy for the Platform employed the 'intervention' menu of the advanced search function using the topic 'surgery' and system self-generated synonyms. The database provided the recruiting countries, and countries were categorised manually into LMICs or high-income countries (HICs) according to the World Bank Development Assistance Committee (DAC) classification. All trials registered as open to recruitment, in follow-up or completed were included.

For the MEDLINE and EMBASE databases, all studies published up until May 2019 inclusive were considered for eligibility. All searches were conducted on 25th June 2019. Titles and abstracts from the identified articles were screened for relevance against the eligibility criteria below. Eligible manuscripts were fully inspected. Reference lists from eligible studies and published systematic reviews were inspected to further identify relevant studies. The search strategy for these databases is described in Appendix 1. In brief, search terms included LMIC countries (as classified by the World Bank DAC list), articles relating to the delivery of clinical trials in any surgical speciality and reporting on barriers and/or facilitators to trial delivery. Non-English articles were excluded to prevent potential misinterpretation of the information.

2.3.3 Manuscript eligibility criteria

Figure 10 illustrates the selection process and displays the PRISMA diagram. The eligibility criteria for manuscripts were:

2.3.3.1 Inclusion Criteria

1. Manuscript type: systematic reviews (+/- meta-analysis), randomised controlled trials, cohort and case control studies, case series, case reports, study protocols.
2. Participants: humans in LMICs.
3. Procedure: any surgical technology or operation defined here broadly as any technology, medical device or procedure targeted at surgical care.
4. Outcome: reports on barriers, challenges or facilitating factors of trial delivery.

2.3.3.2 Exclusion Criteria

1. Manuscript: All editorials, news, comments, letters, technical notes, and conference abstracts.
2. Language: All non-English language articles.
3. Participants: Studies not involving humans, or humans in HICs only.

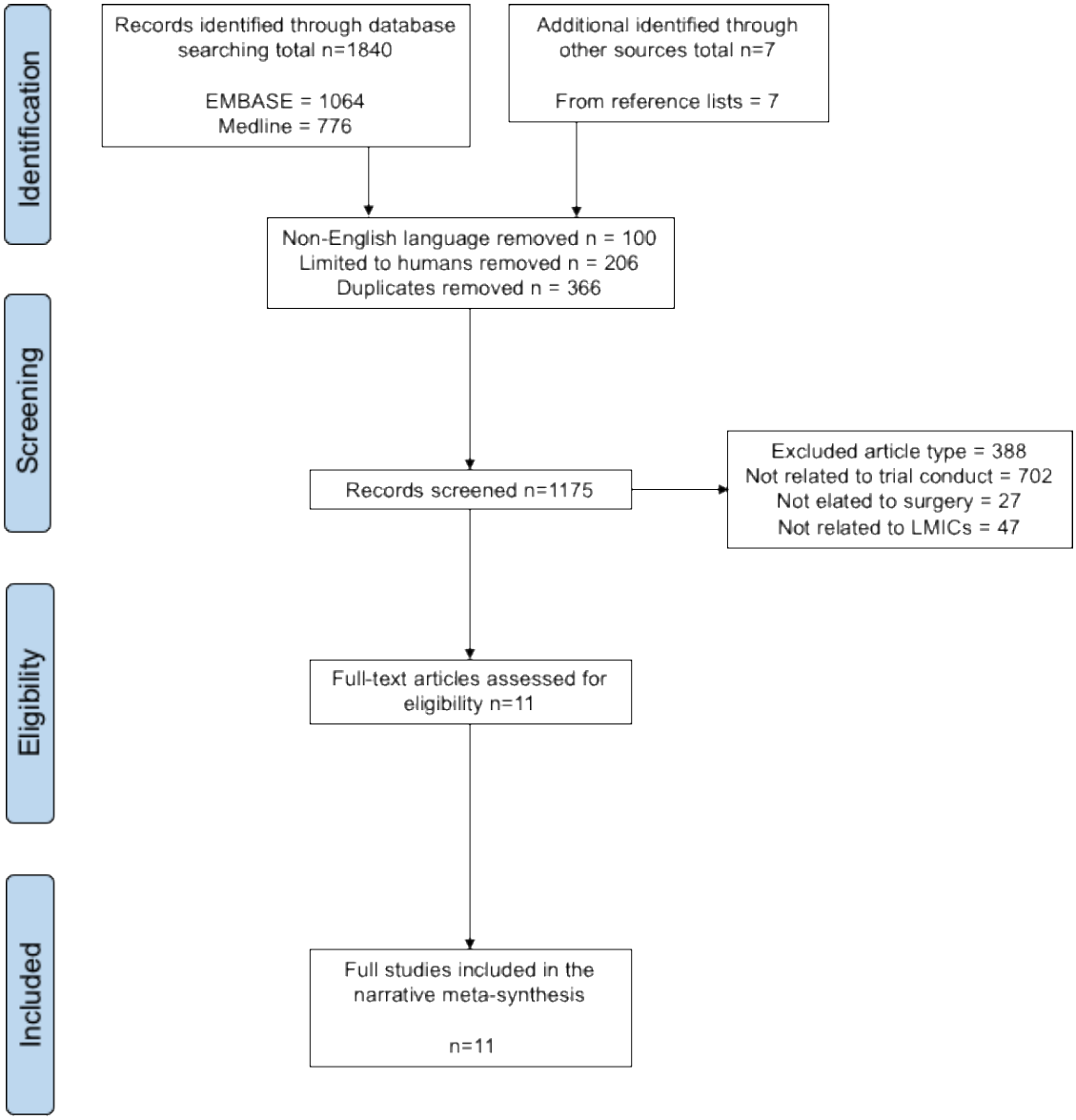


Figure 10: PRISMA diagram of search and eligibility process.

2.3.4 Data extraction and analysis

To identify barriers and facilitators, a meta-synthesis approach guided by Greenhalgh *et al* and Thomas *et al* was used to inductively generate analytical themes from the findings of the included studies, as described and used in previous systematic reviews (142,144–149). All text under the ‘‘results or findings’’ or ‘‘conclusion or discussion’’ section of each article was extracted and entered verbatim into NVivo. This was coded and analysed by WSB using the Framework method for thematic analysis (150). If the article was a review,

then all text within the main body of the article was included. Once the coding process was completed, the meta-synthesis was conducted by organising the data using NVivo. Patterns within the data were observed, themes were identified and refined using an iterative process, and used to draw interpretations before the evidence was then synthesised to provide a narrative relevant to the research questions. This process followed the European Social Research Council Guidance on the Conduct of Narrative Synthesis in Systematic Reviews (151). To improve reliability of the evidence synthesised, identified themes were discussed within the research group, examined and changes made where necessary. This process was repeated until consensus was reached regarding the sufficiency and appropriateness of the themes and subthemes developed. Given the qualitative methodology and synthesis of a heterogenous literature on the topic, formal methods for assessing risk of bias were not undertaken.

2.4 Results

WHO International Clinical Trials Registry Platform (ICTRP) findings

A total of 488,120 (136,327 listed as recruitment ongoing) trials were listed on the WHO ICTRP. Of these, 16,510 (4,823 listed as recruitment ongoing) listed ‘surgery’ (including synonyms) as an intervention. This represents only 3.4% of all registered trials globally. A total of 154,613 (49,931 listed as recruitment ongoing) of all trials registered globally were listed as recruiting from at least one LMIC, representing 31.7% of all registered trials. Within LMICs, 7,077 (2,140 listed as recruitment ongoing) trials listed ‘surgery’ (including synonyms) as an intervention, representing 4.6% of the trials with recruitment from LMICs.

2.4.1 Manuscript demographics

Eleven studies met the inclusion criteria, including five qualitative studies, one mixed methods study and five review articles. The characteristics of the included studies,

including LMICs involved, study design and participant population are summarised in Table 1.

Table 1: Summary of included studies, study design, country, and primary aims.

First author & date	LMIC country/countries	Study design	Participant population	Primary aims
Ibrahim et al, 2015(152)	Chile, Ethiopia, Kenya, Nigeria, Ukraine	Qualitative	Surgeons n=18	Develop a framework for the monitoring international surgical initiatives in LMICs
Vischer et al, 2017(153)	Kenya, Ghana, Burkina Faso, Senegal.	Qualitative	Surgeons, clinical researcher staff n=60	Determine internal factors slowing down clinical trials in Sub-Saharan Africa
Rendon et al, 2017(154)	Brazil	Qualitative	Surgeons n=13	Identify barriers and facilitators experienced in collaborative prospective research in orthopaedic surgery
Aveling et al, 2016(155)	Ethiopia	Qualitative	Surgical staff, clinical research staff n=66	Barriers to implementation of interventions to improve surgical services
Fallah et al, 2017(156)	HIC members working with various LMIC collaborators	Qualitative	Surgeons, anaesthetists, physicians, residents, nurses, academics, and	Framework for improving international surgical teaching collaborations

			administrators n=68	
Conradie et al, 2018(157)	27 African countries	Mixed methods	Surgeons, clinical researcher staff n=134	Barriers to clinical research in Africa
Grover et al, 2017(158)	na	Review	na	Identify challenges to clinical trials in LMICs
Moraes et al, 2013(159)	na	Review	na	Identify challenges to multicentre trials in orthopaedic and trauma surgery
Clement et al, 2018(160)	na	Review	na	Identify the use of qualitative methods in trials globally
Søreide et al, 2013(106)	na	Review	na	Strategies to improve surgical research through international collaboration
Skrzynno et al, 2018(161)	na	Review	na	Challenges in surgical consent in trials

2.4.2 Barriers to surgical trials in LMICs

The thematic presentation of barriers meta-synthesised from the literature are summarised in Table 2, highlighting which references were drawn upon to generate each theme and subtheme. There were four main barrier themes, each having multiple sub themes: i) Lack of human resource capacity; ii) Lack of equipment, technology, and resources; iii) Culture and contexts; iv) Methodology, design and implementation. To

describe the core of each theme, the following narrative draws on examples from the included studies.

Table 2: Meta-synthesised thematic and sub thematic presentation of barriers to delivering surgical trials in LMICs

Number	Thematic barriers	Subtheme	References
1	Lack of human resource capacity	Lack of surgical and allied healthcare workforce Lack of general clinical research delivery workforce Lack of trial methodology and delivery workforce Lack of knowledge and skills Lack of time Lack of incentive or motivation Underdeveloped research culture	(106,152–158)
2	Lack of equipment, technology, and resources	Lack of surgical technology for trial and wider care delivery	(153–155,157,158)

		Lack of data collection and information technology Lack of research and service delivery infrastructure Lack of financial resources	
3	Culture and contexts	Cultural sensitives and a lack of patient/community education Varying ethics and other regulatory affairs Lack of trial adaptation to differing populations and systems Surgeon and researcher attitude to research, randomisation, and influence of surgeon preference	(106,152–155,157,158,160,161)
4	Methodology, design, and implementation	Lack of planning and context understanding Lack of LMIC consultation in design Lack of trial design and delivery knowledge and skills Challenging outcome and data collection	(106,152–154,157,158,160,161)

		Standardising interventions and trial delivery procedures Lack of qualitative process evaluation	

i) Lack of human resource capacity

The lack of human resource capacity was a significant barrier in seven out of the eleven studies. In their mixed methods study, Conraide *et al* highlighted a critical lack of surgical and allied healthcare workforce to conduct the necessary study interventions (157). These are essential to deliver the components of any trial, but the execution of a complex surgical intervention is even more dependent on human resource skillset. In their review article, Søreide *et al* highlighted that the lack of clinical research delivery skills and motivation among the surgical workforce adds to the human resource gap (106). A qualitative paper by Rendon *et al,* exploring barriers to collaborative orthopaedic trial research in LMICs, highlighted that while improving the skillset of personnel is important, researchers often have a limited bandwidth and find it difficult to balance research with clinical delivery (154). Finally, they often experience a personal sense of fatigue from constantly fighting barriers.

ii) Lack of equipment, technology, and resources

Five studies found a lack of equipment, technology, or resources, such as financial resources, was a key barrier. In their qualitative process evaluation of a surgical quality improvement project, Aveling *et al* highlighted that it is essential to audit the amount of functioning equipment from both within and outside the research study (155). This ensures safe and efficient running of the research, but also builds and leaves clinical capacity after the study has finished. In their study involving 27 African countries,

Conradie *et al* found that information technology to collect data and share information was among the most frequently reported barrier (157). Although the internet may have penetrated larger urban centres, rural hospitals (where a large proportion of surgical care is delivered) have little access to the information technologies that are often essential for research. Financial resource is also essential to research delivery. In their review article, Grover *et al* discussed how funding for clinical trials does not always prioritise the conditions or areas of greatest need in LMICs (158). Further, even if clinical trials do demonstrate efficacy in LMICs, researchers are often unable to provide a plan for sustainable implementation of these interventions. Grover *et al* argue that this poses a major challenge to global surgical funding panels and ethics committees (158).

iii) Culture and contexts

The most frequently reported barrier was adapting to the wide range of cultural and contextual factors that are intrinsic to international global surgical research. In an international qualitative study of surgeons from HICs and LMICs, Ibrahim *et al* demonstrated that understanding cultural sensitivities and loco-regional contexts was essential when navigating varying ethical and regulatory affairs, as well as exploring surgeon and researcher attitudes to trials (152). A systematic review by Clement *et al* showed the usefulness of process evaluations and other qualitative methodologies during trials to inform the understanding of culture and context as they examined a total of 615,311 registered trials (160). The authors highlighted that trials of surgical interventions used qualitative methods the least and, in general, use in LMICs was infrequent. In particular, De Skrzynno *et al* highlighted that culturally appropriate patient and public engagement is vital to ensure good conduct during surgical trials (161).

iv) Methodology, design, and implementation

A total of eight studies discussed important barriers concerning the theme of methodological design and trial implementation. Vischer *et al* conducted a qualitative study of internal factors responsible for slowing down trials in Sub-Saharan Africa (153). They identified two broad themes: 'planning' and 'site organisation'. Planning referred to the work done during the design phases of studies. Importantly, there seems to be a chronic lack of LMIC consultation during the trial methodology design stages. This can translate into poorer quality data collection that reduces the overall impact of the trial. These themes were represented in several included articles (152,161). Ongoing site organisation can be monitored and improved with in-built qualitative process evaluations, a theme which was frequently reported the literature (160).

2.4.3 Facilitating strategies to surgical trials in LMICs

The thematic presentation of facilitators meta-synthesised from the literature are summarised in Table 3, highlighting which references were drawn upon to generate each theme and subtheme. There were three main facilitator themes, each having multiple subthemes: i) Collaboration; ii) Flexible and efficient trial designs; iii) Funding and research culture. Facilitators are presented here as strategies to overcome barriers presented above. Often a facilitating factor can be identified as the inverse or counterpoint to a barrier, but in the narrative here, the core of each facilitating theme is discussed to cover distinctive and perhaps cross-cutting ideas to overcome the identified barriers.

Table 3: Meta-synthesised thematic and sub thematic presentation of facilitators to delivering surgical trials in LMICs.

Number	Thematic facilitators	Subtheme	References
1	Collaboration	International HIC-LMIC collaboration Loco-regional collaboration Interdisciplinary collaboration and team working Multi-centre collaboration to increase sample sizes and capacity building Surgical trial leadership	(106,152,154,156–159)
2	Flexible and efficient trial design	External pilot phases LMIC lead planning and trial design Evaluation of implementation and process Cost-effective and efficient design Use of technology in design and delivery	(106,153–155,157–159)
3	Funding and research culture	Financial resources and capacity building Encouraging a research culture, recognising academics	(106,152–155,157–161)

		Professional development	

i) Collaboration

Collaboration was discussed as an essential facilitator in several papers. In particular, Søreide *et al* stressed that international collaboration is mutually beneficial, and Ynoe de Moraes *et al* highlighted the importance of considering loco-regional collaboration within countries (106,159). This is principally important to reduce the urban-rural disparity. Importantly, the interdisciplinarity (between/within healthcare workforce members and collaboration with key partners such as industry and governments) of the collaboration was discussed as a facilitating factor that improved trial delivery (154,156). These collaborations foster surgical trial leadership and multiple centres increases capacity to gain larger sample sizes when necessary and improve generalisability of trial findings. Overall, collaboration is needed to address the key barrier in the lack of human resource capacity, where surgeons and researchers within and between countries establish training and knowledge transfer collaborations.

ii) Flexible and efficient trial design

The majority of the included literature emphasised that local contexts should be considered at every stage of the trial. Particular additional features discussed as facilitating strategies included conducting external pilots and front-loading qualitative evaluations during the design and planning phases (106,153). These can inform the design and prevent avoidable pit falls and failures, as well as pulling key local members of the team into the design process. Using in-built qualitative methodology can allow researchers to evaluate the trial implementation and delivery in real-time, thus adapting to changing situations where needed and boosting efficiency (153,154,160). Overall, it

is essential to keep trials affordable and efficient in their design. The use of digital technologies to collect, store and share data, as well as to deliver training and trial implementation, are further facilitating strategies to improve the efficiency of trial conduct (106,157).

iii) Funding and research culture

Almost all included literature highlighted that adequate funding, and a conducive research culture are essential components for increasing surgical trials capacity globally. Recognising and developing clear career pathways and offering professional development opportunities for clinical academics is key, especially in LMICs (106,152,159). This will encourage new research leadership and ensure academic effort is rewarded, including financially. Creating mutually interesting and beneficial research priorities across countries will develop a deeper, more productive surgical trials research culture whilst ensuring that collaborative large-scale funding and impact can be achieved.

2.5 Discussion

The results of this chapter demonstrate a disproportionately low quantity of surgical trials undertaken globally, which results in a mismatch between randomised evidence and global disease burden. The delivery of standardised interventions and trial procedures, remain a significant challenge for surgical researchers in LMICs. This is compounded by the frequent lack of surgical care and trial research infrastructure. In contrast, focusing on flexibility in trial design, employing additional methods from qualitative research, together with collaboration and training opportunities, facilitate LMIC surgical trial research.

The lack of surgical trials in LMICs is particularly concerning given the contribution that surgical care makes to tackling the global disease burden (4,162). This systematic review provides an insight into the challenges faced by those attempting to deliver this much-needed research. Even in the most difficult circumstances, there are strategies to overcome these barriers which could be employed in future surgical trials. A key strength of this review is the ability to synthesise and display these strategies in one place. Whilst global surgical researchers seek to increase the volume of well conducted trials in LMICs, it is essential that the findings inform policy and produce a change in practice to benefit patients. The use of a qualitative meta-synthesis design permitted the exploration of a broad research question and interrogation of heterogenous evidence from a range of contexts and study designs. This rich synthesis of the evidence, and resulting narrative, does not solely focus on the challenges, but highlights widely useful facilitating strategies for both policymakers and surgical researchers. A weakness of the review is the incomplete representation of the research pathway. Whilst clinical trials are often required to persuade policy makers to adopt an intervention, many other types of research are needed to answer broader questions pertaining to the clinical impact of interventions in the short and long term. An examination of non-trial surgical research in LMICs may identify further gaps and facilitating strategies along the pathway. Another weakness is that only papers written in English were included in the review owing to the lack of translation facilities available to the research team. Some countries are not represented in this review, and as barriers may be context specific, important data could be missing. Further, of the papers included, appraisal of study quality was challenging with such a variety of study designs. Given the lack of literature on the topic, it was felt that an inclusive approach would increase the diversity of the data. Finally, the qualitative methods used in this review are inherently subjective, affected by the researchers' experience and prejudices.

This chapter raises important considerations for both the design and delivery of surgical trials in LMICs. The imperative for global surgical researchers now is to explore the use

of the facilitating strategies outlined in this study within ongoing and future global surgical trials research. For example, standardising interventions within surgical RCTs is essential to derive high quality, meaningful data (163). In LMIC surgical trials, ensuring standardisation across multiple surgeons, hospitals and countries is equally important, but often more challenging. To address this, the current study highlights the need to ensure a flexible and efficient trial design, and to take differing cultures and contexts into consideration. This could be achieved by using the method proposed by Blencowe *et al* to identify the critical component/s of the intervention and trial design that require standardisation, and how much flexibility is permitted whilst maintaining methodological rigor in surgical trials (163). Another facilitating strategy identified is in-building qualitative methodologies during the design and delivery phases of surgical trials. Clement *et al* highlighted that only 0.24% of registered trials reported using qualitative methodologies and only 4% involved surgical interventions (160). The authors suggested that surgical trials can benefit from qualitative methodology to explore surgical behaviour, recruitment issues and factors affecting equipoise. For example, Donovan *et al* embedded a surgical trial within qualitative research and demonstrated the positive impact on recruitment and trial delivery (164). Employing qualitative methodology may be especially important for global surgical trials recruiting in LMICs, where there may be a greater need to identify challenges, explore cultural contexts and the acceptability of interventions. By front-loading qualitative exploration during the trial design phase, researchers will be able to identify and tackle specific human resource training needs, thereby addressing a significant barrier to research upfront. Employing novel approaches to research training such as the Global Competency Framework for Clinical Research, which describes the core competencies for a research team in LMICs and provides e-learning materials, would help address this barrier (102,103,165).

It is important to remember that this chapter focuses only on surgical trials, and there remains a wide range of potential study methodologies that have different utilities in the evaluation pathway of surgical innovation and technology. In later chapters I explore

alternative study designs and their appropriateness depending on the context and research question. The justification for focusing on RCTs here is the importance of these studies to informing decision-making around clinical adoption. In global surgery, the barriers to RCTs identified in this chapter are compounded by the need to evaluate increasing numbers of innovations and technology solutions, and to do so in a timely fashion to address the growing challenges in global surgical provision. There will always be a need for valid randomised, unbiased evidence for new interventions irrespective of the context. Therefore, while this chapter highlights facilitating strategies to improve the design and delivery of surgical trials in LMICs, it remains important to also identify alternative study designs that may be more resource-effective and easier to complete. In this way, more results can be fed back efficiently to policy makers and surgeons and provide the evidence on which to base decisions surrounding innovation adoption.

There is no question that surgical trial research in LMICs has been neglected. Human resource gaps and global trial funding remain unmet challenges and international collaboration from all members of the surgical research community is required. Cultivating surgical research leadership from within LMICs will likely be a critical step in strengthening an international surgical research culture. Addressing the lack of qualitative methodology in surgical trials would likely provide a cross-cutting facilitating strategy that can target multiple elements of the trial design and delivery pathway. With the recent global drive to improve access to surgical care, our findings are relevant to all members of the global surgical trial community, providing facilitating strategies to address the challenges in undertaking surgical trials in LMICs. This will in turn help drive up the overall standard of surgical care globally.

3 IDEAL Stage 2 evaluations to facilitate surgical innovation adoption in LMICs

In Chapter 3 I highlighted the lack of surgical RCTs globally and identified that the limited human resource capacity and research skills gaps are some of the most important barriers to surgical trial delivery in LMICs. Solutions are urgently needed to improve the development of a workforce skilled in the evaluation of surgical innovation to improve surgical care. While this may make the delivery of surgical trials more efficient, we also discussed the need to utilise alternative evaluation approaches that may be more appropriate to conduct. In this Chapter, I explore the role of IDEAL Stage 2 studies and the potential for them to generate sufficient evidence without needing to progress to definitive RCTs in certain circumstances (IDEAL Stage 3). These types of studies may serve as potential facilitators of global innovation adoption and diffusion. The situations where these studies may provide valid alternatives include when the intervention is not novel (Chapter 4) or when the intervention is deemed low risk (Chapter 5). These study designs may increase the pace of innovation adoption as they are simpler, quicker to conduct, and generally less expensive. Because addressing the research skills gap is critical, in this Chapter we also report the findings of an embedded process evaluation exploring the effect of a research skills training programme for an IDEAL Stage 2 study.

3.1 Background

IDEAL Stage 2a and 2b studies are usually used to inform the design and delivery of a future definitive multicentre RCT (IDEAL Stage 3 studies). However, the use of IDEAL Stage 2a and 2b studies as alternatives to Stage 3 studies in LMICs has been underexplored. Where a Stage 3 study is needed, alternative RCT designs have been explored as a potential approach to improving the delivery of clinical trials in LMICs,

such as adaptive designs and platform trials (166). The IDEAL Collaboration has also recently published guidance on when an IDEAL Stage 3 study is not required, such as when the intervention is not novel and no superiority claim is being made, and in such cases they suggest that IDEAL Stage 2 studies will provide the minimum evidence required before adoption (167). In global surgery this scenario often applies, with researchers aiming to inform the adoption of existing and established technologies from one context (e.g., HIC) into new contexts (e.g., LMICs). Superiority may already be established via clinical effectiveness Stage 3 studies in HICs, and therefore no new superiority claim is being made. The effect of this approach on surgical innovation adoption in LMICs remains unclear. In this chapter we present the design of the IDEAL Stage 2b NIHR FIXT Trial: Feasibility of Ilizarov frame fiXation for closed Tibial fractures in Sierra Leone (ISRCTN 51545197) as an example of this approach. To assist with overcoming the barrier of research skills gaps in LMICs for this study design, we also present the evaluation of a research training programme to guide the site initiation of IDEAL Stage 2 studies across LMICs.

3.2 Aims

This chapter aims to present the design of an IDEAL Stage 2 study in Sierra Leone and evaluate the effect of receiving research skills training and trial intervention training to a range of research and clinical staff. This evaluation took place during the initiation of a single centre, non-randomised, before-after surgical trial of a surgical technology intervention in Sierra Leone (The NIHR FIXT Trial). This study also aims to explore the perceptions and experiences of the training intervention in the delivery of clinical trials of surgical technology in a LMIC setting.

3.2.1 Study setting

The study site is a large government referral hospital called Connaught Hospital in Freetown, the capital city of Sierra Leone, and has 300 beds of which 108 are surgical

(76 adult and 32 paediatric). The hospital has 5 functional operating theatres and only one consultant trauma and orthopaedic surgeon. The hospital has 4 postgraduate surgical trainees and is the teaching hospital for the University of Sierra Leone and the College of Medicine and Allied Health Sciences (COMAHS).

3.3 IDEAL Stage 2 study design in LMICs: The FIXT Trial design and rationale

I am the UK-PI of the NIHR FIXT Trial, a non-randomised, unblinded, before-and-after trial of conservative treatment (standard of care) versus operative fixation using the Ilizarov method. This feasibility trial aimed to recruited 20 patients into each arm (40 in total). The key objectives included assessing the safety of Ilizarov frame fixation, proof of clinical efficacy in terms of fracture healing, the effect on patient function and quality of life, and the cost-effectiveness of the technology through a prospective health economics evaluation. The primary endpoint was fracture angulation at 3 months as a marker of functional fracture healing. The CONSORT trial participant flow diagram can be seen in Figure 11.

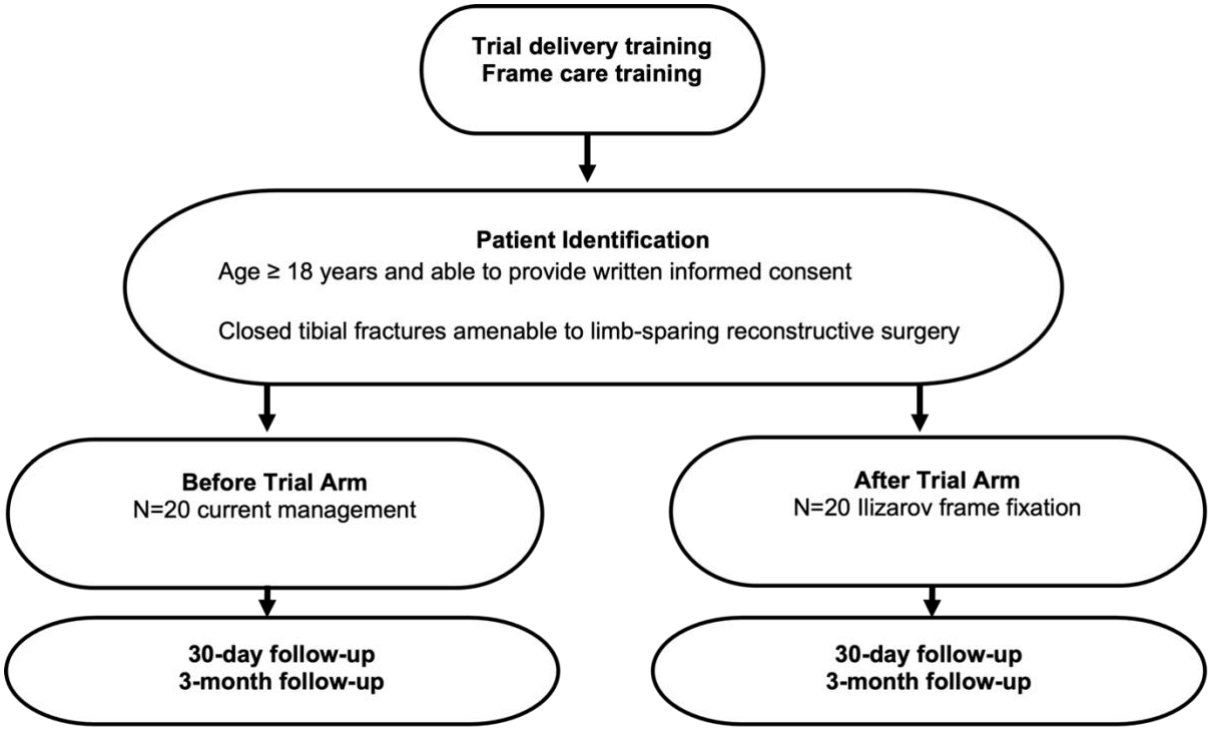


Figure 11: FIXT Trial CONSORT participant flow diagram.

The Ilizarov frame is a circular external fixator, often used in the surgical management of several fractures including long bone fractures such as the tibia. The feasibility and safety of Ilizarov frame fixation for limb-sparing reconstructive surgery has been established in HICs (168–171). The use of this fixation technique in LMICs is not widespread and evidence of its feasibility, efficacy and cost-effectiveness in low-resource settings is lacking (61,62). Such evidence is required to inform policy making and guide wider implementation if it is a safe and cost-effective for fracture management in the low resource setting. Provision of trauma services, including the surgical management fractures, is essential and should be available 24/7 at all first level hospitals (172). Indeed, treatment of fractures is considered one of the three Bellwether procedures; the most essential surgical procedures all hospitals should be able to perform, including laparotomy and caesarean section.

The majority of closed, long bone, lower limb fractures in Sierra Leone are managed conservatively using skin traction techniques, which results in prolonged hospital stays, delayed return to work, and suboptimal functional outcomes (173,174). The purpose of the FIXT trial was to investigate the feasibility of limb-sparing reconstructive surgery with Ilizarov frame fixation for closed tibial fractures as an alternative to conservative management.

This IDEAL Stage 2b study design was chosen for logistical reasons as it was a convenient, simple, and affordable design. The trial intervention (Ilizarov frame fixation) is an established intervention for the management of tibial fractures in HICs and in itself was not surgically novel. In this setting, the context in which the intervention was used (the population and healthcare system) was novel. It could safely be assumed that the clinical effectiveness of the intervention was proven, but the unknown was its application in a low resource environment. An IDEAL Stage 2b design was therefore deemed to be appropriate with outcomes including the feasibility of conducting the research within Sierra Leone, safe application of the technology, and health economics evaluation to inform wider adoption should the intervention be clinically successful.

In keeping with the Medical Research Council (MRC) guidance on complex interventions, this trial had an embedded process evaluation (92,139,175) (Figure12). The process evaluation aimed to assess the contextual factors, implementation issues (fidelity, dose, adaptations, and reach), and mechanisms of impact, including participants responses to and interactions with the intervention, mediators, and unanticipated pathways and consequences. As highlighted in Chapter 3, qualitative methodologies within trials are important facilitating strategies as they provide the researchers with a great understanding of the context, enable adaptive strategies to be incorporated into trial design, and aid in the interpretation of results.

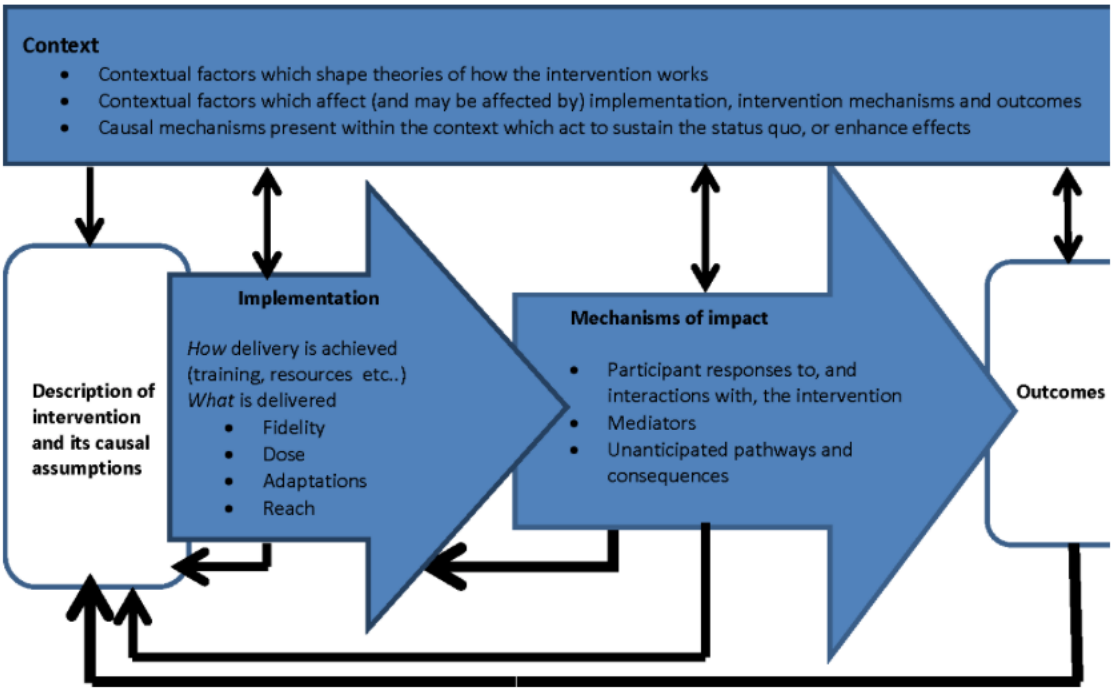


Figure 12: Process evaluation of complex interventions UK Medical Research Council (MRC) guidance (140)**.**

In this circumstance, an IDEAL Stage 3 study was not deemed necessary because the question of clinical effectiveness for the treatment of this condition is already established. What was important in this present study was to establish if any unintended consequences on clinical safety arose when the intervention was implemented in a new context. Embedding process evaluations into Stage 2 studies may facilitate the real-time identification of these unintended consequences. The feasibility of the intervention and how it interacted with current patient pathways was also important to define.

3.4 Research skills training for IDEAL Stage 2 studies

There is a significant research skills gap in LMICS, particularly in Sierra Leone, and addressing this was crucial to delivering the NIHR FIXT trial. The quality of researcher training in the delivery of complex interventions, as well as the assessment of

outcomes, has been shown to significantly impact study quality and outcomes (176). Improved training and reporting of interventions may improve the validity and usability of the results, and enhance the wider implementation of the intervention (177). Suitable training should be available for all staff involved in clinical evaluation studies, regardless of the context, and to ensure that study participants are ethically and safely treated (165).

The training required to deliver a clinical evaluation study of a complex intervention, such as a novel surgical technology, broadly falls into two categories: the researcher training, and the trial intervention training. Researcher training in LMIC evaluation studies has centred around the delivery of Good Clinical Practice training, as well as study-specific data collection and processes (165). Examples include the WHO Good Clinical Practice for trials on pharmaceutical products and the Global Health Network's Global Competency Framework for Clinical Research, which describes the core competencies for a research team in LMICs (102,178) and has been shown to be effective at improving research skills and study delivery (179).

Standardising the intervention via intervention training for clinical staff is important to ensure the intervention, processes and outcome assessment are consistent between patients and researchers(180). In an evaluation study of a surgical technology, the intervention is more than just the surgeon and the technology. The intervention includes all the perioperative, post-operative, and long-term follow-up care. Ensuring consistent application and implementation of the critical components of the intervention improves the delivery of studies and the validity of the findings.

3.5 Methods

This section focuses on the methods used to evaluate a training programme for the NIHR FIXT Trial, which was conducted at the time of trial initiation. Ethical approval

was provided by the Office of the Sierra Leone Ethics and Scientific Review Committee and the School of Medicine University of Leeds Research Ethics Committee (MREC18-001; Appendix 2)

3.5.1 Training programme design

To ensure the training covered all those involved in the delivery of the surgical trial, as well as those involved in the delivery of the complex intervention, two training programmes were designed and delivered to local staff:

1. Researcher training: those who are involved in the identification, recruitment and consent of patients, and collection of data, including study outcomes.
2. Intervention training: those who are involved in the delivery of the intervention, from surgeon to theatre nurses, ward nurses, physiotherapists and any healthcare professional involved with the patient in a caring or therapeutic capacity.

The researcher training delivered content informed by the WHO Good Clinical Practice for trials and the Global Health Network's Global Competency Framework for Clinical Research, as well as FIXT trial specific data collection and processes (102,165,178). The intervention training covered core principles of fracture management, surgical fixation using the Ilizarov method, patient aftercare, physiotherapy, and rehabilitation, in order to cover all facets of the complex intervention.

Both programmes employed techniques from blended learning and active experiential learning theory, where all participants were given access to online pre-course reading material, combined with face-to-face didactic sessions and interactive workshops (181–183). The combination of didactic sessions and interactive workshops aims to improve participants cognitive understanding alongside their practical skills learning. The full programmes for the training are included in Appendix 3.

3.5.2 Training evaluation and analysis

The programmes were evaluated using semi-quantitative paired pre- and post-course paper questionnaires. The barriers to clinical trials identified in Chapter 3 were included in the research training questionnaire, to assess participant agreement. Free text responses and focus group discussions (FGDs) were then used to identify and explore any additional barriers that may exist and explore responses to the questionnaires in more depth. For quantitative data, exploratory analyses were performed, summarising the data using descriptive statistics, including proportions and averages. Differences between pre- and post-course responses were tested for significance using Mann–Whitney U test and Student's t-test for non-parametric and parametric statistics respectively. Where free-text responses were collected, these responses were typed up and included verbatim in the qualitative analysis of the FGDs described below.

The findings from these questionnaires were enriched by further exploration via a FGD after each programme to explore participants views and experiences of undergoing the training. These FGDs were guided by a topic guide that covered their experiences of the training, reflections on what went well and what could be improved, and their perceptions of learning via the course, as well as barriers to trials and training in general. There was one FGD after the researcher training and one FGD after the intervention staff training. There was a small FGD with the two trial coordinators after all the training programmes and trial site initiation visit activity, to explore their overall views and experiences of a surgical trial initiation. FGDs were transcribed verbatim, and transcripts were imported into NVivo (version 12). A framework approach and thematic analysis were used to inductively generate analytical themes from the transcripts (142,144–149)(150).

All training delivery was observed by myself in line with the process evaluation analysis plan described in The FIXT Trial Protocol and with the Medical Research Council (MRC) guidance on process evaluations during trials of complex interventions (139,175,184). To contextualise the results from the paper questionnaires and FGDs, I observed the researcher training and intervention staff training, focusing on the content and quality of the training and staff engagement in the workshops, including any questions staff had regarding the delivery of the trial or intervention.

3.6 Results

3.6.1 Researcher training quantitative results

Twenty-two paired questionnaires were returned from the researcher training participants. The majority were female (n=16; 73%) and half had some previous experience of research (non-trial) (n=11; 50%). Almost all (n=20; 91%) were nurses from surgical wards, accident and emergency and theatre nurses, the remaining were surgical trainees. Only 4 (18%) participants rated their current level of knowledge about clinical research as ‘Good’ or ‘Very good’ on their pre-course questionnaire. After the course 19 (86%) ($p<0.001$) participants rated their current level of knowledge about clinical research as ‘Good’ or ‘Very good’ on their post-course questionnaire. Table 4 and Table 5 outline the influence of certain motivators and barriers respectively for involvement in IDEAL Stage 2 studies. Table 6 summarises course specific feedback.

Identified barriers were ranked from 0-10 by participants (0=not at all a barrier; 10=absolute barrier). Importantly, none of the included barriers were considered ‘absolute barriers; 10/10’ by the group, with ‘previous bad experience in research’ (indicating a poor research culture) and a ‘lack of time’ being perceived by the group as only 4.5-5/10. A key additional barrier that was identified by free text responses and explored in detail in the FGDs was the lack of patient education and engagement.

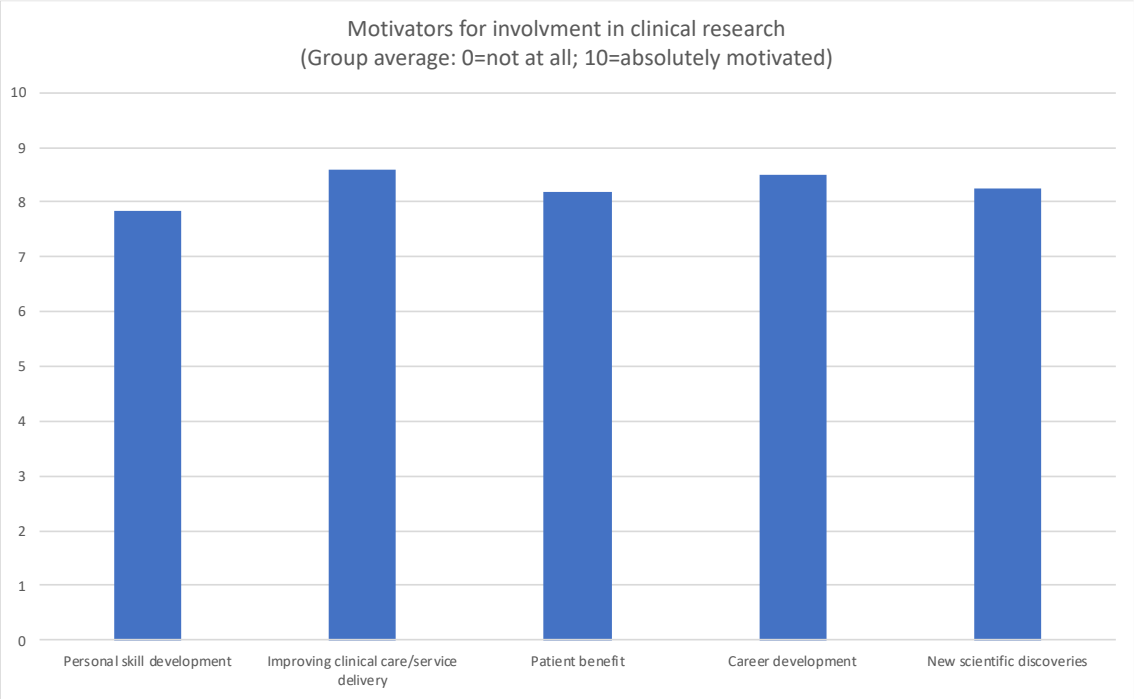


Table 4: Motivators for involvement in IDEAL Stage 2 studies

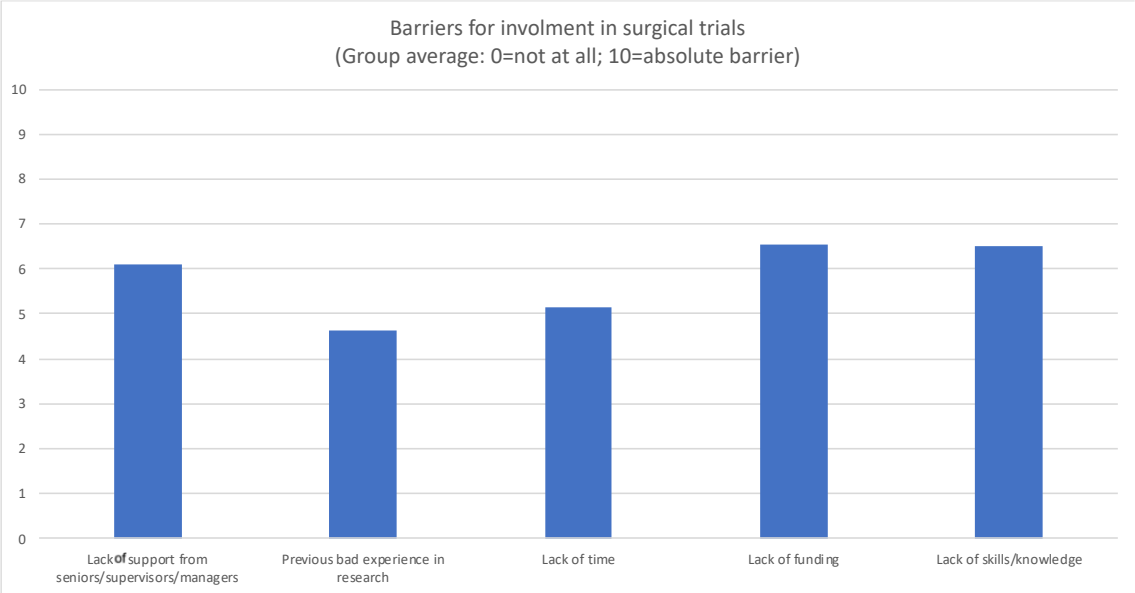


Table 5: Barriers for involvement in IDEAL Stage 2 studies

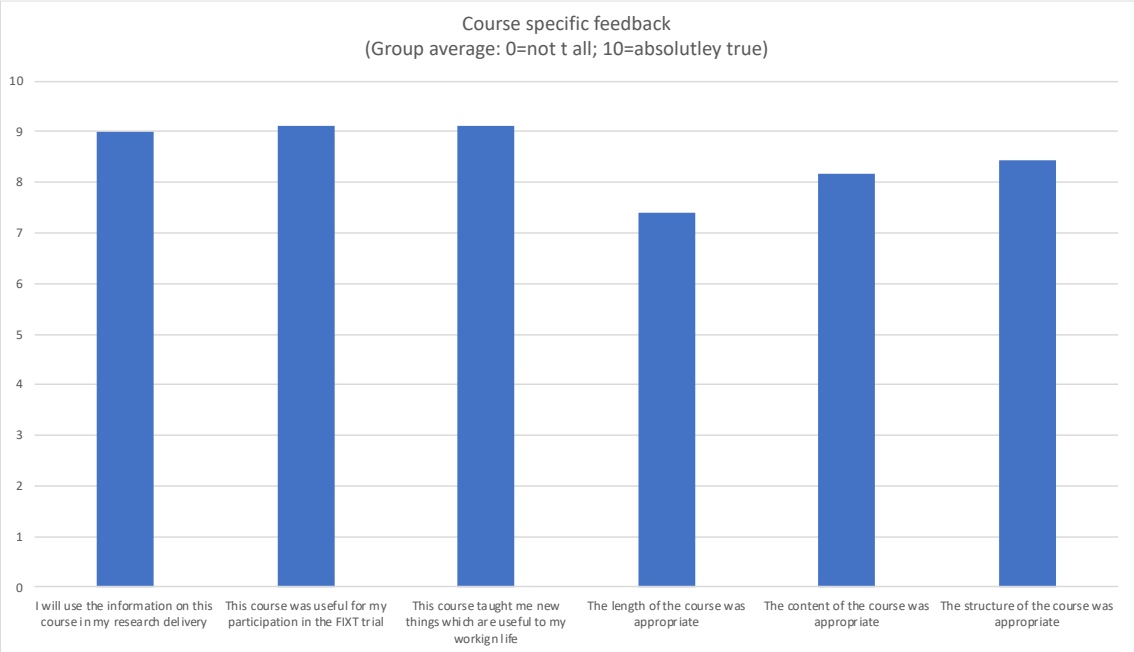


Table 6: Course specific feedback

3.6.2 Intervention staff training quantitative results

Thirty-one paired questionnaires were returned from the intervention staff training participants. Twenty-two provided a response for their gender and the majority (n=14; 64%) were female. Almost all (n=29; 94%) were nurses from surgical wards, accident and emergency, physiotherapy and theatre nurses, the remaining were surgical trainees. Ten (32%) had previous exposure to a patient with an Ilizarov frame before. Approximately half (n=14; 48%) of participants rated their current level of knowledge regarding the care of patients with Ilizarov frames as ‘Good’ or ‘Very Good’ on their pre-course questionnaires. After the course 29 (90%) (p=0.01596) participants rated their current level of knowledge about clinical research as ‘Good’ or ‘Very good’ on their post-course questionnaire. Table 7 outlines the influence of certain barriers to the implementation of this complex intervention in this setting. Table 8 summarises course specific feedback. The barriers to implementation of this technology intervention largely align with existing literature. A key additional barrier that was identified in the free text responses and explored in detail in the FGDs was the lack of interdisciplinary working both during training and usual working life.

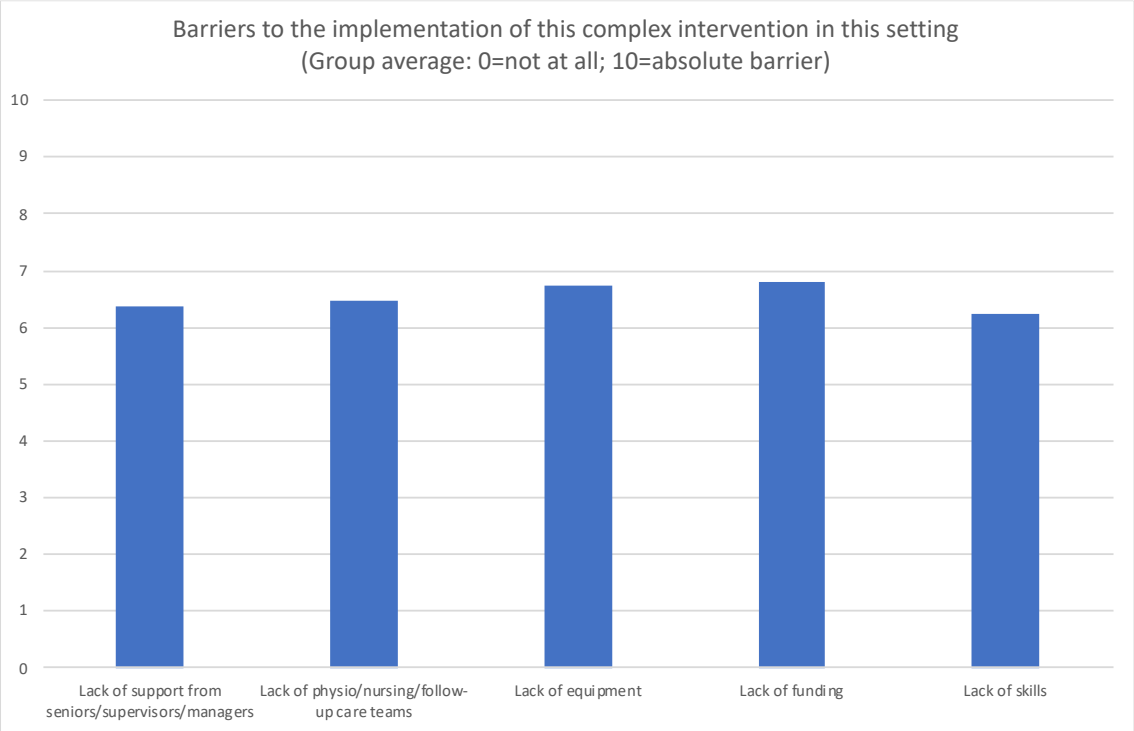


Table 7: Barriers to implementation of this complex intervention in this setting

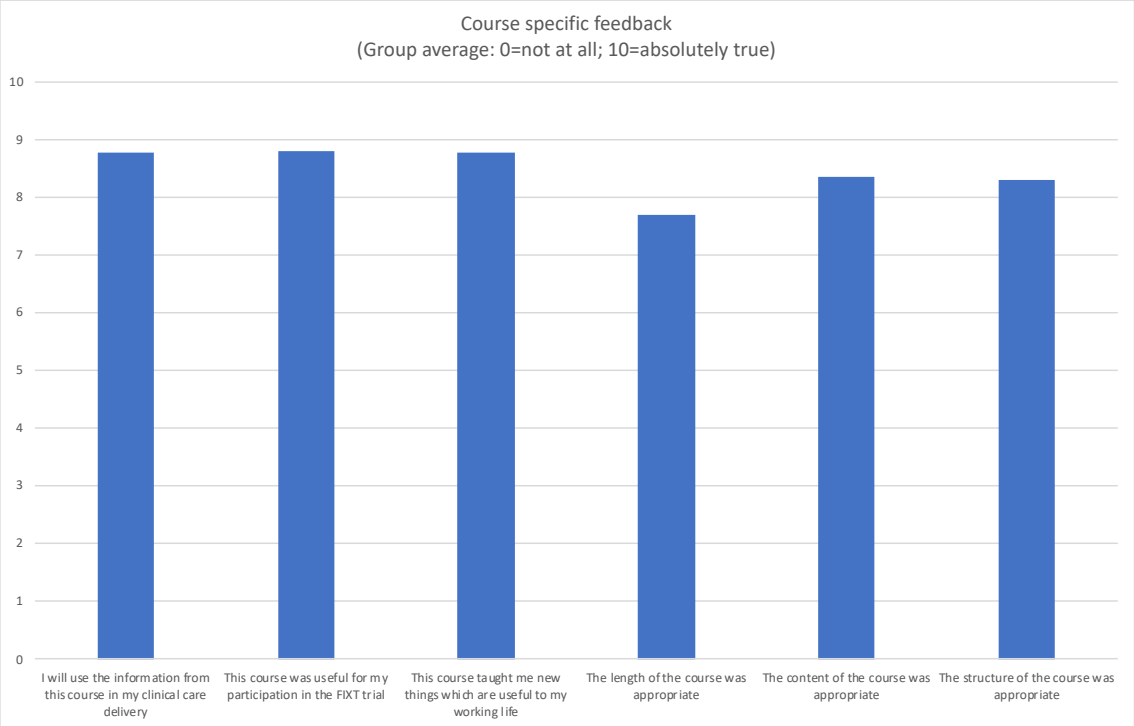


Table 8: Course specific feedback

3.6.3 Training programmes and trial initiation qualitative results

The results of the 3 FGDs and free-text results were analysed and considered as a whole, to provide a summary of the main themes and subthemes of establishing a surgical trial in an LMIC setting.

Training programme observations were conducted and fed into the qualitative analysis. It is important to note that LMIC settings can vary. This setting was observed to be of an extremely resource constrained, and naive to both surgical trials and many of the elements of this complex intervention. Table 9 summarises participant demographics of the 3 FGDs.

FGD	**Length** minutes:seconds	**Participants**
Researcher training	35:37	10 (1 matron, 1, surgical trainee, 3 staff nurses, 3 surgical ward nurses, 2 nurse anaesthetists)
Intervention staff training	32:35	10 (1 matron, 1 consultant general surgeon, 3 staff nurses, 3 surgical scrub nurses, 2 nurse anaesthetists)
Trial coordinators	24:53	2 (trial coordinators)

Table 9: Participant demographics of the FGDs

Five main themes emerged:

i. Interdisciplinary working
ii. Trial initiation management
iii. Training the trainers using technology
iv. Patient education and engagement

v. Desire for professional development opportunities

The transcripts and field notes that contributed to this data total more than 10,000 words.

3.6.3.1 Interdisciplinary working

The delivery of IDEAL Stage 2 studies of surgical technologies at the study site was a brand-new concept for the participants. However, other training programmes in related subjects had been conducted in the past, but these were often limited to the doctors:

"Nurse: Sometimes nurses are not invited to attend such trainings and participate in research, so we really want to learn these things."

The delivery of surgical care is an interdisciplinary process and surgical trials are no different. The involvement of multiple disciplines from the surgical team was valued by the participants:

"Surgical trainee: I really liked the mixture of people, it is good to train the nurses, anaesthetists, theatre staff, usually this doesn't happen. At this is a teaching hospital, we need to carry everyone along, so I really enjoyed the past two days."

The lack of interdisciplinary working was seen as a barrier to research and technology implementation. Overcoming this, by involving all disciplines in training and trial delivery, is essential to successful trial delivery and technology implementation.

3.6.3.2 Trial initiation management

Organising the delivery of a trial initiation is a complex task. Although involving multiple disciplines was valued by participants, sometimes the differing responsibilities made it challenging to manage and engage all participants fully:

“Surgeon: the timing, the doctors, some of them also wanted to attend, but because we have our early morning meetings at 8 o’clock, so that time frame of starting, they need to go to these meetings and both of us attended these so according to the programme we could not all make these timings.”

Managing the expectations of the participants and addressing the needs in knowledge and skills was challenging. Engagement in the learning by participants was in the main good, with many sensible and useful questions and discussions. A significant challenge was ensuring enough time was allocated to the training session without taking essential healthcare staff away from their routine duties for too long. The balance was hard to strike. Employing practical learning techniques was valued by participants:

“Nurse: On my own part, generally for the last 2 days and trainings concerning the fixation, the timings were very short. Because when you think about the contents, the contents we had for the time, the time was too short. Because the hands on, the hands on was good, when you think of how the Ilizarov is used.’

It was noted that further practice would be required as the trial began, and this suggestion was led by more experienced nursing team members who suggested a cascade learning approach with their colleagues:

“Nurse: the intraoperative fixation and assembling the equipment takes some time and takes some practice for you to know when and how to anticipate the request of the surgeon. So, if they can have it down at the theatre so that we can play around with it when they are less busy so that they can.”

3.6.3.3 Training the trainers using technology

Because the training interventions were short and at the beginning of the trial, the participants were keen to ensure they could develop their learning and highlighted that even in extremely resource limited settings, technology can be used to deliver this learning:

"Surgeon: I was just thinking, in the future, if we can organise online updates things like webinars, that would be fantastic."

Some of the senior nurses said they valued the idea of accessing such online material and delivering future training episodes to their colleagues.

"Nurse: Yes, what I am thinking is if you can send to me, because for me the nurses will need to access. The doctors and medical students can access yes but for me I am worried about what the nurses can access. So, if it is sent to me, it's like if we have a time like in the surgical department, what I will do is download it into my laptop and we can then have a small projection maybe."

3.6.3.4 Patient education and engagement

From the perspective of the training programme participants, engaging patients in research, as well as a lack of patient education, were among their top concerns in terms of a barrier to successful trial delivery.

"Nurse: ...the patients at Connaught have one of the highest levels of illiteracy, so I've been there before, the patients do not know what research is, sometimes it is difficult to explain it all to them and collect reliable data to analyse."

"Surgical trainee: And also, the cultural beliefs, people don't like elaborate information, research surgery, they will be asking why is this needed. They won't understand why this data is needed. So, the beliefs, level of literacy and the knowledge of the researchers.'

Cultural beliefs also pose a potential barrier when it comes to consenting to research or surgical care, and in the patient's and patient's family's 'trust' in healthcare:

"Nurse: coming back to what you said about cultural beliefs. Some of them, even though they are eligible for consent, they go back to their family members and ask them if they should be part of the study. Some of them are really dependent on what

their family members think. Maybe, they [themselves] will be willing to, but sometimes he [family members] tell them they are not going to."

Some felt that this challenge will increase as the trial progresses:

"Nurse: What I foresee is that, when we start with a particular patient, no problems, but for you to complete, it will be a big problem. Because as soon as they are discharged, some of them leave and will go against medical advice, they will go to traditional healers. From my experiences in research, the doctors are treating them in hospital but then they leave they may not come back to the nurses, so they will leave, it's like informal withdrawal. So, it's very difficult."

Separate from research participation in general, some had patient engagement related concerns specific to the intervention, largely because the intervention was so novel in this setting:

"Nurse: ...especially their [patients] beliefs for them they will be asking questions and then they won't be compliant because they will say 'why do you want to use me as a test rabbit, why not put some pins in, rather than out?' They will want to know 'what is this thing, it is too bulky, how do you want me to put on my trousers?' So, several questions, so the information and education for patient is going to be a challenge unless you are really really, like you have been trained and you can get the patient to keep on, because it is going to be a continuous process. ...some of them will go home and apply some traditional herbs, some will go home and fidget with the screws, and they come back, and they call you, yes so the patient education."

Developing effective patient and public involvement (PPI) strategies, as well as health education programmes, that are context and culturally specific for local populations, is going to be vital if we are to ensure surgical trials are ethically delivered and disadvantaged populations have the chance to participate if they wish.

3.6.3.5 Desire for professional development opportunities

There is a lack of post-graduate training for healthcare professionals in Sierra Leone and it was clear from the participants how valuable the training was for their development and capacity building:

"Surgeon: This Ilizarov apparatus is timely, the workshop itself is very informative. The formatting is excellent, the only thing is I think we need more time, and the frequency of these workshops should be increased, because it is capacity building and training at the same time."

There was a sense that regular and more frequent trainings were highly sought after. This may be facilitated by effective use of technology for education:

"Nurse: We pray that this will not be the end, and that we have more trainings."

"Nurse: thank you very much, this is my first time in research like this. I never knew about this intervention (the frame), this is my first time. I think it will have a great impact, and we pray that it will continue and not only this one, but will do more other stuff, other trainings."

The participants were highly motivated to attend the training and hoped for future opportunities to develop their skills. They were motivated for personal development reasons, but also motivated to keep the care of patients at the centre of their work:

"Nurse: To improve myself as a nurse, and to give back to my community at the healthcare facility."

"Surgical trainee: Generally, I am the kind of guy who likes to make use of opportunities to improve the patient's quality of care. I always jump at these opportunities. Personally, I like new discoveries and I know I can help patient care. So, for all of us, we need opportunities to improve patient care, so being part of the trial and this training has helped me personally and also to improve our patient's healthcare."

3.7 Discussion

The aim of this chapter was to explore the use of IDEAL Stage 2 studies as facilitators of surgical innovation adoption in LMICs, and to evaluate the effect of receiving

research skills training and trial intervention training on a range of research and clinical staff participants within an LMIC context. Through conducting mixed-methods analysis, including multiple FGDs with a wide range of participants, I was able to gain a wide variety of insights by using an inductive analytical process with the flexibility to include emergent theoretical ideas in addition to *a priori* concepts. This allowed me to retain diversity and complexity in the analysis with respect for the uniqueness of individual cases, as well as find comparative themes and patterns.

Participants of this surgical trial initiation were motivated to undertake surgical trials and valued the combination of research skills and intervention delivery training, as well as the chance to learn alongside their multidisciplinary team colleagues. They felt that more time was needed in some areas, and that some of the most significant challenges as they move forward in their roles as trial or care deliverers lie in the engagement of patients with surgical care in general, let alone the surgical trial itself. Future research is needed to explore the use of technology in training and the involvement and engagement of patients and the public. Participants felt that the training they received had increased their knowledge and understanding, as well as prepare them for the trial and surgical care provision in the future.

The data from this study is limited to the context in which it was collected and may not be valid in other contexts. Data saturation was quickly reached, and I am satisfied with the recurrence of themes across a wide demographic.

Resources necessary to conduct IDEAL Stage 2 studies are lacking, not just equipment and materials but importantly education and training. The motivation is there, but if the number and quality of IDEAL Stage 2 studies in LMICs is to increase, robust human resource training and rigorous, well planned trial initiation strategies are essential. This study confirms that these perceptions are shared by LMIC researchers and identifies interdisciplinary training and working, together with context specific PPI

initiatives as key facilitators for these studies. The results of this chapter highlight that training to conduct IDEAL Stage 2 studies is well received by LMIC researchers and healthcare professionals. Importantly, it is possible to efficiently deliver training during a single site initiation visit.

Strengths of this study are recognised. The interdisciplinary nature of participants meant that teams who were working together, learned together which aims to bridge the gap between clinical and trial commitments through integrated delivery of care and research. The design of the training programme was tailored to the needs of this specific trial yet remained grounded on the Global Health Network's Global Competency Framework for Clinical Research. Finally, the mixed-methods evaluation through feedback questionnaires and qualitative focus groups provided rich detail and valuable insights that can inform future research. Limitations are also recognised. The training programme was relatively short. A key piece of feedback from participants was that they wished to have more time to learn. Indeed, other LMIC research training programmes can be much longer in duration, such as the Structured Operational Research and Training Initiative (SORT IT) programme that consist of three one-week workshops over 9 months (185). A longer training programme would have been more costly, more demanding on the participants time regarding competing clinical service provision and may be unnecessary for programmes pertaining to specific individual projects such as in this study.

In conclusion, this chapter establishes that despite the relative lack of resources (material and human), there is a demonstrable willingness to participate in surgical research and, in particular, early phase surgical trials in LMICs. To increase research capacity and capability, and secondarily drive up the quality of care, investment needs to be focused on overcoming the barriers highlighted in this study, many of which are not costly to implement.

4 An IDEAL Stage 2b feasibility randomised controlled trial in a LMIC: The VITAL Trial

In Chapter 4, I described the use of IDEAL Stage 2 studies in LMICs to improve surgical innovation adoption and highlighted opportunities to address the human resource and research skills gap to increase the quantity and quality of these studies. In this Chapter, I report on the full delivery of an IDEAL Stage 2b study in Sierra Leone called the VITAL Trial: A feasibility randomised controlled trial of Virtual reality technology to Improve surgical Training in SierrA Leone. I highlight important considerations for future use of this study design. Training surgeons is expensive and relies on expert supervision. Virtual reality (VR) may enhance acquisition of knowledge and skills, but there is limited evidence on its applicability in LMICs. Furthermore, Chapters 3 and 4 identified training as a key unmet need, and highlighted that technology enhanced learning tools may be a strategy to overcome workforce training barriers. The aim of this Chapter was to conduct a context-specific IDEAL Stage 2b feasibility RCT of smartphone VR in LMICs and explore the use of IDEAL Stage 2 studies as appropriate designs for low-risk interventions.

4.1 Introduction

Training surgeons is expensive and time-consuming because it relies on expert supervision, and frequently involves skill acquisition on a high volume of cases to reach proficiency (186). Delivering an effective healthcare service requires several inter-connected elements, including essential medicines and technologies, infrastructure, and a skilled workforce (187). The WHO highlights that significant investment in healthcare professional education is required to realise UHC by the year 2030 and address the estimated global shortage of over 7.2 million healthcare providers (188).

The shortfall in healthcare professional education is especially pronounced in LMICs, which have the lowest workforce densities (188). Strategies are needed to address this workforce deficit, as well as the quality and relevance of the healthcare training.

Advances in simulation and immersive technologies, such as virtual reality (VR), may address these challenges by providing a safe and scalable training environment (186). The use of technology enhanced learning tools with immersive technologies may facilitate the acquisition of basic skills and knowledge in advance, reserving limited time in theatre or mentored teaching for the acquisition of more complex material (189). Several studies have explored the use of immersive technologies to supplement and enhance surgical training and have demonstrated efficacy, but highlight that at present such technologies cannot completely replace traditional training (190–193). Evidence is still lacking to inform the use of these technologies in surgical training, particularly in LMIC settings. One study from Rwanda demonstrates the feasibility of simulation-based training to improve operative skills when delivered as a brief training intervention. The study highlights that LMICs have the same drivers as high-income countries to adopt simulation and immersive technologies as part of surgical training, and additional drivers specific to LMICs may include high trainee-trainer ratios, limited number of operating rooms, and reliance on short-term training from visiting international trainers (194).

Innovations in the way training is delivered has explored the principle of ‘flipped classroom’ or ‘reverse classroom’ where the sequence of self-directed study or homework and lessons are reversed (195–197). The aim of this pre-course working is to enhance the learning during the time-limited mentored sessions within classroom teaching. This technique has been shown to improve engagement and knowledge acquisition, and the incorporation of simulation based learning, for example with virtual reality and other video assisted learning technologies, within the field of surgical skills training demonstrates the same benefit (196,198).

Whilst educational resources and opportunities are limited in LMICs, the use of mobile smartphones is prevalent and opens the possibility of using this medium as an educational training platform (199). Aligning a training intervention to technology that already exists and is prevalent in the population reflects frugal innovation thinking and VR accessed via smartphones may have powerful disruptive potential in this context. The aim of this study was to assess the feasibility of smartphone-based VR for surgical simulation and to evaluate the effect of VR on learning as part of a flipped classroom hands-on surgical training course in Sierra Leone.

4.2 Methods

4.2.1 Study setting

The study was conducted in Freetown, Sierra Leone, as a collaboration between the Leeds NIHR Global Health Research Group in Surgical Technologies (GHRG-ST), Connaught Hospital and CapaCare NGO. Study participants were government employed surgical trainees or surgical officers in the CapaCare Surgical Training Programme (129).

4.2.2 Lower limb amputation

Lower-limb amputation was chosen as the surgical topic for the hands-on training course and VR module. It is a frequently performed operation in Sierra Leone and other LMICs where the rates of trauma and chronic lower limb infection are particularly high (129,200) (201–203). The pre-course learning and the hands-on course focused on the indications, perioperative management, and operative technique for lower limb amputation.

4.2.3 Trial design

The study was designed as an assessor-blinded, parallel group, feasibility randomised controlled trial, following the CONSORT extension statement checklist for feasibility studies (204). Ethical approval for the study was obtained from the University of Leeds School of Medicine Research Ethics Committee (MREC 19-016; Appendix 4) and the Sierra Leone Scientific Ethics Review Committee. To be eligible for the study, participants had to be a current surgical trainee or graduate of a government or CapaCare Surgical Training Programme and able to attend a 2-day training course.

Recruitment took place seven days before the hands-on training course during a course promotion site visit where potential participants were invited to find out more about the study. All participants had to provide written informed consent. Participants were allocated 1:1 to either VR training or non-VR training using stratified block randomisation using a random number generator. It was not possible to blind participants, but assessors were blinded to allocation. Stratification factors included previous surgical experience and training programme affiliation (Government or CapaCare). Baseline demographic data included current training grade, number of lower limb amputations observed/performed and previous use of VR and other video assisted learning tools.

As the trial was designed to assess the feasibility and intervention fidelity, a power calculation was not considered appropriate. A sample size of 30 (15 in each arm) was deemed sufficient based on recommendations of 10-20 participants per group to assess feasibility outcomes (205,206). The trial ended on completion of the hands-on course following assessment of learning.

4.2.4 Intervention description

All participants in both the VR and non-VR group had access to pre-course learning and a hands-on training course using a flipped classroom approach. The surgical topic covered was lower-limb amputation in LMICs. The pre-course learning for both the VR and non-VR group included printed written material, consisting of information and illustrations about the technique of lower limb amputation in the form of a booklet. In addition, those randomised to the VR group received pre-course VR training. The pre-course material available seven days prior to a two-day hands-on course for all participants.

Trainees randomised to the VR group were given VR Shinecon 2.0 headsets that convert smartphones into head mounted displays (Manufacturer: VR Shinecon; Model number: 1629_VRSHINECON) and access to two 30-minute VR modules, which covered below knee amputation (BKA) and above knee amputation (AKA). The amputation modules were based on live operations previously filmed at Leeds Teaching Hospitals, UK, in collaboration with Medical Realities Ltd (London, UK), and narrated by a consultant vascular surgeon. The modules focussed on critical anatomy and operative steps during amputation. There were two video feeds, one from a 360-degree Vuze+ camera (Humaneyes Technologies Ltd., Israel) that was mounted on a tripod and positioned at the foot end of the operation table. A ‘surgeon’s eye view’ that captured the detail of the operative field was filmed using a Sony (Tokyo, Japan) HVR-Z5E digital camcorder mounted on a Hague multi-jib held above the table.

Participants were trained by technical support staff from Medical Realities in the use of the VR headsets and how to navigate through the modules. The training modules were accessible through an application which was free to download to their smartphones from the App Store or Google Play Store. If the participant did not have a compatible phone, or no phone at all, Samsung (Seoul; South Korea) Gear VR headsets with Samsung Galaxy S9 phones were made available to loan for the study period.

All participants were instructed to engage with their pre-course learning material at least once prior to the hands-on course. Data on pre-course learning engagement was collected via self-reported questionnaires after the hands-on course. All participants were invited to attend the 2-day hands-on training programme. The course was delivered using an interactive approach employing a combination of didactic lectures, practical demonstration and hands-on simulation covering the critical steps of above and below knee amputation including skin marking, neurovascular bundle ligation, and bone shaping and division. The course was delivered by surgeons from the UK and Sierra Leone. On completion of the study, all study participants were given a VR headset with access to the VR modules.

4.2.5 Outcome measures

The primary outcomes were participant recruitment and retention rates, and VR intervention fidelity. Recruitment success was defined as 80% of eligible participants agreeing to be enrolled in the study. Successful retention was defined by less than 10% attrition rate. Successful VR intervention fidelity was defined as at least 80% of the VR group successfully completing the VR modules at least once measured by participants self-reporting their completion on questionnaires after the hands-on course.

Secondary outcomes explored other key aspects of the study design such as:

- Information on the rate of unblinding, as defined by the assessor reporting knowledge of participant allocation
- Adherence to protocol, and reasons for nonadherence, as defined by the number of participants who cross-over assessing group contamination rate.
- Intervention fidelity: rate of VR failure, defined as the inability to use or access the VR training when required.

- The acceptability of the VR as a learning tool, and whether it may benefit training through increased engagement in learning, including:
    - The acceptability and engagement of the learning objects (VR technology or pre-course booklet only) via a modified Web-based Learning Tools (WBLT) Evaluation Scale (207,208).
    - The acceptability and engagement with pre-course learning in a flipped classroom approach, and the hands-on course itself using course feedback questionnaire.
    - Whether there was evidence that the VR module in a flipped classroom approach improves skill acquisition via OSATs assessment score (Objective Structured Assessment of Technical Skills) (Appendix 5) and knowledge acquisition via a Multiple-Choice Questions (MCQ) paper (Twelve questions).

OSATs assessment scores are validated measures of hands-on procedural skill acquisition that can be applied to a range of clinical skill domains. The assessors of the OSATs and MCQs assessments were blinded to study group allocation. It was not possible to blind the research team or the participants to group assignment.

4.2.6 Statistical analysis

Participant baseline characteristics are summarised descriptively for the whole study cohort and by intervention group. The number of participants completing each component of the training programme was recorded. Quantitative outcome measures are presented using summary statistics for the whole study cohort and by intervention group.

4.3 Results

Thirty eligible participants consented and were randomised to the VR group (n=15) or the non-VR group (n=15). The CONSORT trial participant flow diagram can be seen in Figure 13. The mean age of participants was 32.3 years (SD = ± 5.8). Twenty-four (80%) participants were male, representing a male-to-female ratio of 4:1. The mean years of surgical experience was 2.7 years (SD = ± 2.24). The majority were general surgical trainees (n=26; 86.7%). Twenty-eight participants (93.3%) owned a smartphone, and all had previously used educational applications on their device. Only two participants (6.67%) had prior experience of immersive technology. Baseline characteristics are summarised in Table 10.

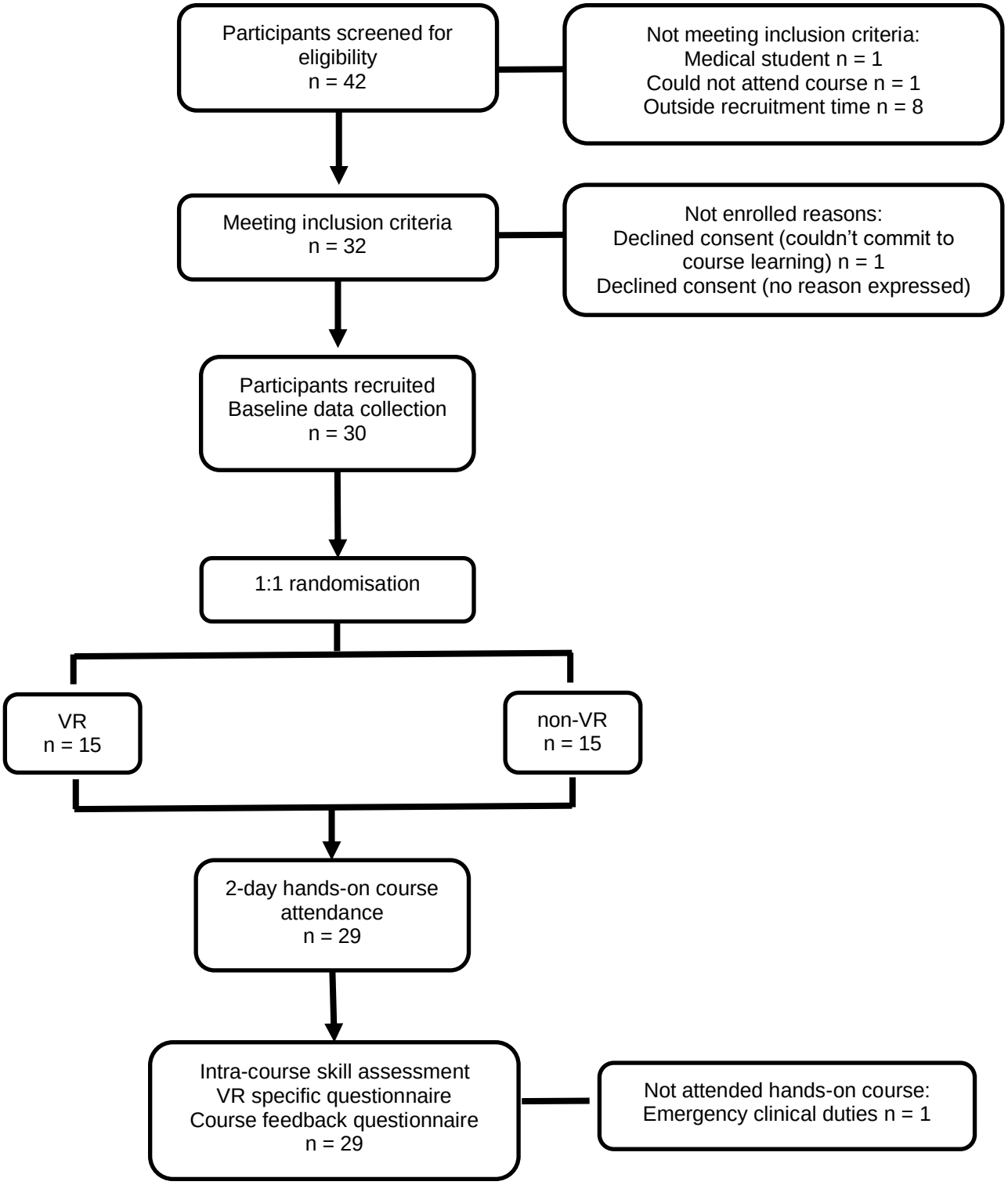


Figure 13: VITAL Trial CONSORT trial participant flow diagram.

Table 10: Baseline participant characteristics

Variable	All participants n = 30	VR group n = 15	Non-VR group n = 15
Experience (Years; Mean ± SD)	2.7 ± 2.24	2.53 ± 2.07	2.87 ± 2.47
Age (Years; Mean ± SD)	32.3 ± 5.8	31.7 ± 4.0	32.9 ± 7.3
Sex M:F	24:6	11:4	13:2
Government training (N; %)	21 (70%)	10 (66%)	11 (73%)
CapaCare Surgical Training Programme (N; %)	9 (30%)	5 (33%)	4 (27%)
Speciality			
General Surgery (N; %)	26 (87%)	13 (87%)	13 (87%)
Obstetrics and Gynaecology (N; %)	3 (10%)	2 (13%)	1 (7%)
Trauma and Orthopaedics (N; %)	1 (3%)	0	1 (7%)
Smartphone use			
Owned a smartphone (N; %)	28 (93%)	14 (93%)	14 (93%)
Number of educational apps on smartphone	2.8 (IQR 2-4)	3.2 (IQR = 2-4)	2.4 (IQR= 1-3)
Previous use of immersive technologies (N; %)	2 (7%)	0	2 (14%)

Feasibility outcomes for the 14-items used to evaluate methodological issues for feasibility research are presented in Table 11. These items are derived from previous methodological research (209,210).

Table 11: Summary of findings against 14 methodological issues for feasibility research

Methodological items	Findings	Evidence
1. What factors influenced eligibility and what proportion of those approached were eligible?	Ineligibility was only found in two screened participants: due to not including medical students and being unable to attend the hands-on course	30 agreed to participate, only two screened declined to consent. More may have consented if sample size was larger.
2. Was recruitment successful?	Yes. Recruiting success was defined as 80% of eligible participants agreeing and being recruited into the study. A larger sample size is possible with a larger hands-on course capacity and recruitment window.	30 out of 32 (93.8%) eligible participants agreed to take part and were recruited. There were many more that may have been eligible had a larger recruitment window been used.
3. Did eligible participants consent?	Yes. The majority of participants agreed to consent.	Only 2 did not wish to consent.
4. Were participants successfully randomised?	Yes. Randomisation processes worked well.	Table 10 shows that baseline group differences were minimal.
5. Were blinding procedures adequate?	Yes. Assessors of MCQ and OSATs and course faculty were blinded to assignment throughout.	Assessors and faculty were not present during pre-course learning and participants did not disclose their assignment during the course.
6. Did participants adhere to the intervention?	Yes. Successful adherence to the intervention was defined as at least 80% of the VR arm participants	100% of participants completing the VR at least once. Six (40%)

	successfully completing the VR modules at least once.	completed the VR modules more than once.
7. Was the intervention acceptable to the participants?	Participants were keen to engage with the VR intervention. Acceptability was measured by refusal to engage with the VR modules	All participants engaged with the VR at least once, and 40% engaged with it more frequently.
8. Was it possible to calculate intervention costs and duration?	An economic evaluation was not conducted.	-
9. Were outcome assessments completed?	Reasons for missing outcome assessments were participant withdrawal (n=1)	29 (96.7%) of participants had complete outcome assessments.
10. Were outcomes measured those that were the most appropriate outcomes?	All outcomes were deemed valid and appropriate.	Participant-completed forms were largely complete (missing data points in 3 instances)
11. Was retention to the study good?	Successful retention in the study was defined by less than 10% attrition rate.	29 (96.7%) participants were successfully retained throughout the trial
12. Were the logistics of running a multi-centre trial assessed?	No. This was a single-centre feasibility trial.	-
13. Did all components of the protocol work together?	The components of the trial and the intervention itself worked in this feasibility study	Adherence to the intervention and study processes met the pre-determined criteria and show feasibility of progressing to full RCT if needed.

14. Did the feasibility/pilot study allow a sample size calculation for the main trial?	No. A sample size for a future full RCT was not calculated from the data in this study.	While our study suggests trends, meaningful effect size estimates are not possible given inherent imprecision of the data at small sample sizes

4.3.1 Eligibility, recruitment, and randomisation

Between 1st and 8th of November 2019, 42 trainees were screened for eligibility to the study. Two trainees did not meet the inclusion criteria; one was a medical student, and one could not attend the hands-on course. Eight trainees were not enrolled because they were outside the recruitment period. A total of 32 trainees met the inclusion criteria, but one declined to consent as they felt unable to commit to the pre-course learning, and one declined consent but did not want to express a reason. Recruitment and consent processes were deemed successful as 30 eligible trainees consented and were randomised to either the VR group (n = 15) or non-VR group (n = 15). The randomisation process produced VR and non-VR groups matched in terms of stratification factors, age, and gender. The outcome assessors (MCQ and OSAT markers) and course faculty were blinded to participant allocation, which was maintained throughout the study. There was no cross-over of participants between the two intervention groups.

4.3.2 Adherence to the intervention

Of the 30 recruited participants, 29 (96.7%) successfully completed the two-days hands-on course. One had to withdraw shortly before the hands-on course due to emergency clinical duties. Intervention adherence exceeded the pre-specified success

rates with 100% of participants completing the VR at least once. Six participants (40%) completed the VR modules more than once. Twelve (80%) of the VR group could access the modules on their own mobile phones; one did not have a smart phone, and two did not have the necessary in-built hardware (accelerometer) and were provided with a loan device. The VR modules were completed a total of 21 times by the 15 participants in the VR group. Only on one occasion (4.7%) was a participant unable to access the VR due problems opening the application on their phone, which was later resolved. In the non-VR group, all participants reported reading the pre-course booklet at least once. In the VR group, 12 (80%) used the pre-course booklet alongside the VR modules.

4.3.3 Outcome assessment

All participants who attended the hands-on course (n=29) completed the outcome assessments. 100% completed the modified Web-based Learning Tools (WBLT) evaluation, the course feedback questionnaire, the MCQs and the OSATs. The results of the MCQs and OSATs assessments are presented in Table 12. This study was not powered to identify effect for these measures by the VR group had larger mean scores achieved for both OSATs and MCQs, suggesting a trend in favour of VR for educational effectiveness

Table 12: Outcomes from practical skills (OSATs) and knowledge (MCQ) acquisition assessments

Variable	All participants	VR group mean	Non-VR group
OSATs (Mean ± SD)	28.1 ± 6.3	29 ± 6.0	27.3 ± 6.7
MCQ (Mean ± SD)	15.5 ± 3.0	16 ± 2.8	15 ± 3.3

Engagement in learning and perceived fulfilment of learning objectives was collected via the modified Web-based Learning Tools (WBLT) and course feedback questionnaires and compared between groups. As compared to the non-VR group, the VR group recorded increased perceived learning before the hands-on course and increased engagement with the pre-course learning. As compared to the non-VR group, the VR group also recorded higher engagement in the hands-on course itself. A full breakdown is presented in Table 13.

Table 13: Engagement in learning and perceived meetings of learning objectives throughout the trial.

	VR group: Percentage selecting each response					Non-VR group: Percentage selecting each response				
Statement	***Strongly agree***	***Agree***	***Neutral***	***Disagree***	***Strongly disagree***	***Strongly agree***	***Agree***	***Neutral***	***Disagree***	***Strongly disagree***
Perceived meeting of learning objectives										
1. I understand the indications for lower limb amputations (LLA)	86%	7.10%	7.10%	7.10%	0%	60%	40%	0%	0%	0%
2. I understand the pre-operative optimisation of LLA patients	92.90%	7.10%	0%	0%	0%	53.30%	40%	6.70%	0%	0%
3. I understand the anaesthetic considerations of LLA	71.40%	28.60%	0%	0%	0%	26.70%	46.70%	20%	6.70%	0%
4. I understand the use of prosthetics/orthotics	50%	50%	0%	0%	0%	21%	71.40%	7.10%	0%	0%
5. I understand the skin marking and incisions required for a BKA	85.70%	14.30%	0%	0%	0%	86.70%	6.70%	6.70%	0%	0%
6. I understand the skin marking and incisions required for an AKA	92.90%	0%	7.10%	0%	0%	86.70%	6.70%	6.70%	0%	0%
7. I can identify the neurovascular anatomy during a BKA	50%	35.70%	14.30%	0%	0%	46.70%	40.00%	13.30%	0%	0%
8. I can identify the neurovascular anatomy during a AKA	57.10%	28.60%	14.30%	0%	0%	46.70%	46.70%	6.70%	0%	0%
9. I can ligate vessels and nerves correctly	85.70%	7.10%	7.10%	0%	0%	46.70%	46.70%	6.70%	0%	0%
10. I can divide and shape the tibia and fibula during BKA	85.70%	7.10%	7.10%	0%	0%	53.30%	33.30%	13.30%	0%	0%
11. I can divide and shape the femur during AKA	85.70%	7.10%	7.10%	0%	0%	60.00%	26.70%	13.30%	0%	0%
12. I understand how to create skin flaps and close for BKA	78.60%	21.40%	0%	0%	0%	57.10%	35.70%	7.10%	0%	0%
13. I understand how to create skin flaps and close for AKA	78.60%	21.40%	0%	0%	0%	57.10%	35.70%	7.10%	0%	0%
14. I understand how to manage post-operative complications	78.60%	21.40%	0%	0%	0%	35.70%	57.10%	7.10%	0%	0%
15. Overall, I feel more confident performing lower-limb amputations now	71.40%	21.40%	0%	7.10%	0%	57.10%	35.70%	7.10%	0%	0%
Feedback on the hands-on course										
Learning										
1. I felt I learned new things during the course	100%	0%	0%	0%	0%	85.70%	14.30%	0%	0%	0%
2. I learned skills that will be useful to my clinical practice	100%	0%	0%	0%	0%	85.70%	14.30%	0%	0%	0%

3. The lectures helped me learn	92.90%	7.10%	0%	0%	0%	85.70%	14.30%	0%	0%	0%
4. The practical sessions helped me learn	100%	0%	0%	0%	0%	92.90%	7.10%	0%	0%	0%
5. The group discussions were useful for my learning	71.40%	28.60%	0%	0%	0%	86.70%	14.30%	0%	0%	0%
Design										
6. The lectures were well designed	42.90%	50.00%	7.10%	0%	0%	57.10%	42.90%	0%	0%	0%
7. The practical sessions were well designed	78.60%	14.30%	7.10%	0%	0%	78.60%	21.40%	0%	0%	0%
8. I had enough time to learn on the course	42.90%	42.90%	14.30%	0%	0%	21.40%	42.90%	21.40%	14.30%	0%
9. The overall structure of the course was well designed	50.00%	42.90%	7.10%	0%	0%	57.10%	35.70%	7.10%	0%	0%
Engagement										
10. I found the course enjoyable	85.70%	14.30%	0%	0%	0%	53.30%	40.00%	6.70%	0%	0%
11. I attended every session	100%	0%	0%	0%	0%	66.70%	20.00%	13.30%	0%	0%
12. I would recommend the course to colleagues	71.40%	28.60%	0%	0%	0%	80.00%	13.30%	6.70%	0%	0%
13. I found attending the course easy	71.40%	28.60%	0%	0%	0%	26.70%	53.30%	13.30%	0%	0%
14. The course met my expectations	78.60%	21.40%	0%	0%	0%	46.70%	40.00%	13.30%	0%	0%
15. I have gotten a lot out of attending this course	85.70%	7.10%	7.10%	0%	0%	73.30%	26.70%	0%	0%	0%
Feedback on the pre-course learning tools										
Learning										
1. Working with the learning object helped me learn	71.80%	28.60%	0%	0%	0%	40.00%	60.00%	0%	0%	0%
2. The written content from the learning object helped me learn	69.20%	30.80%	0%	0%	0%	33.30%	60.00%	6.70%	0%	0%
3. The graphics, animations and pictures from the learning object helped me learn	64.30%	35.70%	0%	0%	0%	13.30%	60.00%	26.70%	0%	0%
4. The learning object helped teach me a new concept	71.40%	28.60%	0%	0%	0%	26.70%	73.30%	0%	0%	0%
5. Overall, the learning object helped me learn	76.90%	23.10%	0%	0%	0%	42.90%	57.10%	0%	0%	0%
Design										
6. The learning tool was unnecessarily complex to use	0%	14.30%	21.40%	35.70%	28.60%	6.70%	6.70%	13.30%	46.70%	26.70%
7. The instructions and guidance in the learning object were easy to follow	57.10%	21.40%	21.40%	0%	0%	46.70%	40.00%	13.30%	0%	0%
8. The learning object was easy to use	50.00%	42.90%	7.10%	0%	0%	40%	53.30%	6.70%	0%	0%
9. The learning object was well organised	71.40%	28.60%	0%	0%	0%	46.70%	53.30%	0%	0%	0%
Engagement										

10. I liked the overall theme of the learning object	57.10%	42.90%	0%	0%	0%	46.70%	53.30%	0%	0%	0%
11. I found the learning object engaging	85.70%	7.10%	7.10%	0%	0%	33.30%	66.70%	0%	0%	0%
12. The learning object made learning fun	71.40%	28.60%	0%	0%	0%	35.70%	35.70%	28.60%	0%	0%
13. I would like to use the learning object again	100%	0%	0%	0%	0%	40%	60.00%	0%	0%	0%
14. I was able to use the learning object whenever I wanted	46.20%	23.10%	7.70%	23.10%	0%	26.70%	66.70%	6.70%	0%	0%
15. I think the learning object is user friendly	92.90%	7.10%	0%	0%	0%	42.90%	50.00%	7.10%	0%	0%
Feedback on the flipped classroom design										
Learning										
1. I felt the learning I did before the course prepared me well for the course itself	50.00%	42.90%	0%	7.10%	0%	28.60%	50.00%	14.30%	7.10%	0%
2. I made the most of my learning before the course	35.70%	35.70%	7.10%	21.40%	0%	7.10%	57.10%	14.30%	21.40%	0%
3. I learned new things before the course	28.60%	35.70%	28.60%	0%	7.10%	14.30%	64.30%	14.30%	7.10%	0%
4. I revised existing knowledge before the course	35.70%	35.70%	7.10%	14.30%	7.10%	28.60%	21.40%	42.90%	7.10%	0%
5. Overall, doing learning before the course made me gain more knowledge during the course	50.00%	21.40%	14.30%	14.30%	0%	42.90%	42.90%	7.10%	7.10%	0%
Design										
6. I think learning before the course was useful	76.90%	7.70%	7.70%	7.70%	0%	57.10%	28.60%	14.30%	0%	0%
7. I had enough time to learn before the course	23.10%	38.50%	15.40%	7.70%	15.40%	21.40%	42.90%	21.40%	14.30%	0%
8. I had the right materials and resources to learn before the course	21.40%	21.40%	42.90%	14.30%	0%	42.90%	50.00%	7.10%	0%	0%
9. Doing pre-course learning improved my experience of the course itself	35.70%	28.60%	21.40%	14.30%	0%	42.90%	50.00%	7.10%	0%	0%
Engagement										
10. I liked the overall structure of learning before the course delivery	50.00%	21.40%	28.60%	0%	0%	64.30%	28.60%	7.10%	0%	0%
11. I found the pre-course learning engaging	50%	14.30%	35.70%	0%	0%	35.70%	57.10%	7.10%	0%	0%
12. I enjoy learning before courses	42.90%	42.90%	14.30%	0%	0%	50.00%	42.90%	0%	7.10%	0%
13. I would do pre-course learning for future courses	64.30%	35.70%	0%	0%	0%	92.90%	7.10%	0%	0%	0%
14. In the future, I will carry out my pre-course learning in the same way I did this time	42.90%	14.30%	28.60%	7.10%	7.10%	50.00%	28.60%	7.10%	0%	14.30%
15. I enjoy learning in my spare time	78.60%	0%	14.30%	0%	7.10%	57.10%	35.70%	7.10%	0%	0%

4.4 Discussion

Despite the technical challenges of working in low resource settings, this study has shown that it is feasible to conduct an IDEAL Stage 2b study of smartphone VR surgical training in a LMIC. VR as part of a flipped classroom learning approach is acceptable to surgical trainees with high rates of engagement before and during a hands-on course. Given the high engagement in the pre-course learning and completion of the hands-on course, intervention adherence and fidelity were deemed to be a success.

A key strength of this study is the assessment of the potential implementation of the VR intervention within a simple IDEAL Stage 2b study with short data collection time points. This was useful as it allowed for contextualisation of VR use both within and beyond future studies. I explored how VR could be used alongside existing training courses to enhance the effect of these educational methods in a blended learning approach. VR is a platform technology and the specific content that could be delivered is wide ranging. This may form important components of multiple training pathways. This training intervention was evaluated according to the Kirkpatrick model of training evaluation that assessed the immediate reaction after the course and perceived learning via questionnaires, and the results of new knowledge on behaviour and skills via hands-on and MCQ assessments (211).

Another strength is the exploration of smartphone-based VR. Some immersive technology applications require prohibitively expensive hardware, such as the mixed reality platform HoloLens by Microsoft (212). While these technologies may bring benefits for certain applications, this adds an additional barrier to adoption in terms of cost and access to extra equipment. Although a recent report demonstrated

smartphone adoption was modest and varied across countries within Sub-Saharan Africa, exploring technologies that more closely align to existing hardware may improve adoption (199). The rate of smartphone adoption is increasing in many countries, and in our study the majority of participants owned a device. Indeed, even if they did not currently own a smartphone, our participants were digitally knowledgeable and engaged well with the VR technology, requiring only minimal instruction. Smart phone ownership is more frequent in younger, more educated populations, possibly explaining the high rates in our study (199). Reliable internet and modest speeds are required for many technology-enhanced learning tools. Again, while the rate of internet use is growing, the majority of Sub-Saharan African populations have no or limited access (213). A headset is still an additional item of equipment required to use the smartphone as a head mounted display for a VR application, but these are becoming very low cost, reducing this barrier to adoption (214). Immersive technologies such as VR have the potential to dramatically alter surgical training in both low and high-income countries. There are other barriers to adoption aside from technical and equipment aspects. Decisions regarding how the technology augments and relates to 'traditional' training formats, through to cultural shifts in the way new training methods are perceived by patients and surgeons are both important areas of enquiry. To overcome these barriers and persuade key stakeholders to adopt these training technologies, further evaluation is needed.

Limitations of this study are also recognised. It is not possible to draw conclusions about the educational effectiveness of VR technology for surgical training. While our results may show trends to favour VR, in terms of skills and knowledge acquisition, the study was not powered or designed to test this hypothesis. Hypothesis testing in feasibility studies is inappropriate and firm conclusions cannot be drawn either way from an underpowered study (210,215). Although no contamination was reported in our study, trainees were enthusiastic and eager to engage with the VR technology. It is possible that the VR was shared between groups without self-reporting, and future

studies may benefit from the inclusion of a more sophisticated method to detect contamination.

This present chapter raises important considerations for surgical training in LMICs and globally. As smartphone technology use and internet access continues to increase, there is a real opportunity to leverage this technology for surgical training. Whilst immersive technology is unlikely to replace surgical mentorship, it has potential to enhance the limited training available globally by shortening the learning curve and providing improved patient safety due to augmented use of non-human simulation and practice. Performing surgery is a complex and encompassing experience requiring simultaneous use of prior knowledge, practical skills, situational awareness, and real-time problem solving. Other evidence supports our preliminary findings that engagement in learning experience, and therefore experiential knowledge acquisition, is increased when an immersive modality (such as VR) is used (216,217).

This IDEAL Stage 2b study was designed to assess if VR was a worthwhile target for future investigation and investment as a technology solution. Using immersive technologies in LMICs is feasible and these should form part of the solution to address the lack of a trained global surgical workforce.

5 Examining the global surgical innovation pathway

In Chapter 3 I highlighted the importance of IDEAL Stage 3 studies and identified in the literature strategies to overcome the barriers to conducting these in LMICs. Chapters 4 and 5 presented the design and findings from conducting two IDEAL Stage 2 studies in LMICs focused on improving the research skills gap, a barrier to efficient evaluation and adoption of innovative surgical technology and developed the argument for these study designs to be deployed as practical, efficient evaluation methodologies for rapid assessment and adoption of novel-to-context surgical technology. The purpose of this Chapter is to explore the global surgical innovation pathway more fully and ascertain what other study designs and practices are employed by the surgical community in LMICs on a global scale. As well as mapping current practice in evaluation study designs, the types of technologies and corresponding adoption practices has also been considered. This Chapter builds on the work earlier in the Thesis and provides prerequisite evidence to inform the design and synthesis of the novel Global Surgical Innovation Framework that is presented in full in Chapter 7.

5.1 Introduction

A comprehensive understanding of the evaluation pathway for surgical innovation in LMICs is lacking. Attempts have been made for medical devices more broadly through the WHO's Health Technology Assessment (HTA) (99). However, evidence indicated that for surgical interventions, only 38% had undergone a formal HTA in LMICs (vs 69% in HICs) (218). This discrepancy suggests a lack of applicability or usability for surgeons in LMIC settings and could be due to design of the HTA guidance. As described elsewhere in this Thesis, the IDEAL Framework was developed to advance the evaluation of surgical innovation specifically, but it's used in LMICs is extremely

limited. Understanding current practices in evaluating and adopting surgical innovation may indicate which areas of this guidance needs amending to increase the appropriate evaluation of surgical innovation in LMICs.

5.1.1 Aims

The primary aim of this Chapter is to understand the current practices surrounding technology development, evaluation, dissemination, and adoption in LMIC settings through a global online survey and semi-structured interviews (SSIs) with LMIC and HIC surgeons and researchers. The secondary is to derive targets for adaptations to the IDEAL Framework that may increase the relevance and effectiveness of future recommendations to overcome challenges for surgeons and researchers working in LMICs. A full presentation of the novel framework components and their derivations is provided in Chapter 7.

5.2 Methods

Identifying barriers and facilitating factors present in the evaluation pathway of surgical innovation in LMICs was conducted via a global mixed methods study involving a semi-quantitative online survey and SSIs with key informants to corroborate, expand and contextualise the findings further. Consenting adults, who were either surgeons and/or researchers involved in surgical care or surgical technology development, from an LMIC or working within a LMIC who can read and speak English were included in this study. For the purposes of this study, LMIC was defined as any country appearing on the Development Assistance Committee (DAC) List of Official Development Assistance (ODA) Recipients.

Ethical approval for this study was granted by the School of Medicine Research Ethics Committee, University of Leeds (MREC 18-102; Appendix 6).

5.2.1 Online survey design and execution

A cross-sectional survey using a self-reported, anonymised, voluntary, online, questionnaire conducted in English was designed. This design was appropriate as it facilitates rapid collection of contemporaneous data from a large sample of eligible participants across multiple disciplines and countries. The content of the survey covered participant demographics including location and work setting, experience of surgical technology evaluation, and then progressed to cover barriers and facilitating factors to conducting each IDEAL stage study design in their context. Finally, participants could then include other study designs and potential facilitating strategies they felt should be considered throughout the evaluation pathway. There were several open text-box response opportunities throughout the survey so that respondents could expand on their answers or provide additional suggestions that they felt were important.

The survey was piloted with a group of surgeons and healthcare professional from Sierra Leone to assess and ensure face and content validity. During the pilot, focus group discussions on the design and content of the survey identified missing or surplus topics, and ensured the phrasing and flow of the survey was optimised before disseminating more widely.

To provide a generalisable and representative evidence base globally, the survey was disseminated using snowball sampling through relevant associations, groups, and collaborations in a range of high-income countries (HICs) and LMICs. Key mailing lists and interest groups were approached for dissemination, including GlobalSurg

Collaborative, G4 Alliance, Association of Rural Surgeons of India, West African College of Surgeons, and the College of Surgeons of East, Central and Southern Africa. Social media such as Facebook and Twitter were used to expand reach to a broader audience. Data was collected over a 12-week period in 2019.

5.2.2 Semi-Structured Interviews

All respondents to the online questionnaire were also invited to consent to being approached and receive more information about the interviews. Interviews were conducted via face-to-face discussions where possible, but video teleconference platforms were also used. All interviews were in English language. Interviews were conducted by a researcher (WSB) trained in qualitative methods. Interviews were audio recorded and later transcribed verbatim. The initial items in the interview topic guide were based upon the areas covered by the questionnaire to ensure the results were aligned and that the interviews provided an opportunity to expand on insights gained from the interview stage. These initial items were discussed, refined, or added too based on feedback from the pilot alongside the questionnaire itself.

5.2.3 Data Analysis

Descriptive statistics were used to summarise demographics and categorical or Likert scale question responses. Open text-box responses in the survey were analysed and included in the thematic analysis. Descriptive statistics and tabulation were be performed on Microsoft Excel Version 16.50.

Qualitative interview data analysis was an ongoing and iterative process. Preliminary analysis began during data collection, as new themes and connections within the data are explored. This involved the interviewer conducting a reflective debrief after each

interview and noting key ideas. The content or procedures for subsequent interviews was modified accordingly. Thematic analysis structured using the Framework method was employed to analyse the complete data and inductively identify themes (150). This approach was chosen as it is designed to identify commonalities and differences in qualitative data, before focusing on relationships within the data, leading to descriptive or explanatory conclusions clustered around themes. Following this, the wider research team assessed the emerging themes and contributed to the iterative refinement and interpretation of the results through within-team discussion.

5.3 Results

5.3.1 Participants

The online survey yielded 66 responses representing experience from 40 countries. Twenty-eight (42.4%) described themselves as a Consultant Surgeon/Attending Physician and 23 (34.8%) as a Trainee/Resident Surgeon. Nine (13.6%) reported being a Researcher/Academic/Trialist/Methodologist. The remaining respondents reported being an Obstetrics & Gynaecology (n=5; 7.6%), Surgical Associate/Surgical Officer (n=2; 3%) and Anaesthetist/Anaesthesiologist (n=2; 3%). Four (6.1%) recorded ‘other’. Three-quarters of respondents were male 50 (75.8%). The majority (n=46; 69.7%) worked in public hospitals in urban settings (n=56; 84.8%). The respondent demographics are summarised in Table 14. Nine (13.6%) respondents expressed an interest and were included in the interview stage.

Table 14: Respondent demographics and places of work

Professional experience		**Hospitals currently working with**	
Consultant Surgeon/Attending Physician	28	**No. of beds**	
Trainee/Resident Surgeon	23	less than 50	6
Researcher/Academic/Trialist/Methodologist	9	50-99	7
Obstetrician/Gynaecologist	5	100-199	7
Surgical Associate/Surgical Officer	2	200-499	15
Anaesthetist	2	500-999	17
Other	4	1000+	14
Surgical specialty experience		**Type of hospital**	
General	41	Public	46
Trauma & Orthopaedics	11	Private	7
Obstetrics & Gynaecology	10	Mixed public and private	8
Paediatric	7	NGO/charity	5
Neurological	6	**Area served**	
Urological	5	Urban	56
ENT	4	Rural	10
Plastic and reconstructive	2	**Countries currently working in**	
Vascular	2	India (11), Sierra Leone (11), United Kingdom (11), Nigeria (8), Uganda (8), Ghana (4), Brazil (3), Colombia (3), Pakistan (3), South Africa (3), Turkey (3), Bangladesh (2), Bolivia (2), Botswana (2), Egypt (2), Ethiopia (2), Mexico (2), Netherlands (2), Rwanda (2), United States (2), Zambia (2), Cameroon (1), Canada (1), China (1), Denmark (1), France (1), Haiti (1), Ireland	
Anaesthetics	2		
Ophthalmology	1		
Cardiac	0		
Other	3		

5.3.2 Experience of evaluating innovation

The majority (n=48; 72.7%) had experience in clinical research (with living humans), and the remaining either had experience with pre-clinical research (n=15; 22.7%) or had no prior experience (n=15; 22.7%) (some respondents had a combination of experience). The spread of evaluation experience mapped against IDEAL stages is shown in Figure 14, with the majority having experience in IDEAL Stage 2 studies. The conduct of IDEAL Stage 1 studies was relatively uncommon among the study participants. The majority (n=48; 72.7%) of participants felt that conducting Stage 1 study designs in LMICs was realistic in their experience. The majority of participants felt that conducting IDEAL Stage 2a and 2b studies was realistic in their experience (n=51; 77.3% and n=44; 66.7% respectively). For IDEAL Stage 3 studies, just over half (n=35; 53%) felt this design was realistic in their experience. Finally, 48 (72.7%) of participants felt IDEAL Stage 4 studies were realistic in their experience.

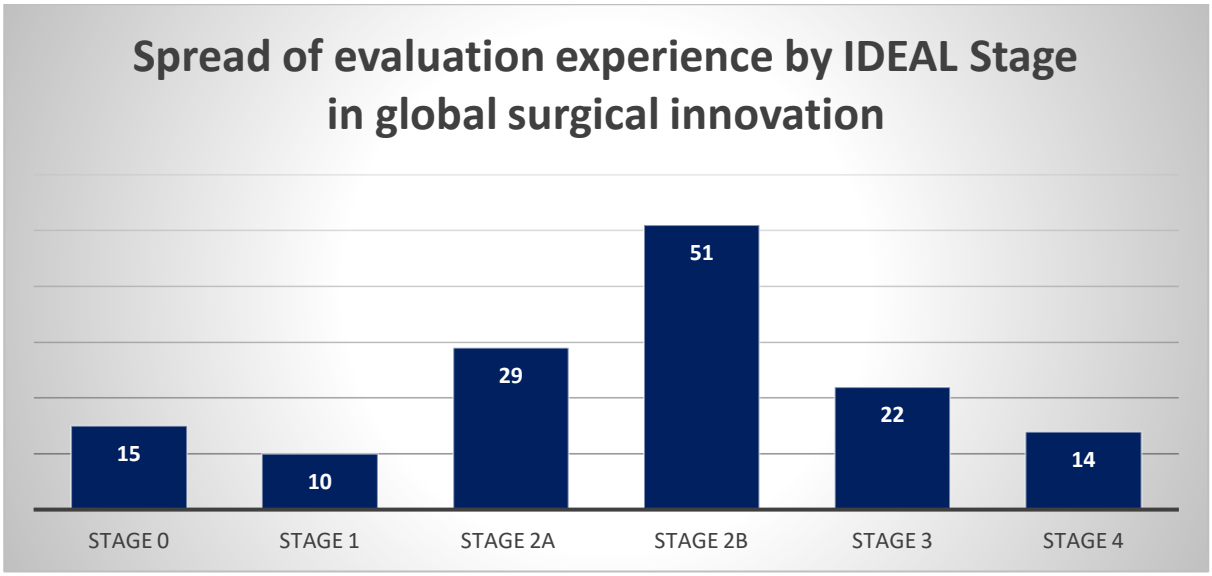


Figure 14: The number of respondents who have undertaken a study at each IDEAL Stage (short descriptors were used to describe the IDEAL Stages).

Three quarters (n=49; 74.2%) had experience evaluating surgical technologies and the spread of technologies evaluated is shown in Figure 15. The respondents reported

that technologies and innovations were most frequently adopted either based on colleague recommendation or based on clinical evaluation in countries other than their own (Figure 16). However, almost half (n=30; 45.4%) perceived the need for evidence from a locally conducted RCT before adopting a technology/innovation that is in established use in a context other than their own (Figure 17).

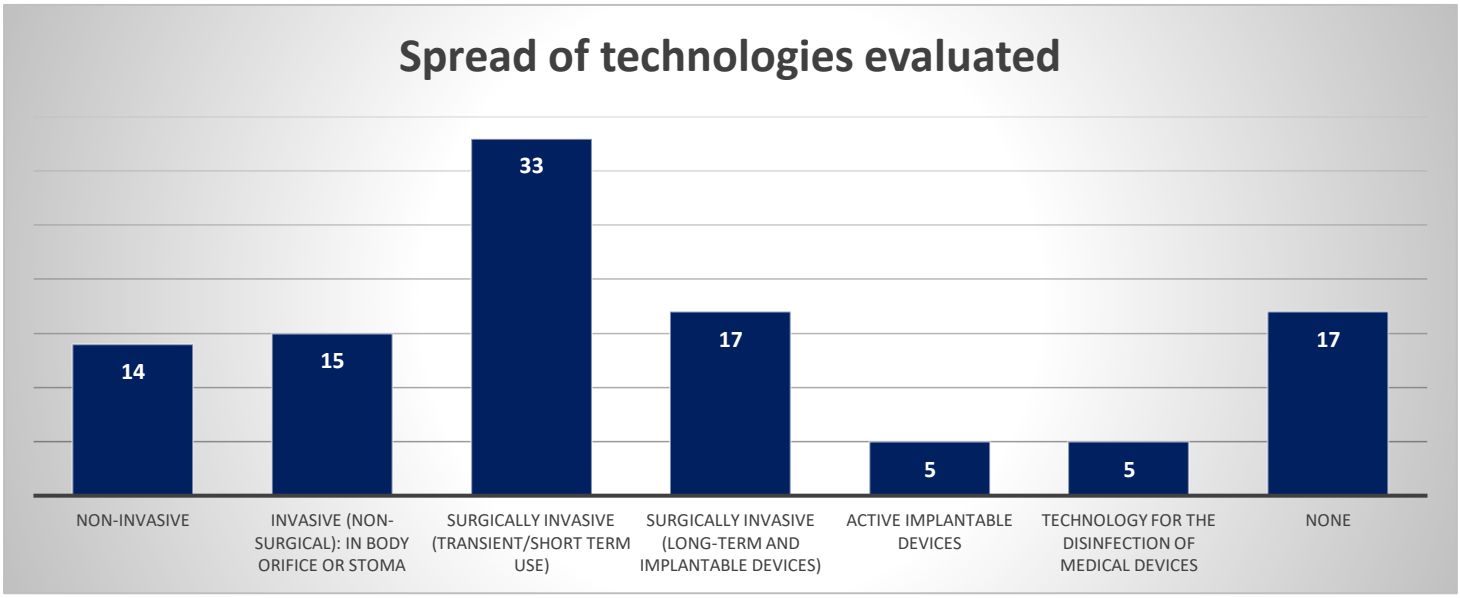


Figure 15: The number of respondents who have undertaken a study with each category of surgical technology (short descriptors were used to describe with examples).

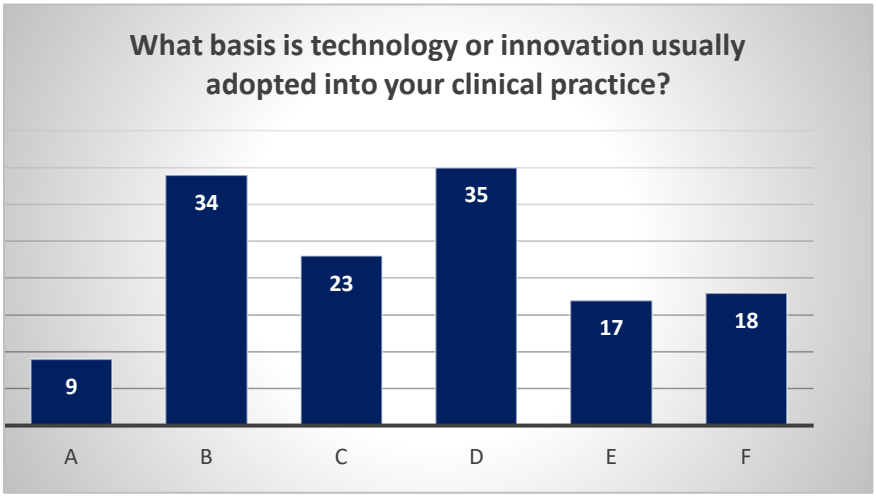
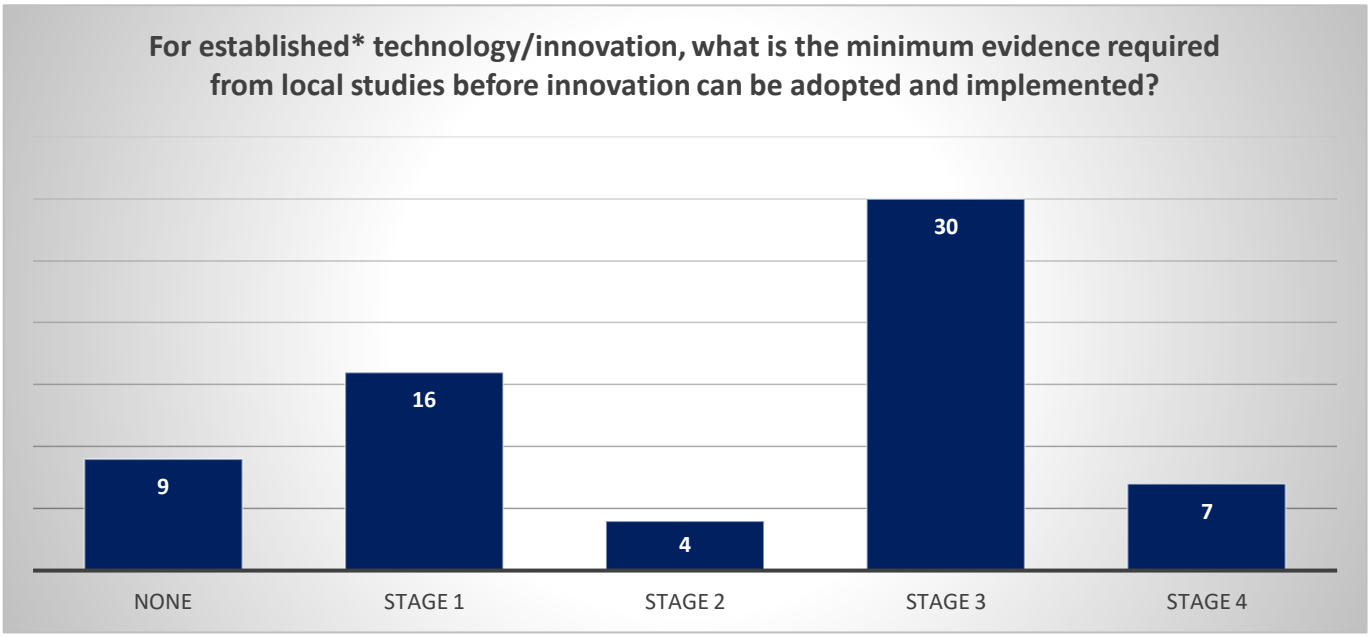


Figure 16: The basis of current technology or innovation adoption in the respondent's experience.



*Question asked: "An innovation/technology is evidence based and in routine use in a different setting to your own. In your opinion, what is the minimum evidence base required from studies conducted in your setting before it can be implemented and adopted?"

Figure 17: Respondent's perceptions around evidence required from local studies before adopting a technology/innovation in established use in a context other than their own.

5.3.3 Qualitative interview findings

Emergent through exploration of barriers and facilitators in surgical innovation evaluation in LMICs, four key themes that were deemed important to consider when evaluating surgical innovation highlighted initially in the survey and then built upon through discussions during the interviews.

Theme 1 - Frugal innovation in device development
Theme 2 - Evaluating the same technology/innovation in multiple contexts
Theme 3 - Additional methodologies important in evaluation of surgical innovation in LMICs
Theme 4 - Support for researchers along the evaluation pathway

5.3.3.1 Theme 1 - Frugal innovation in device development

Several respondents had experience working on surgical technologies at the IDEAL Stage 0 phase (pre-clinical). One of the main reasons for engaging in device development arose from the barriers associated with donation of medical devices from HICs to LMICs. "*Most of the time these do not work and end up in a donation graveyard*". This is because these devices were not specifically designed for use in these contexts and a lack of consumables or issues with maintenance and repair limit the device usability. Concepts pertaining to the principle of frugal innovation arose on multiple occasions. This frequently involved ensuring devices were "*lower-cost*" but also recognised that "*the innovation itself must be context specific*" with the need for "*adaptive technology*" specific for surgical care in LMICs, noting that the "*cultural acceptance of intervention, viability and sustainability in developing countries*" is paramount.

5.3.3.2 Theme 2 - Evaluating established technology/innovation in multiple contexts

The original IDEAL Framework was created with the evaluation of completely novel interventions in mind and specifically excluded established or existing technologies. In global surgery however, surgeons are often faced with the need to evaluate technology already established in one context (often HICs) and they need to decide how best to progress in the context they currently work in. "*The effectiveness, or appropriateness, of an intervention is absolutely context specific"* if for example the "*training or additional equipment or follow-up*" is not available. There is a need to help researchers generate context specific design both in intervention and study design, and to inform this a "*kind of pre-analysis to assess the intervention and context readiness*" may be useful. A specific issue that was frequently discussed was whether there is a need to avoid having to repeat IDEAL Stage 3 (definitive RCTs) in every possible context due to impracticalities and stifling innovation adoption: "*It's not about is A better than B, it's about can we reproduce the safety results in this setting*". IDEAL 2 studies were revealed as the most common types of studies conducted by respondents in this study. This was often because, when evaluating a technology in a new context, they "first want to make sure the innovation is safe, then identify where the risks lie" and if the researchers could acquire "*similar results without excess harm*" via these studies then they felt the technology/innovation could be adopted. However, this depends on how similar the contexts are, and if very different the majority of survey respondents felt the need to repeat a Stage 3 study.

5.3.3.3 Theme 3 - Additional methodologies or disciplines important in evaluation of surgical innovation in LMICs

A frequently discussed topic arose from the need to incorporate additional methodologies or disciplines into existing IDEAL stages to increase the relevance of the framework for surgical researchers in LMICs. "*The research question, make sure it*

is relevant and specific to our needs". Often it is about "*why and how they [intervention] works in this area*" recognising the need for qualitative methodologies to explore these topics in more detail. There is a frequent desire to "*focus on the training and implementation of the new technology*" and methods from implementation science were frequently raised as examples. Health economics evaluations were seen as very relevant both by survey participants and interviewees, especially in LMICs where there is a need to "*think of it as a public health issue and identify local and low-cost solutions".*

5.3.3.4 Theme 4 - Support for researchers along the evaluation pathway

A frequently discussed issue was the effect of the *"lack of background knowledge in the basics of research methodologies"* on evolution and innovation adoptions. One respondent simply summarised the main areas of support needed as "*money, knowledge, time*" explained further as funding to deliver research, better understanding of evaluation methods needed and protected time or workforce support to deliver the studies. To help with this, "*effective local and international collaboration is essential*" and "better training and understanding in innovation pathways" need to be fostered.

5.4 Discussion

This Chapter captured the perceptions and experiences of innovation in global surgery from a wide range of interdisciplinary professionals. Respondents had a breadth of experience with backgrounds from each IDEAL Stage and a variety of different technology categories evaluated. Insights into the current practice of innovation adoption in global surgery and the evidence basis upon which it is adopted has been defined for the first time via this study. Four key themes and accompanying narrative contribute to evidence gathered elsewhere in this Thesis and provide a robust

foundation for the proceeding Chapter 7 that outlines the first iteration of the Global Surgical Innovation IDEAL Sub-Framework.

The most frequent study design conducted by respondents in this study was that of IDEAL Stage 2b with a drop off seen at the transition to Stage 3. Reasons for this could include the relative ease in conduct of Stage 2 studies when compared to Stage 3, both in terms of methodological challenges and sample size or funding constraints. Stage 2 studies are also often quicker to design and conduct, perhaps making them more attractive for surgeons and researchers when seeking to address urgent unmet clinical needs. One theory could be that respondents felt that IDEAL Stage 3 studies were not needed at that moment in time for the evaluation of the technology in question. Indeed, this was explored in detail during the interviews as an area of contention and led to the emergence especially of theme 2 where the need to avoid unnecessary Stage 3 studies was apparent. However, the data demonstrates that a majority of respondents still felt minimum evidence base derived from Stage 3 studies was required before technologies could be adopted. Within the findings of this Chapter, there seems to be a disconnect between perceived need for Stage 3 studies and the actual reality of current evidence generation approaches. Deciding if a Stage 3 study is needed and then selecting the most appropriate design elements is therefore of critical importance along the global surgical innovation pathway.

An IDEAL Stage 2b study may be the appropriate study design to inform innovation adoption especially in two main circumstances. Firstly, if the intervention is deemed low risk, meaning that the risk of causing patient or participant harm through delivering the intervention was deemed to be low, perhaps because safety and efficacy has been defined elsewhere but in a different context. Secondly, if the feasibility of delivering the technology solution itself in this new context and the intervention fidelity are not known, and once known, the innovation could be adopted. As discussed in Chapters 4 and 5, IDEAL Stage 2 studies are also useful for the efficient evaluation of interventions that

are non-novel, meaning their clinical efficacy is established elsewhere, before adopting in a particular context. The findings from this Chapter demonstrate that if existing evidence demonstrates efficacy, then doing an IDEAL Stage 2 study in this way, the need for a Stage 3 study before adoption is negated unless the context is very different, or unless unintended consequences are demonstrated at the Stage 2 phase. In this way, an increase in the efficiency of innovation adoption and global diffusion through utilising Stage 2 studies could be gained, which in turn would improve patient outcomes. To put it another way, IDEAL Stage 2 studies on their own could be used as rapid evaluation methods for low risk or non-novel interventions to quickly make decisions about which innovation to adopt. Further to this, the discussion surrounding theme 3 highlights that there are different study designs not encompassed in the current IDEAL Framework that may serve equivalent or even more appropriate functions. After the evaluation at Stage 2 is performed, a surveillance evaluation could be propagated thereafter, to continue to monitor for unforeseen consequences. The boundaries of such a surveillance evaluation in terms of scope and length of time must be carefully defined and will likely vary depending on the innovation and context.

Chapter 4, aside from the demonstrating a training programme required for the set-up of IDEAL Stage 2 studies, also highlighted additional benefits compared to other designs including the relative simplicity, small size and shorter duration required. This supports the theoretical explanation as to why the majority of respondents in this Chapter had experience in this study design. Further, these factors mean that IDEAL Stage 2 studies may improve surgical innovation diffusion globally by rapid and context-specific evaluations. A key gap in the current understanding of this process is the recognition of when (and if) a context-specific Stage 2 study is sufficient on its own to guide local adoption. This will be explored in Chapter 7 more fully. For example, following the completion of a Stage 2 study, if one believes the evidence is satisfactory to adopt then the researcher has avoided the need for a Stage 3 study. However, as the original recommendations for IDEAL Stage 2 studies include informing the design

of a potential future Stage 3 study, if the researcher then feels a Stage 3 study is needed, they would have conducted a worthwhile evaluation that will improve the delivery and design of such a study. In this way, whether or not a Stage 3 study is deemed necessary, it remains clear that an IDEAL Stage 2 study will improve the timely adoption of appropriate surgical innovation in LMICs.

More respondents had experience with IDEAL Stage 0 (pre-clinical) than Stage 1 or 4. Work in this pre-clinical stage may be prevalent in global surgery because context specific innovations often do not exist or are not easily accessible to surgeons in LMICs. This may reflect the need for respondents to innovate new solutions themselves to address local needs. Theme 1 emerged largely because of the prevalence of pre-clinical early phase innovation where the principles of frugal innovation are extremely relevant to ensure innovations are low-cost, accessible to surgeons in LMICs and context specific. Findings on the spread of technologies evaluated demonstrate a mixed picture, however the majority of technologies were classified as surgically invasive for short term or transient use. Examples include surgical instruments and other devices used intra-operatively. Technologies in this classification that are widely available to HIC surgeons may be unsuitable (due to reliance on certain sterilisation techniques or consumables), hard to procure or unfamiliar in terms of training and operative experience for LMIC surgeons. Therefore, there is an apparent innovation pressure felt by respondents to develop and evaluate frugal innovations in global surgery, derived from LMIC needs and experiences.

Theme 4 is centred around the need to support researchers in LMICs deliver appropriate and context specific evaluation studies that are most suitable to inform the adoption of global surgical innovation. Chapters 4 and 5 of this Thesis describe the evaluation of a researcher training programme and the use of virtual reality as a training tool respectively. The findings from the current Chapter demonstrate that this focus on training for study delivery is highly valued by LMIC surgeons and researchers.

The lack of training may be a contributory factor to the lack of evaluation at Stage 3 and 4 of the pathway evidenced by the survey component. Evidence from this and other Chapters in this Thesis directly inform the inclusion of recommendations surrounding researcher training Framework presented in Chapter 7.

The two most frequently reported bases upon which innovations are adopted in global surgery as reported by respondents in this Chapter were recommendation from colleagues or were based on evidence generated via evaluation in countries other than their own. This finding demonstrates the importance of local and global champions for the widespread dissemination of evidence-based context specific innovations, perhaps including exemplars and use of case studies to encourage and inform adoption. The fact that innovations are often adopted on the basis of evidence from a limited number of countries is unsurprising, given the global lack of surgical research described in Chapter 3. This finding reinforces the need to break down barriers to the evaluation of innovation in multiple contexts, especially LMICs where the majority of respondents of this study work. Locally derived, context-specific evidence was seen as highly important by those interviewed and approaches to generating appropriate evidence efficiently are therefore a key focus of the Framework outlined in Chapter 7.

In summary, this Chapter builds on the preceding Thesis work to provide targets from the results to inform the adaptation to the IDEAL Framework for evaluating innovation in surgery, increasing its relevance of recommendations for surgeons and researchers in LMICs. Key strengths of this Chapter include involving a wide range of participants from different backgrounds, geographies and contexts which increases the generalisability of the findings. Recommendations based on these findings are therefore derived from and shaped by surgeons and researchers in LMICs ensuring the guidance is itself context-specific, relevant, and accessible. This study was split into two parts, a semi-quantitative survey, and a series of qualitative interviews. This mixed

methods approach is a further strength of this Chapter as it permitted deeper exploration of key themes identified.

Limitations are also recognised. Firstly, the study was conducted in English only. This means I may have missed valuable information from non-English speaking participants. Furthermore, many countries are not represented among the participants despite efforts from the research team to ensure as wider representation of contexts as possible. Other specialties related to surgical care were also not well represented including emergency medicine, radiology, cancer care and intensive care. Views and experiences from these specialties may have provided new insights and valuable clarifications to our recommendations. Despite endeavours to reach those respondents who have experience in rural settings, the majority of respondents appeared to work in urban centres. This is a frequently occurring phenomenon within the global surgery literature and further research is needed to explore approaches that maximise reach and input from rural contexts (219). A final limitation recognised is that only a small number of interviews were conducted. Despite this, data saturation was reached and there was considerable repetition of themes across the participants suggesting the themes identified are generalisable. In qualitative research, emphasis is placed on the content, meaning and quality of the data rather than quantity and it is not felt that the limited number of interviews adversely effected the results in a fundamental way. Nevertheless, further interviews would have increased the range of backgrounds and perspectives included in the analysis.

Unlike Chapters 3, 4 and 5 that all focused on specific IDEAL Stages, this Chapter attempted to examine the whole innovation pathway including all stages and cross-cutting/pan-stage issues, whilst reinforcing through further exploration the evidence gathered from earlier work in this Thesis. This was essential to address the primary aim of the Thesis as a whole body of work and completes the prerequisite evidence

generation prior to drafting the initial Framework components for development in Chapter 7.

6 The Global Surgical Innovation IDEAL Sub-Framework

This Chapter pulls together the collective learning and evidence generated throughout the preceding systematic review of the literature, the conduct of two surgical trials, and a global survey and interview study mapping the current surgical innovation evaluation pathway in LMICs. It is clear from this combined evidence that IDEAL Stage 3 studies are still important, and their conduct needs to be adapted to make them more likely to succeed in low-resource environments; that context-specific IDEAL Stage 2 studies may be powerful study design options for rapid and efficient adoption informing evaluations in lieu of Stage 3 evidence in a particular context; and that additional recommendations are needed to overcome the barriers imposed on the current innovation evaluation pathway. This Chapter presents the first completed iteration of the Global Surgical Innovation IDEAL Sub-Framework, a principles-based framework and decision-making aid for identifying the most appropriate evaluation methodology for a given context and describing corresponding strategies to deliver evaluation and inform adoption. Importantly, this Framework is derived from the experiences and guidance from LMICs surgeons and researchers themselves, and so represents the first truly LMIC context-specific guidance for surgical innovation evaluation. The impact of this Framework will be tested during real-world application as it informs future evaluation practices, and the resulting impact on innovation adoption is measured and monitored.

6.1 Introduction

There persists a global lack of evaluation in surgical innovation and this is compounded by limited utilisation of context and surgery specific guidance to inform the process (16,98). Several challenges associated with generating evidence for novel surgical innovations include the complexity of the intervention, standardisation of critical

intervention components and completing appropriately designed and powered evaluations that persuade policy makers and surgeons to translate their widespread adoption (98). In 2009 and 2019, The IDEAL Framework was first published and updated respectively to address these challenges: it provided a structured set of recommendations to inform innovators and researchers in the systematic scientific development and evaluation of surgical innovation (95,98). IDEAL stands for Idea, Development, Exploration, Assessment, Long-term study and consists of 4 stages. Briefly, Stage 1 focuses on a small number of participants and the evaluation usually takes the form of structured case reports where the main outcomes are proof of concept related. Stage 2 is split into 2a and 2b. 2a still includes a small number of selected participants in a single group design and aims to document the development of the evolving procedure or technology. 2b builds on this using collaborative prospective cohort studies and feasibility randomised controlled trials (RCTs) to build clinical consensus around indications and quality of delivery, focusing on feasibility and short-term clinical safety outcomes. Stage 3 seeks definitive comparative evidence of clinical and cost effectiveness, normally involving multicentre RCTs with longer follow-up time points. Finally, stage 4 takes the form of long-term surveillance studies such as registries or routine databases. Here the focus is on ensuring and maintaining standards. In 2016, the IDEAL-D Framework modified the Framework to include considerations specifically for medical devices, including recommendations for the pre-clinical development in a new IDEAL Stage 0 (109).

In 2015, the Lancet Commission on Global Surgery generated a roadmap to scale up global surgical care by 2030 (1). One of the key enabling factors to achieve the targets set out by the Commission is the development of novel technologies and adoption of appropriate innovation. Many of the challenges faced in designing new surgical technologies and thereafter generating the necessary evidence to inform safe adoption are even more onerous in low-resource environments, especially when evaluating innovations across multiple contexts (106). Often low and middle-income countries

(LMICs) have unique, context-specific challenges that complicate the process (142). Facilitating strategies to overcome or mitigate these barriers do exist, but there is a lack of comprehensive guidance for surgical innovation and technology evaluation for LMICs.

6.2 Aims

The aim of this Chapter is to identify the adaptations required to transform the IDEAL Framework into a relevant, context-specific set of surgical innovation evaluation guidelines for LMICs surgeons and researchers.

6.3 Methods

6.3.1 Framework components and derivation

New additional recommendations within the Global Surgical Innovation IDEAL Sub-Framework were derived by mapping the perceived barriers and facilitating strategies to the corresponding original recommendations for the IDEAL Framework Stages. Additional evaluation methodologies or new Framework components that were generated from the data collection were then added. Multiple components of this Thesis were utilised in deriving the Framework presented in this Chapter. Chapter 3 provided a range of components surrounding the conduct of IDEAL Stage 3 studies in LMICs from the analysis of the systematic review. Insights from conducting IDEAL Stage 2 studies in LMICs were derived from Chapters 4 and 5. The breadth of the innovation pathway in its entirety was explored in Chapter 6 and provided a range of insights for multiple stages as well as the derivation cross-cutting or pan-stage components. A Logic Model was created to depict how the Global Surgical Innovation IDEAL Sub-Framework could be used, and how it could help to solve contextual

innovation problems. These proposals have been used to help bridge the theory-research-practice divide in global and public health initiatives (220,221).

A draft version of the Global Surgical Innovation IDEAL Sub-Framework was presented at a workshop during the IDEAL Virtual Congress 15-16th April 2021 bringing together clinicians and researchers from all over the world including colleagues from LMICs. Participants of this workshop were sent written materials detailing the proposed components of the Sub-Framework as well as background and rationale to the study in general, including links to the freely accessible original IDEAL papers. They were asked to provide verbal feedback during the workshop which was held over Zoom® (Zoom Corporation, San Jose, USA), or they could feedback written information before or after the workshop over email. Participants were encouraged to provide opinion (agreement or disagreement) on the included recommendations. Areas of disagreement were debated collaboratively, and modifications made accordingly. Further detail on areas of contention is provided in the commentary within the results section and is presented as the final argument summary and outcome to be taken forward in this version of the Sub-Framework. Areas of agreement were then included and taken forward in the recommendations presented below. Any additional modifications and suggestions were discussed and incorporated into the Global Surgical Innovation IDEAL Sub-Framework. The resulting Framework is presented in this Chapter.

6.4 Results: The Global Surgical Innovation IDEAL Sub-Framework

The recommendations presented below aim to address the issues and themes raised throughout the evidence gathered in this Thesis and following further discussion of the initial draft Sub-Framework at the workshop. A summary comparison of the features

characterising the original IDEAL and Global Surgical Innovation IDEAL Sub-Framework recommendations at each stage is presented in Table 15. It is important to note that this builds upon, rather than replaces, the original IDEAL Framework and IDEAL-D Framework recommendations which can be freely accessed here (98,109): https://www.ideal-collaboration.net .

Table 15: Brief comparison of the features characterising the original IDEAL/IDEAL-D and Global Surgical Innovation IDEAL Sub-Framework recommendations at each stage.

Original IDEAL/IDEAL-D Stage of Innovation	**Global Surgical Innovation IDEAL Sub-Framework Recommendations and considerations**
Pre-IDEAL **Stage selection**	
Silent but recognised: Theoretical exercise only	Conceptual decision-making aid provided to select appropriate stage to enter the pathway based on rapid appraisal of existing evidence.
Stage 0 **Frugal Innovation and Context-Centred Design**	
Calls for standards for publication/registration of preclinical data need to be established	Shifts focus to the design and development elements of innovation pre-clinically and calls for consideration of the context-specific processes, human factors, system, and regulatory issues employing principles of frugal innovation.
Stage 1 **Local safety review and intervention modification for context**	
First-in-human studies with compulsory confidential reporting of all wholly new innovations	Recognition that much of the innovation to be evaluated in global surgery is not first-in-human and if so, this stage may not need to be duplicated. If a traditional Stage 1 study is not needed, then we recommend a formal requirement that researchers perform a theory or experienced based safety review and modification of the intervention to fit the context before progressing to a full-scale Stage 2 study.

Stage 2a and 2b **Key diffusers of innovation**	
2a) Small uncontrolled cohort studies, usually single centre, with consecutive case reporting and explanation of innovation development. Focus on technical details and feasibility. 2b) Explanatory or feasibility RCTs, usually smaller in scale, focusing on safety and feasibility outcomes. Can be efficacy trials.	Also suitable for established innovation in a new context to facilitate rapid feasibility and safety concerns mitigation. Focus on checking the results aren't dissimilar to other existing data in other contexts and capturing and displaying any unexpected consequences/outcomes arising from new contexts. We recommend augmenting these studies with in-built qualitative process evaluations and implementation science methodologies.
Stage 3 **Beyond the traditional RCT**	
Randomised controlled trials, ideally multi-centre, appropriately statistically powered. Aim to assess clinical effectiveness of interventions.	Consider any study specific training needs required to deliver Stage 3 studies that often have a range of complex methodological components above and beyond studies in other Stages. Employ adaptive trial designs by implementing protocol-driven pre-planned interim evaluations that use prespecified updates/amendments decision rules. Consider master protocols and platform trial designs for large trials across multiple countries. As with Stage 2 studies, include in-built qualitative process evaluations and consider phased/hybrid RCT-implementation evaluation designs.
Stage 4 **Engage with mixed-methods registries sooner**	
Comprehensive registries and databases for recording rare events, long-term outcomes and challenges in use.	Registries should be employed as soon as possible in the evaluation of innovation, including in conjunction with earlier stages. These should be mixed methods, involving a digital

	database capturing clinical safety concerns and rare events, as well as an on-going qualitative analysis to identify and address challenges with sustained innovation adoption specific to the context.

Pan-Stage Considerations

Some considerations are recommended for each stage and form more largescale guidance for implementing the innovation evaluation pathway globally:

- Emphasis on employing in-built, protocol driven mixed methods approaches at each stage
- Ensuring human resource training (both research methods and innovation/technology use training)
- Fostering innovation culture guided by frugal innovation principles
- In-built health economics evaluations to help make decisions about appropriate adoption and choose between innovations
- Loco-regional and international collaboration driven by LMIC researchers
- Pan-stage leadership of LMIC researchers, surgeons and patients/public in design, evaluation and adoption of innovation
- Supporting researchers via training, methodological support, securing funding and identifying dissemination and advocacy opportunities

A Logic Model depicts how this new Sub-Framework could be used and how it interacts with external circumstances that are pertinent to the innovation pathway in global surgery, and its constituents are summarised briefly below (222) (Figure 18):

1. Situation – description of the current state of things, the unmet need/s or problem/s
2. Inputs – resources required, your 'investment'
3. Outputs – the activity you actually do/need to do

4. Outcomes – short term, intermediate, long term/impact
5. External environment – factors that affect outcome but outside the model's control
6. Assumptions – conditions needed for success

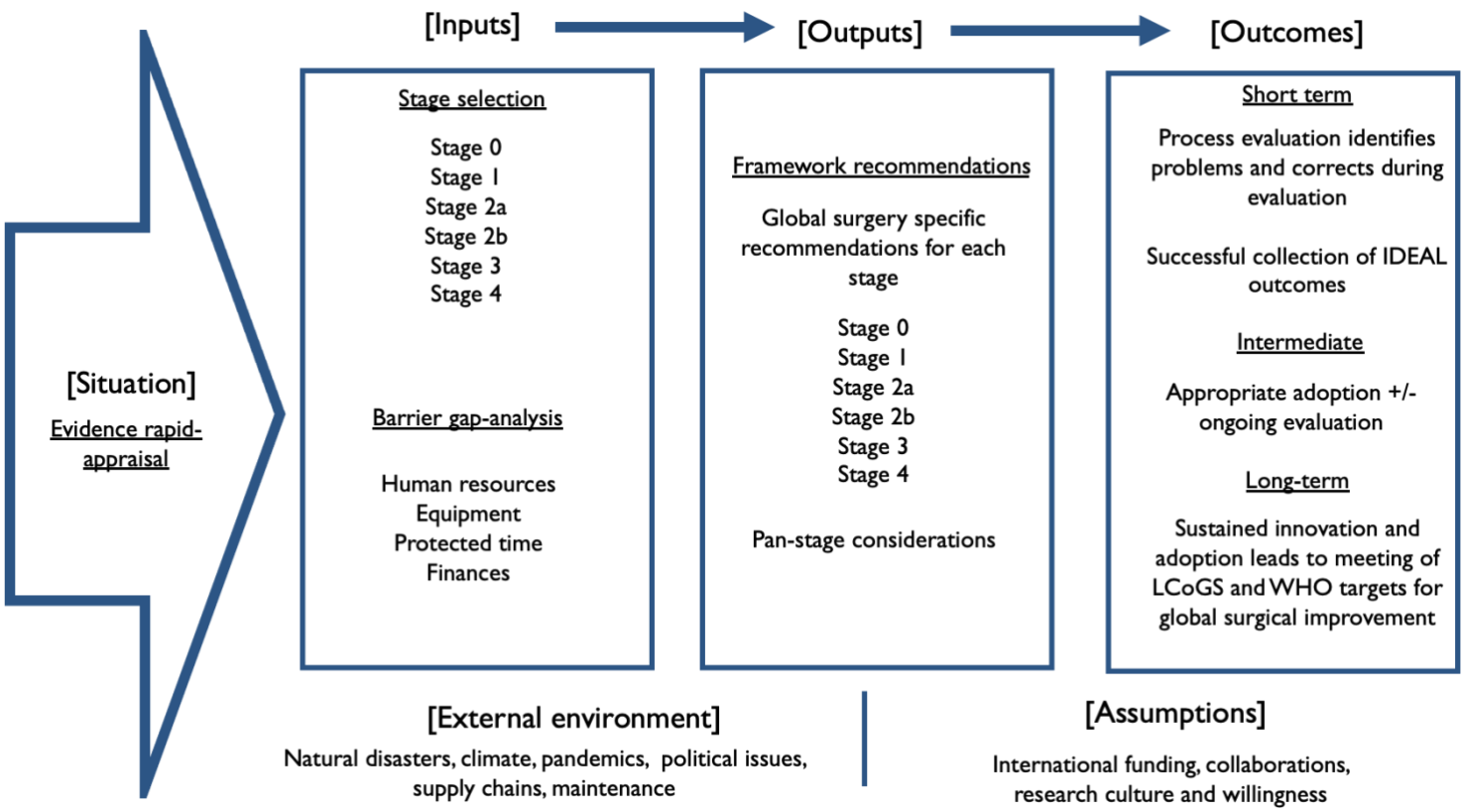


Figure 18: Logic Model depicting how the Framework user may consider the recommendations in relation to other factors before, during and after the evaluation process. Arrows depict relative flow of decisions/considerations for the six components of logic models (Situation, Inputs, Outputs, Outcomes, External environment, and Assumptions).

An expanded presentation of the new or additional recommendations, or modifications to the original IDEAL recommendations is discussed below.

6.4.1 Pre-IDEAL: Stage Selection

The first recommendation of this Sub-Framework is for a new Stage to help the researcher decide where to enter the evaluation pathway. This recognises the fact that often, LMIC surgeons are not aiming to evaluate interventions that are novel in themselves, but rather that they want to apply them safely to their own context. Decisions on the context-relevant evidence required to achieve a balance between benefits of swift innovation adoption and risks of potential harm through under-evaluation should be made in collaboration with regulators, innovators, surgeons, and patients themselves. For this reason, we recommend consulting local key policy makers, legal and regulatory stakeholders to ensure legally and ethically aligned decisions are being made. The Pre-IDEAL: Stage Selection tool is provided to help focus this exercise and review of the evidence in the form of a high-level decision-making aid (Figure 19). If the innovation/technology is completely novel and first-in-man studies have not been conducted yet, then the researcher should begin with Stage 0 and progress sequentially no matter what the context.

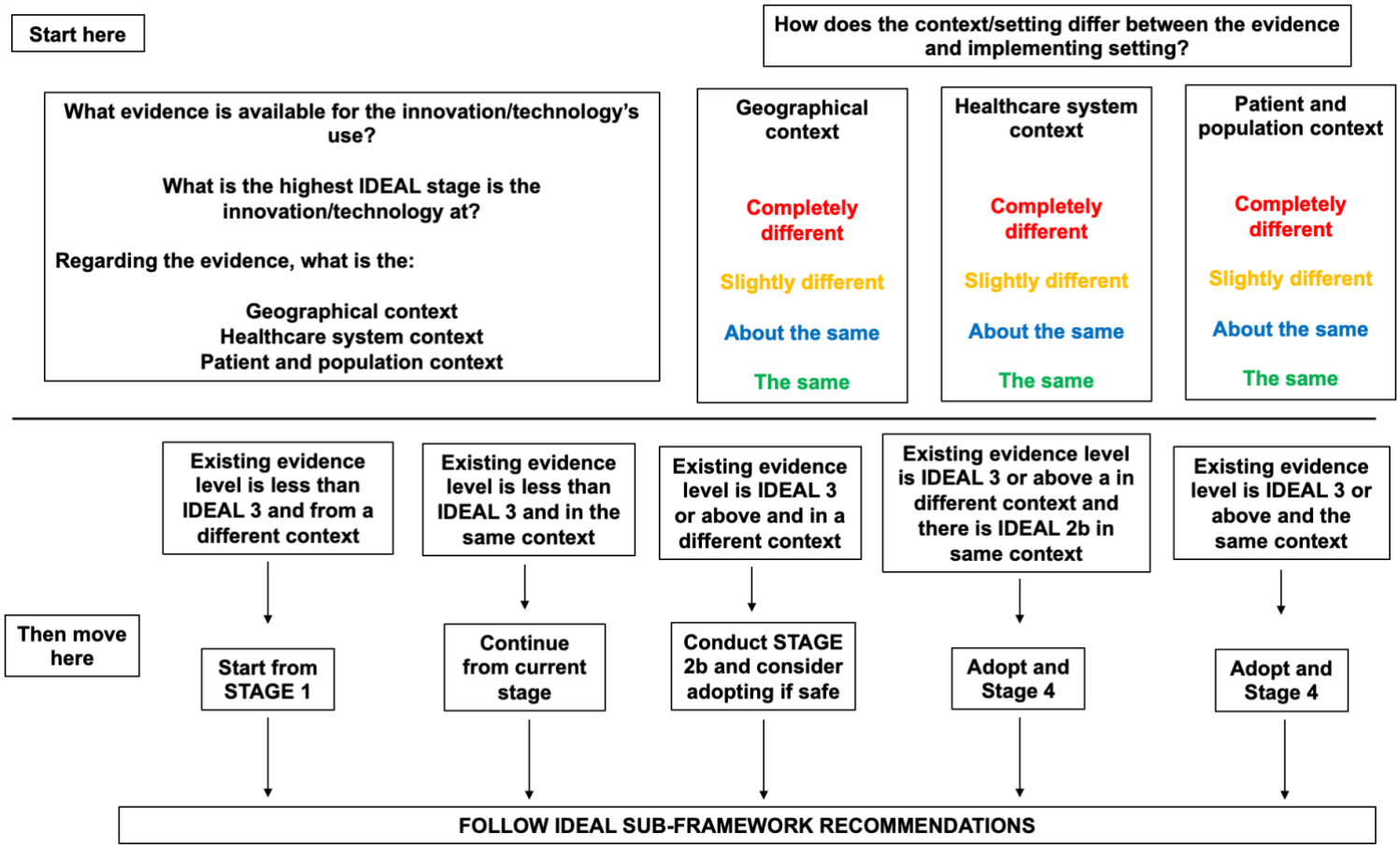


Figure 19: Pre-IDEAL: Stage Selection tool. This decision-making aid is designed to help the user identify the necessary existing evidence, how this relates to their context and then guides them to suitable study designs.

6.4.2 IDEAL Stage 0: Adopt principles of Frugal Innovation and Context-Centred Design

Present in the original IDEAL-D Framework, this stage is retained in this new Sub-Framework with a shift in focus which calls upon the researcher to ensure that the principles of frugal innovation are adhered to during the initial design of any new innovation. Frugal innovation refers to the concept of doing better with less. By concentrating on user-centred design, focusing on core functionalities, reducing cost

and waste, frugal innovation can produce elegant, context-specific solutions to complex problems(12,29). We recommend researchers employ context-centred design principles to ensure all the processes, human factors, regulatory and system considerations relevant to the intended context of use are considered, including consideration of the innovation's acceptability to differing contexts and populations.

6.4.3 IDEAL Stage 1: Local safety review and intervention modification for context

The original IDEAL Stage 1 is compulsory for all wholly new innovations and all first-in-human studies to be internationally registered, and the Sub-Framework endorses this. However, if the first-in-human studies have already been completed, then at this stage the Sub-Framework highlights the need to return to stage selection. We expect that for most established innovation, supplementary Stage 1 studies in new contexts/populations/systems may not be required. If a traditional Stage 1 study is not needed, then we recommend a formal requirement that researchers perform a theory or experienced based safety review and initial modifications of the intervention to fit the context before progressing to a full-scale Stage 2 study. This should be conducted with consideration of contextual factors including healthcare system, patient population and geographic factors. It is important to note that key outcomes from IDEAL Stage 2a studies include safety outcomes.

6.4.4 IDEAL Stage 2a and 2b: Key diffusers of innovation

This Sub-Framework recommends the use of these study designs especially for when established technology/innovation is to be evaluated in a new context. Given the relative simplicity of these studies, they can facilitate rapid, cost-effective feasibility evaluations and safety concerns mitigation. The focus here is on checking the results

of new evaluations aren't dissimilar to other existing data in other contexts, while capturing and displaying any unexpected consequences/outcomes arising from new contexts. It may be reasonable that if the results are acceptable at this stage, then adoption with ongoing monitoring via a registry is acceptable without the need for IDEAL Stage 3 studies. We strongly recommend augmenting these Stage 2a/b studies with in-built qualitative process evaluations to provide context about how the innovation is interacting with the environment and users/patients. The iterative evaluation cycles described in IDEAL 2a could be further strengthened by learning from the phased/hybrid evaluation-implementation cycles seen in implementation science techniques, thereby combining elements of clinical effectiveness and implementation research to enhance public health impact (223). This could be represented as an IDEAL Stage 2a/b study followed by implementation and monitoring via a registry (IDEAL Stage 4 study) with an ongoing process evaluation. IDEAL Stage 2a and 2b studies are recommended for innovations that are non-novel (i.e. clinical effectiveness is established elsewhere) or low-risk (such as educational interventions) and because of the ability to perform this rapidly across multiple contexts with relative ease, they can be considered as suitable methods to increase the global diffusion of innovation by providing necessary context-specific evidence for safe and swift adoption.

6.4.5 IDEAL Stage 3: Beyond the traditional RCT

Much of this Sub-Framework provides guidance on if and when an IDEAL Stage 3 study may not be needed. This depends on existing levels of evidence and its relevance to the specific context and decisions about this are aided by Figure 19. In essence, an IDEAL Stage 3 study is always required if no Stage 3 study has been completed for a specific innovation in any context at all. It may be avoided if Stage 3 evidence exists in a different context and the results are confirmed via a Stage 2a/b study in the new context in question. There is precedent from a recent report for researchers to avoid the need for Stage 3 studies where not required because there is

an opportunity to improve the efficiency and cost-effectiveness of the innovation pathway (167). However, there are plenty of circumstances where an IDEAL Stage 3 study is required, in which case, the original IDEAL guidelines on design and conduct of RCTs should be followed. The Sub-Framework highlights additional considerations including alternative trial designs for global surgery. For example, cluster randomized trials may be more appropriate for public health interventions and stepped wedge designs are often considered when there is already evidence the intervention is likely to be effective (i.e. prior evidence of efficacy), and when phased implementation is desirable or inevitable (224). Employing adaptive trial designs by implementing protocol-driven pre-planned interim evaluations that use prespecified updates/amendments decision rules may also increase the efficiency and success of Stage 3 studies (166). Consider master protocols such as platform trial designs to evaluate multiple interventions (or populations) through concurrent Stage 3 sub-studies. As with Stage 2 studies, we recommend researchers include in-built qualitative process evaluations and consider phased/hybrid RCT-implementation evaluation designs to improve the interpretation of results in context, and the sustained uptake of innovation into future clinical practice.

6.4.6 IDEAL Stage 4: Engage with mixed-methods registries sooner

In many instances, the researcher in global surgery innovation already has the necessary evidence base but wishes to have a structured way of monitoring for any unexpected consequences and to identify challenges in the innovations use once adopted. In this Sub-Framework, we recommend that registries be created and maintained as soon as the innovation is in use to maximise the chance of detecting difficulties and minimising the risk of missing safety concerns. These registries should employ a mixed-methods approach including preferably a digital database to capture clinical safety concerns combined with an on-going qualitative analysis over time with innovation users and relevant policy makers to ensure challenges with sustained

adoption are identified and addressed. These Stage 4 studies can be started immediately if otherwise evidenced innovations are being adopted in a new context or started soon after or in combination with earlier stages during the innovation pathway. It is recommended that Stage 4 studies in this way should be the terminus stage even when intervening stages are not required (for example moving straight from Stage 2a/b to Stage 4 if no Stage 3 is required).

6.4.7 Pan-Stage Considerations

There are a range of considerations that are universal or relevant to all stages and these are summarised below. A frequently recurring recommendation is the need to employ mixed methods approaches as these tend to capture more information about how the innovation is being developed and adopted for and within a given context. The Sub-Framework puts a greater emphasis on this. Importantly, many researchers may need training support to deliver these additional methodological considerations and novel training programmes need to be developed and easily accessible. Examples of evaluating training programmes can be seen in Chapters 4 and 5 of this thesis. Training may also be required for the use of the innovation itself, especially if it is new to the context, and any evaluation needs to be designed with this consideration in mind. Efficient and cost-effective evaluation is critical to ensure context-specific innovation is safely and quickly adopted. For this reason, understanding and applying the principles of frugal innovation to thought processes, device design and evaluation delivery may be beneficial. It may also be helpful to conduct in-built or standalone health economics evaluations to help make decisions about appropriate adoption and choose between innovations in different contexts/populations. Collaborating between urban and rural centres loco-regionally, and then internationally should be multi-directional but led by LMIC researchers. This collaboration should be pan-stage, with leadership from LMIC researchers, surgeons and patients and the public in the design, evaluation, and adoption of innovation. Researchers may need ongoing

methodological support, and assistance in securing funding opportunities, as this was cited as the number one facilitating factor by participants in this study.

6.5 Discussion

This Chapter combines evidence gathered throughout the preceding body of work and aims to produce a coherent framework that combines the lessons learned and corresponding recommendations from previous Chapters. The resultant Global Surgical Innovation IDEAL Sub-Framework is a novel framework that increases the relevance and applicability of the IDEAL innovation evaluation pathway for surgical researchers working in LMICs. It adds to existing IDEAL recommendations and proposes new and valuable tools and considerations with the aim of improving the evaluation pathway of global surgical innovation.

This Sub-Framework is derived from evidence gathered from all Chapters of this Thesis and shaped by the workshop feedback. Chapter 3 provided insights into the barriers and facilitators of surgical trials in LMICs. This was important in the formation of initial recommendations for when a Stage 3 study is required and how different approaches to this stage of evaluation may improve the delivery of these studies in global surgical contexts. Chapter 4 was critical for providing insight into researcher training and approaches to this cross-cutting recommendation for all evaluation in LMICs. This Chapter also highlighted potential uses of IDEAL Stage 2 studies when the intervention in question is not novel in general, just novel to a specific context. Chapter 5 described how a technology such as VR may improve training in global surgical contexts. This may also be useful for evaluation deliver training as well, where VR could be used to teach surgeons the intervention, or how to ethically recruit patients to study and collect data appropriately. Chapter 5 further provided insight into the use of Stage 2 studies for interventions deemed low risk, which impacted recommendations of

the use of Stage 2 designs as rapid evaluation approaches for innovations to facilitate the global diffusion of innovation. Chapter 6 was contributory to a wide range of the Sub-Framework recommendations, providing initial insight into other areas of the innovation pathway in global surgery as well as cross-cutting or pan-stage recommendations that the community felt were highly relevant throughout the generation of evidence to inform innovation adoption in LMICs for surgical care. As previously described, the evidence from these Chapters was supplemented with insights from the wider literature and this formed the initial draft components that were presented for final inclusion or modification at the IDEAL workshop.

Although the first full iteration of the Sub-Framework is presented here, further work is required to verify and iterate some of the principles described in this initial version. Areas for development centre around the use of IDEAL Stage 2 studies in lieu of Stage 3 studies. The Sub-Framework highlights benefits of Stage 2 studies compared to other designs including the relative simplicity, small size and shorter duration required. While the Sub-Framework provides decision-making aids, further real-world assessments of when (and if) a context-specific Stage 2 study is sufficient on its own to guide local adoption will be required. It is essential to note when IDEAL Stage 2b studies may be most beneficial as the appropriate study design for rapid assessment and informing adoption. The decision-making aids provided above try to address this challenge by essentially guiding users to perform a rapid critical appraisal and selection of the corresponding most suitable Stage accordingly. This process was favoured by members of the workshop who valued direction as to where to start along the pathway when considering evaluating an existing technology in a different context. However, the current process is subjective and may be misinterpreted. It also assumes ability to access and appraise evidence effectively. Prospective evaluation of the real-world use of these decision-making aids will be highly useful in providing further definition of their use, or in identifying alternative tactics to select the appropriate stage, including when repeating certain stages in differing contexts can be avoided. This is critical because

innovation adoption needs to be done in an efficient way globally, that limits waste and ensures that safe and effective innovation is adopted to benefit patients as swiftly and widely as possible.

A further area for development includes the involvement of local legal and regulatory entities in the use and adoption of the Sub-Framework itself. Regulatory processes differ from country to country, and while a universal principle of this Sub-Framework is to guide users to consult and engage with the necessary local authorities, it remains to be seen how best this Sub-Framework is used alongside national and local guidance in differing LMICs. This Sub-Framework certainly does not aim to replace or supersede local, national, or international regulatory and legal standards or processes. Understanding how the recommendations in this Sub-Framework work with regulatory guidance will be essential to ensure its safe use. A challenge here will be in doing this for a wide range of countries that may have different processes. One way this could be avoided is by simply stating that surgeons and researchers should ensure all local / applicable regulatory guidance is adhered to first and foremost before considering the recommendations in the Sub-Framework. This may be adequate on its own, but it may be more useful to ensure the recommendations intrinsically do this in any case. This is certainly what was attempted in the current iteration. The most important consideration in this area of development remains the effective collaboration with the various regulatory bodies, especially in relation to the necessary requisite evidence before adoption.

A final area for development includes understanding how the impact of this Sub-Framework will be measured and monitored as it is used in the global surgical community. Impact may be measured by analysis of the number of innovations reporting to being evaluated through using this Sub-Framework, as well as mapping the spread of geographical use and technologies evaluated. Collecting feedback on strengths and areas for improvement on this current version will be essential to

improve its use further, and ensure the recommendations are safe and easily interpreted. Monitoring of the Sub-Framework's use during its implementation is needed to ensure unintended consequences are addressed accordingly. Examples may include misinterpretations of the recommendations, barriers to access such as available translations, and issues where recommendations contradict or are confused with other guidance. Currently unknown or unforeseen issues may also be discovered, and monitoring needs to be real-time, at scale and pragmatic.

To continue work in these development areas, a task force has been established within the IDEAL Collaboration including regulatory representatives, led by WSB, to capture data and extract from it lessons for future modifications. Final terms of reference for this task force are being drafted currently, but it is anticipated that this group will meet virtually multiple times per year and aim to include a face-to-face meeting and accompanying delegate workshop at the IDEAL annual conference. The remit of this group will be to collate and interpret feedback on the Sub-Framework and make consensus driven amendments accordingly, as well as facilitating the widespread implementation of the Sub-Framework by disseminating its impact and troubleshooting its use. Providing a pathway to impact for studies that have been conducted using this Sub-Framework is also critical. A collaboration has been created with the open access British Medical Journal Surgery, Interventions, & Health Technologies that seeks to provide guidance for the reporting of these global surgical innovation studies and no-cost publication LMIC researchers. This process would provide a positive feedback loop where LMIC studies are disseminated effectively with evidence from the use of the Sub-Framework used to guide its further development and dissemination.

A strength of this Chapter is that it aims to align the development of this new guidance to the original IDEAL Framework, an established and evidence-based tool specifically for surgical innovation evaluation. This Sub-Framework did not seek to reinvent anything; the value added is the transformation of high-quality guidance into a more

applicable and appropriate tool for global surgeons. It is important to note that this is the first version of the Sub-Framework and further iterative development will need to occur with even wider inclusion of specialties, geographies, and contexts to clarify and improve the guidance further.

To help users of this Sub-Framework best utilise the guidance, they are invited to visit the IDEAL Collaboration website (https://www.ideal-collaboration.net) for accompanying information and access to services including methodological support, study conduct and pathways to publication and impact.

7 Discussion

7.1 Aims and objectives of this work

The main aim of this PhD was to investigate how surgical innovation occurs in LMICs, the barriers to innovation, strategies to increase innovation research capacity and capability, and the steps needed to increase the efficiency of clinical translation and adoption of surgical innovation for LMICs globally. Specific objectives were:

1) To conduct a systematic review of the literature to identify how surgical technology is evaluated in LMICs and the barriers and facilitating strategies to evaluation.
2) To conduct a research training exercise in Sierra Leone and evaluate a new training methodology to increase research capacity and capability.
3) To conduct a feasibility study in Sierra Leone investigating the use of virtual reality technology to enhance clinical training and improve the uptake and outcomes from surgical interventions.
4) To develop a Framework to increase the efficiency of clinical evaluation studies of surgical technologies in LMICs.

The completed body of work provides a robust and comprehensive overview to help show how innovation in global surgery can be improved across a wide range of contexts by focusing on breaking down barriers to evidence generation to inform the adoption of innovation.

7.2 Conclusions

7.2.1 Chapter 3: Systematic review and meta-synthesis

This systematic review and narrative meta-synthesis demonstrated the substantial global lack of surgical trials (IDEAL Stage 3 studies) compared to non-surgical clinical trials, and that this disproportionately affected LMICs. Following this, the study went on to identify barriers and facilitators to delivering these evaluations in LMICs from within the literature. This study showed us that collaboration, flexible and efficient trial designs, and improving funding and research culture can overcome the lack of human resource, equipment, technology, and challenges with research culture and methodological issues.

The findings from this study went on to inform the design of questionnaires used in Chapter 4 and provided key insights that informed several recommendations in Chapter 7's Sub-Framework. Surgical trials or IDEAL Stage 3 studies were selected as the evaluation method to conduct this in-depth study on because these studies have been historically required to persuade policy makers and surgeons to adopt innovation and are also some of the most challenging to conduct. Before questioning when exactly these studies were needed in global surgical innovation, if at all, I wanted to ensure this important study design was covered. Having focused on how to break down barriers to the conduct of Stage 3 studies in LMICs for surgical innovation, the next step was to explore the key issue of training for evaluation delivery and focus could now be given to IDEAL Stage 2 studies.

7.2.2 Chapter 4: Training for IDEAL Stage 2 studies

The importance of training to conduct evaluations of surgical innovation in LMICs is a central idea throughout much of this Thesis in general. Chapter 4 explored this in

detail, evaluating a trial initiation that included two training programmes, one for those delivering the intervention and one for those conducting the research. This was set within the delivery of an IDEAL stage 2 study in Sierra Leone investigating the feasibility and safety of the Ilizarov external fixator for tibial fractures. Fundamentally, this Chapter demonstrated that despite considerable barriers to conducting evaluations in the study setting, the motivation from the participants to gain new skills and knowledge in the evaluation of innovation is substantial.

The training programmes were designed based on the established WHO Good Clinical Practice for trials and the Global Health Network's Global Competency Framework for Clinical Research. It was found that with study specific modifications, such a training programme can improve the perceived knowledge rating of participants. Through further exploration via qualitative FGDs, this Chapter demonstrated the importance of five key themes when designing training programmes for evaluations of global surgical innovation. While these are useful in and of themselves, they directly inform the design of Chapter 5 (Theme iii - Training the trainers using technology) as well as advising several recommendations in Chapter 7.

7.2.3 Chapter 5: The VITAL Trial (Stage 2b study)

In this feasibility randomised controlled trial, the feasibility of using VR to train surgeons in LMICs was confirmed. Contributing to the evidence from this Thesis surrounding the importance of training in surgical innovation, this Chapter affirms the use of VR in training which may include research skills training. The recruitment target was hit and adherence to the intervention was high, exceeding pre-defined success rates. This demonstrated that even in challenging environments, participants were able to access and engage with VR as a training intervention. The intervention was deemed acceptable by participants as an adjunct to existing training opportunities such as hands-on courses. There was no contamination between groups and retention was

excellent, with only one participant being unable to complete the study due to competing clinical commitments that took priority. This suggests that the study design was feasible and indicates its suitability to be taken forward into a larger study if deemed necessary, or to inform similar studies investigating different types of technology enhanced learning tools.

Participants in the intervention group had improved MCQ and OSATs scores (knowledge and practical skill assessments respectively). These can only be interpreted as trends, as this study was not powered to assess educational effectiveness. What is clear is that among those that received the intervention, engagement in learning was significantly higher and this has been shown to improve knowledge and skills acquisition.

The results of this study could now be used to inform the design of a larger, definitive randomised study exploring the educational effectiveness. The findings from this Chapter confirmed the feasibility of VR technology in this context and therefore, precisely where this definitive study takes place may not be important. Further, it may not be necessary to conduct a repeat Stage 3 study because several are emerging from multiple contexts as evidence of education effectiveness for VR continues to grow. It may be that combining this body of evidence in the literature with the feasibility confirmation from this Chapter is enough to persuade surgical trainees and trainers to adopt this innovation more widely.

7.2.4 Chapter 6: Global survey of innovation pathway

The innovation pathway in global surgery is complex and the understanding of current practices surrounding the evaluation of surgical innovation in LMICs is documented in this Chapter. The findings from this Chapter build on the preceding ones that focused

on Stage 2 and 3 Studies to present an understanding of innovation evaluation across all the IDEAL stages. Respondents had most experience with Stage 2 studies and perceived a need for Stage 3 studies for innovation from different contexts. This finding highlights the importance of both Stage 2 and 3 studies along the innovation pathway, but further exploration at interview stage revealed that Stage 2 studies may be useful for rapid evaluation in multiple contexts.

Themes emerged through interviews that were informed by the findings from the survey phase of the study. These themes centred around frugal innovation in the early stage of the pathway, evaluation approaches particularly useful in LMIC contexts because they help overcome barriers, and once again the need to support researchers with guidance and training on methodological considerations, study selection and research training. These findings were directly informative for the creation of the Sub-Framework presented in Chapter 7.

7.2.5 Chapter 7: The Global Surgical Innovation IDEAL Sub-Framework

The entire body of work in this Thesis contributed to this Chapter that sought to pull together evidence gathered thus far into a coherent set of recommendations that informed how the IDEAL Framework may best be used in global surgery. The resulting Global Surgical Innovation IDEAL Sub-Framework had its draft components challenged and debated at a workshop involving key stakeholders before the final version is presented fully in this Chapter. Recommendations at each IDEAL Stage are put forward, together with a collection of decision-making aids designed to help the LMIC surgeon or research select the most appropriate evaluation approach for a given innovation, and then design and conduct this in such a way that minimises the effect of barriers.

The Sub-Framework still requires real-world evaluation itself and subsequent development. This will be taken forward and conducted in due course and this Chapter summarises some of the key issues with this as well as describing a strategy in place to address these.

7.3 Limitations

When attempting to generate evidence for a global audience, global representation is exceptionally important. Pan-nation, pan-profession representation is a worthy aim but is often unrealistic given practical constraints. While this Thesis provides many examples of endeavours to include a range of disciplines and countries, truly global representation was not achieved. The studies in Chapters 4 and 5 were both conducted in the same country (Sierra Leone). While data from Chapters 3 and 6 did include several other nations (and indeed, the inclusion criteria was certainly global), the findings from this Thesis may not be fully generalisable to all contexts. To overcome some of these limiting factors, future evaluations could target specific countries and contexts felt to be lacking in this current body of work.

Of note is the lack of opinions from patients and the public in this Thesis. This was partly because the many of the research aims set out to explore the barriers and facilitators of surgical innovation evaluation as perceived by those actually innovating and evaluating. However, this work would be strengthened by further exploration and incorporation of the views of patients in the further development and implementation of the Sub-Framework. Indeed, Chapter 4 demonstrated that participants of the trial initiation training programmes felt that patient education and engagement was critical to effective evaluation of innovation. Because of this, the task force described in Chapter 7 that will deliver the implementation strategy for the Sub-Framework will include intrinsic patient engagement. This will be particularly important when dealing with

acceptable evidence requirements and taking risks with innovation, because patients are often the ones who feel the consequences of when things go wrong.

As previously mentioned in other areas of this Thesis, qualitative data is not concerned with sample sizes. Nonetheless, in some areas participant numbers were small and this may compromise the validity of some of the findings. However, in both the FGDs and interviews throughout the Chapters, repetition of concepts did become apparent despite the range of demographics and therefore data saturation emerged. A further mitigating strategy to account for this limitation was the inclusion of a range of methods to collect and analyse data including questionnaires, surveys, FGDs and interviews. This mixed methods approach permitted a thorough understanding of perceptions and experiences surrounding the topics in question.

The quantitative work conducted in this Thesis primarily focused on defining intervention feasibility or informing the Sub-Framework components and recommendations. As such, conclusions as to the effect on outcomes of the interventions or impact of the Sub-Framework cannot be drawn at this stage. This will need to be explored in future work.

7.4 Meaning of this work and implications for future research

7.4.1 Evaluation, implementation, and adoption of the Sub-Framework itself

This body of work primarily focusses on identifying and overcoming barriers to evaluating innovation in global surgery and produces a piece of coherent guidance to inform how this could be done for surgeons, innovators, and researchers in LMICs. However, a meta-evaluation of this guidance will be needed in and of itself. The Sub-Framework, although evidence based via the work collated in this Thesis, will need to

be tested in the real-world if widespread, effective adoption of the Sub-Framework is to be achieved. An implementation strategy with in-built monitoring and evidence capture will be needed and this represents the next substantial piece of future research in this area. This should include the key stakeholders already engaged in this thesis with additional emphasis on patients and the public, regulatory bodies and pan-nation engagement perhaps coordinated by bodies such as the WHO.

Evaluating the implementation of the Sub-Framework will provide evidence for further iterations and improvements in the recommendations, thereby increasing their relevance and value further. Testing the theories underpinning the recommendations in a range of contexts and innovations will provide a rich understanding of how to evaluate surgical innovation in LMICs on a global scale to improve access to safe and effective innovations for patients and surgeons.

7.4.2 Advocating for the neglected surgical patient

There persists a fine balance between over and under evaluation of innovation. Central to this balance is the need to ensure safe and effective innovations are widely and swiftly adopted without being burdened by unnecessary additional evaluation. But where can the line be drawn in the most ethical place possible? It is the aim of this Thesis to investigate the barriers to innovation in LMICs and provide strategies to improve innovation evaluation and increase the efficiency of clinical translation and adoption of LMICs globally. In championing for efficient innovation practices, it could be argued that this Thesis perhaps advocates for leaning toward the side of under evaluation. I hope it is clear from the rigorous discussions of methodological approaches and timely and appropriate yet efficient evaluation that it is not under evaluation that is being advocated, but the ‘minimum effective dose’ of evaluation that is required. That is, the necessary evaluation for a specific innovation in a specific context and no more. In this way, this Thesis encourages global surgeons, innovators,

and researchers in LMICs to think very carefully about evaluating innovation and provides them with guidance to do this.

Seeking out and rapidly yet (appropriately) rigorously evaluating innovation to inform adoption is an act of advocacy for the neglected surgical patient who otherwise would have to go without. The global burden of surgical disease and lack of access to safe, affordable, and timely surgical care remains painfully apparent. Evidence based innovation and technology can be the mechanism through which this enormous unmet need is finally met.

7.5 Summary

In conclusion, the work in this Thesis provides a robust evidence base for the Global Surgical Innovation IDEAL Sub-Framework by combining systematic searches of the literature in this field with data from a comprehensive range of mixed methodology research. It can be summarised that adaptations to the IDEAL Framework for evaluating surgical innovation has increased the relevance and applicability of the guidance for surgeons and researchers working in LMICs. The theories underpinning this work now need to be tested in the real-world for a wide range of contexts and innovations.

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Faculty of Medicine and Health Research Office

School of Medicine Research Ethics Committee (SoMREC)

Room 9.29, level 9
Worsley Building
Clarendon Way
Leeds, LS2 9NL
United Kingdom

& +44 (0) 113 343 1642

Date 21/09/2018

Dr William Bolton
School of Medicine
Faculty of Medicine and Health
Worsley Building
Clarendon Way
LEEDS LS2 9NL

Dear Dr Bolton

Ref no: MREC18-001

Title: Feasibility of Ilizarov frame fiXation for closed Tibial fractures in Sierra Leone: The FIXT Trial

Your research application has been reviewed by the School of Medicine Ethics Committee (SoMREC) and we can confirm that ethics approval is granted based on the following documentation received from you and listed below.

Document	*Version*	*Date Submitted*
FIXT_CF_PE_FIXT trial patients interview_v0.2.doc	2	21/09/2018
FIXT_CF_PE_frame care training observation_v0.2.doc	2	21/09/2018
FIXT_CF_PE_healthcare provider interview_v0.2.doc	2	21/09/2018
FIXT_CF_PE_trial deliverer interview_v0.2.doc	2	21/09/2018
FIXT_CF_PE_trial delivery training observation_v0.2.doc	2	21/09/2018
FIXT_PIS_AFTER ARM_v0.5.docx	2	21/09/2018
FIXT_PIS_BEFORE ARM_v0.5.docx	2	21/09/2018
FIXT_PIS_PE_FIXT trial patients interview_v0.2.docx	2	21/09/2018
FIXT_PIS_PE_frame care training observation_v0.2.docx	2	21/09/2018
FIXT_PIS_PE_healthcare provider interview_v0.2.docx	2	21/09/2018
FIXT_PIS_PE_trial deliverer interview_v0.2.docx	2	21/09/2018
FIXT_PIS_PE_trial delivery training observation_v0.2.docx	2	21/09/2018
MREC 18-001 committee comment_WSB responses.docx	2	21/09/2018

MREC 18-001 UoL_FIXT_Ethics_v0.5.doc	2	21/09/2018
MREC 18-001 UoL_FIXT_Ethics_v0.4.doc	1	14/08/2018
MREC 18-001 FIXT_PE_topic guide_healthcare provider_v1.0.doc	1	14/08/2018
MREC 18-001 FIXT_PE_topic guide_patients_v1.0.doc	1	14/08/2018
MREC 18-001 lower limb functional index.pdf	1	14/08/2018
MREC 18-001 Sample_UK__English__EQ-5D-5L_Paper_Self_complete_v1.0__ID_24700.pdf	1	14/08/2018
MREC 18-001 FIXT_CF_PE_FIXT trial patients interview_v0.1.doc	1	14/08/2018
MREC 18-001 FIXT_CF_PE_frame care training observation_v0.1.doc	1	14/08/2018
MREC 18-001 FIXT_CF_PE_healthcare provider interview_v0.1.doc	1	14/08/2018
MREC 18-001 FIXT_CF_PE_trial deliverer interview_v0.1.doc	1	14/08/2018
MREC 18-001 FIXT_CF_PE_trial delivery training observation_v0.1.doc	1	14/08/2018
MREC 18-001 FIXT_PE_topic guide_trial deliverer_v1.0.doc	1	14/08/2018
MREC 18-001 FIXT_PIS_PE_FIXT trial patients interview_v0.1.docx	1	14/08/2018
MREC 18-001 FIXT_PIS_PE_frame care training observation_v0.1.docx	1	14/08/2018
MREC 18-001 FIXT_PIS_PE_healthcare provider interview_v0.1.docx	1	14/08/2018
MREC 18-001 FIXT_PIS_PE_trial deliverer interview_v0.1.docx	1	14/08/2018
MREC 18-001 FIXT_PIS_PE_trial delivery training observation_v0.1.docx	1	14/08/2018
MREC 18-001 FIXT_PIS_BEFORE ARM_v0.4.docx	1	14/08/2018
MREC 18-001 The FIXT Study_Protocol_v1.3.pdf	1	14/08/2018
MREC 18-001 FIXT_CF_v0.3.doc	1	14/08/2018
MREC 18-001 FIXT_PIS_AFTER ARM_v0.4.docx	1	14/08/2018

Please notify the committee if you intend to make any amendments to the original research ethics application or documentation. All changes must receive ethics approval prior to implementation. Please contact the Faculty Research Ethics Administrator for further information (fmhuniethics@leeds.ac.uk)

Ethics 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, any risk assessments 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.

We wish you every success with the project.

Yours sincerely

Jennifer Blaikie
Senior Research Ethics Administrator, the Secretariat
On behalf of Dr Naomi Quinton, Co-Chair, SoMREC

Appendix 3: FIXT Training Course Programmes

NHS
National Institute for Health Research

External Fixation using the Ilizarov Circular Frame

9-10TH JANUARY 2019 09:00 – 16:00
Connaught Hospital, Freetown, Sierra Leone

TRAINING PROGRAMME DAY 1 9th JANUARY		
Time	**Topic**	**Lead Facilitators**
08:00-09:00	Breakfast and Registration	-
09:00-09:30	Introduction to the Ilizarov method and history	Mr Sandy Wood
09:30-10:00	Fracture management in Sierra Leone with Ilizarov	Dr Ibrahim Bundu
10:00-11:00	WORKSHOP 1 – Equipment familiarisation • Wires, halfpins, rings, frame assembly • Basic principles of frame construction and Ilizarov equipment	Mr Sandy Wood Dr Ibrhaim Bundu Mr Anthony Howard Dr Will Bolton
11:00-11:15	*Refreshment break*	-
11:15-11:45	Acute fracture management, closed, open and reduction	Mr Anthony Howard
11:45-12:30	Circular frame mechanics and frame design	Mr Sandy Wood
12:30-13:30	WORKSHOP 2 – Construction of a basic frame around a simple mid-shaft tibial fracture • Tibial diaphyseal fracture fixation • Basic principles and applied techniques	Mr Sandy Wood Dr Ibrhaim Bundu Mr Anthony Howard Dr Will Bolton
13:30-14:00	*Lunch break*	-
14:00-14:30	Principles of pinsite care and life with a frame	Ms Teresa Chippindale
14:30-15:00	Principles of physiotherapy for frame patients	Mr Anthony Howard

15:00-16:00	WORKSHOP 3 – Practical pinsite dressings and physio demonstrations. Divide into two halves and swap half way. • Pinsite care (Led by Teresa) • Practical physiotherapy (Led by Anthony)	Ms Teresa Chippindale Mr Anthony Howard
16:00-16:15	Close and plan for tomorrow	Mr Sandy Wood and Dr Ibrahim Bundu

TRAINING PROGRAMME DAY 2 10th JANUARY

Time	Topic	Lead Facilitators
08:00-09:00	Breakfast and Registration	-
09:00-09:45	Intra-operative use of the Ilizarov frame: Role of the scrub nurse	Ms Claudia Whitcombe and Mr Sandy Wood
09:45-10:45	WORKSHOP 4 – In theatre setting (Mock theatre frame processes session) • Use of the frame equipment in theatre • Role of the scrub nurse	Mr Sandy Wood Dr Ibrhaim Bundu Ms Claudia Whitcombe
10:45-11:00	*Refreshment break*	-
11:00-11:30	Frame specific post-operative complications	Mr Anthony Howard and Dr Will Bolton
11:30-12:00	The UK experience: In-patient nursing care of frame patients	Ms Teresa Chippindale
12:00-12:30	Discharge and follow-up pathways for frame patients in Sierra Leone	Dr Ibrahim Bundu
12:30-13:00	Patient information and life with a frame leaflet and advice	Ms Teresa Chippindale
13:00-13:30	*Lunch break*	-
13:30-14:30	WORKSHOP 5 – FIXT trial overview • Nursing care for frame patients • Role play of nursing care on ward • Role play of follow-up care and physio	Dr Will Bolton and Dr Ibrahim Bundu
14:30-14:45	*Refreshment break*	-

14:45-15:45	WORKSHOP 6 • Group discussion, feedback, trouble suiting, re-cap	Mr Sandy Wood Dr Ibrhaim Bundu Dr Will Bolton
15:45-16:00	Close and feedback forms	Mr Sandy Wood and Dr Ibrahim Bundu

You will be given hardcopy handouts of the lectures and materials in a workbook together with links to online resources. If you have any questions about any of the content, please contact the Principal Investigators:

Dr Ibrahim Bundu (Connaught Hospital) bunduibrahim@gmail.com
Dr Will Bolton (University of Leeds) w.s.bolton@leeds.ac.uk, Whatsapp: +44 7803 336202

NIHR Global Health Research Group Surgical Technologies | Leeds | UK | e: c.a.harris@leeds.ac.uk | website: www.ghrgst.nihr.ac.uk Twitter: @GHRG_ST | Facebook: facebook.com/GHRGST

NHS
National Institute for Health Research

Research Induction for The FIXT Trial

6-8TH JANUARY 2019 09:00 – 16:00

Connaught Hospital, Freetown, Sierra Leone

TRAINING PROGRAMME DAY 1 6th JANUARY
For ALL Researcher Staff

Time	Topic	Lead Facilitators
08:00-09:00	Breakfast and Registration	-
09:00-09:30	Introduction to Team – UK, Sierra Leone, Trial Coordinators	Dr Ibrahim Bundu and Dr Will Bolton

09:30-10:30	Introduction to The FIXT Trial	Dr Ibrahim Bundu and Dr Will Bolton
10:30-11:00	*Refreshment break*	-
11:00-13:00	Research Principles (Interactive session) • Informed consent • Recruitment • Ethics • Trial documentation	Ms Bonnie Cundill and Dr Will Bolton
13:00-14:00	*Lunch break*	-
14:00-15:00	WORKSHOP 1 – Identifying and consent for FIXT Participants • Process of screening, assessing eligibility and identifying patients for FIXT • Potential participant scenarios • Informed consent role play • Participant information sheet run through	Ms Bonnie Cundill Dr Ibrhaim Bundu Dr Will Bolton Mr Alasdair Fellows
15:00-16:00	WORKSHOP 2 – Eligibility and registration to FIXT • Consent • Eligibility assessments • Registration and formalising entry into the trial	Ms Bonnie Cundill Dr Ibrhaim Bundu Dr Will Bolton Mr Alasdair Fellows
16:00-16:15	Close and feedback forms	Dr Ibrahim Bundu and Dr Will Bolton

NIHR Global Health Research Group Surgical Technologies | Leeds | UK | e: c.a.harris@leeds.ac.uk | website: www.ghrgst.nihr.ac.uk Twitter: @GHRG_ST | Facebook: facebook.com/GHRGST

TRAINING PROGRAMME DAY 2 7th JANUARY
For ALL Researcher Staff

Time	Topic	Lead Facilitators
08:00-09:00	Breakfast and Registration	-
09:00-10:00	Data collection in FIXT – The Case Report Forms	Dr Will Bolton

10:00-13:00	WORKSHOP 3 – Completion of the Case Report Forms for FIXT • Role play of data collection • Completing the form packs • Sources of data *Refreshment break in the middle*	Ms Bonnie Cundill Dr Ibrahim Bundu Dr Will Bolton Mr Alasdair Fellows
13:00-14:00	*Lunch break*	-
14:00-14:30	Dissemination and next steps after FIXT	Dr Will Bolton
14:30-16:00	WORKSHOP 4 – Trial conduct and delivery • The FIXT Protocol • Adverse event reporting • GCP, data collection, storage and participant safety • CRF completion and follow-up data collection • Trouble shooting • Trial research office final set up, trial packs, and laptop storage Trial Coordinators to be introduced to the database by Alasdair	Ms Bonnie Cundill Dr Ibrahim Bundu Dr Will Bolton Mr Alasdair Fellows
16:00-16:15	Close and feedback forms	Dr Ibrahim Bundu and Dr Will Bolton

TRAINING PROGRAMME DAY 3 8th JANUARY
For the Principal Investigators and Trial Coordinators

Time	**Topic**	**Lead Facilitators**
08:00-09:00	Breakfast and Registration	-
09:00-10:00	Data storage – paper forms, laptop database	Mr Alasdair Fellows
10:00-12:00	WORKSHOP 5 – Introduction to the laptop and database • Using REDCap • Logins • Trouble shooting	Ms Bonnie Cundill Dr Ibrahim Bundu Dr Will Bolton Mr Alasdair Fellows
12:00-13:00	*Lunch break*	-
13:00-14:00	Data entry into the database, processes and protocols	Mr Alasdair Fellows

14:00-16:00	WORKSHOP 6 – Using the database for FIXT • Entry of mock data • If things go wrong • Double data entry • Data back up • Data upload	Ms Bonnie Cundill Dr Ibrahim Bundu Dr Will Bolton Mr Alasdair Fellows
16:00-16:15	Close and plans for tomorrow	Dr Ibrahim Bundu and Dr Will Bolton

You will be given hardcopy handouts of the lectures and materials in a workbook together with links to online resources. If you have any questions about any of the content, please contact the Principal Investigators:

Dr Ibrahim Bundu (Connaught Hospital) bunduibrahim@gmail.com
Dr Will Bolton (University of Leeds) w.s.bolton@leeds.ac.uk, Whatsapp: +44 7803 336202

Appendix 4: Research Ethics Committee Approval for VITAL Trial

The Secretariat
University of Leeds
Leeds, LS2 9JT
Tel: 0113 3431642
Email: FMHUniEthics@leeds.ac.uk

UNIVERSITY OF LEEDS

School of Medicine Research Ethics Committee (SoMREC)

Dr William Bolton
Clinical Research Fellow
Leeds Institute of Medical Research
School of Medicine
Faulty of Medicine and Health
Office 7.19, Clinical Sciences Building
St James's Hospital
LEEDS LS9 7TF

01 November 2019

Dear Will

Ref no: MREC 19-016

Title: The VITAL Study: Virtual reality technology to Improve surgical Training in SierrA Leone

Thank you for submitting your documentation for the above project. Following review by the School of Medicine Research Ethics Committee (SoMREC) I can confirm a conditional favourable ethical opinion based on the documentation listed below, received at date of this letter *and subject to the following conditions which must be fulfilled prior to the study commencing:*

1. **C19 – Please clarify what digital data will be saved and where (e.g. the secure University M drive)**

2. **The Participant Information Sheet (PIS) should statement regarding withdrawal form the focus group (FG) should state '*you*' rather 'participants may withdraw prior to…" i.e. second person pronoun so it is consistent with the rest of the PIS**

3. **The Consent Form statement regarding withdrawal should be amended to be in line with the statement on the PIS and use the first person pronoun in line with the rest of the consent document**

4. **A separate statement should be added that if quotations are used, these will be anonymous and the statement should be in the first person pronoun**

5. **The formatting on the consent form for points 6 & 7 should be addressed prior to use**

The study documentation must be amended as required to meet the above conditions and submitted for file and possible future audit. Once you have addressed the conditions and submitted for file/future audit, you may commence the study and further confirmation of approval is not provided.

Please note, failure to comply with the above conditions will be considered a breach of ethics approval and may result in disciplinary action.

Document Received	*Version*	*Date Received*
VITAL_Ethics_UoL_application form_v0.2	0.2	25/10/2019
MREC 19-016 Signed Risk Assessment_v0.2	0.2	01/11/2019
VITAL_CF_v2.0	2.0	25/10/2019
VITAL_course programme	1.0	25/10/2019
VITAL_PIS_v2.0	2.0	25/10/2019
In country approval letter from Sierra Leone VITAL Study	1.0	23/10/20196
VITAL_FGD_topic guide_v1.0	1.0	19/09/2019
The VITAL Study_protocol_v0.6	0.6	19/09/2019

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 Administrator for further information FMHUniEthics@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 SoMREC takes no responsibility for you gaining access to staff, students and/or premises prior to, during or following your research activities.

You are expected to keep a record of all your approved documentation, as well as documents such as sample consent forms, risk assessments and other documents relating to the study. This should be kept in your study file, and may be subject to an audit inspection. If your project is to be audited, you will be given at least 2 weeks notice.

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.

The committee wishes you every success with your project.

Yours sincerely

Dr Naomi Quinton
Co-Chair, School of Medicine Research Ethics Committee

Appendix 5: Objective Structured Assessment of Technical Skills (OSATS) form

Objective Structured Assessment of Technical Skills (OSATS)

Assessor (name):

Global rating scale of operative performance *Please circle the number corresponding to the candidate's performance for each category, irrespective of training level*				
Respect for Tissue:				
1	2	3	4	5
Frequently used unnecessary force on tissue or caused damage by inappropriate use of instrument		Careful handling of tissue but occasionally caused inadvertent damage	Consistently handled tissues appropriately with minimal damage	
Time and Motion:				
1	2	3	4	5
Many unnecessary moves		Efficient time/motion but some unnecessary moves	Clear economy of movement and maximum efficiency	
Instrument Handling:				
1	2	3	4	5
Repeatedly makes tentative or awkward moves with instruments by inappropriate use of instruments		Competent use of instruments but occasionally appeared stiff or awkward	Fluid moves with instruments and no awkwardness	
Knowledge of Instruments:				
1	2	3	4	5
Frequently asked for wrong instrument or used inappropriate instrument		Knew names of most instruments and used appropriate instruments	Obviously familiar with the instruments and their names	
Flow of Operation				
1	2	3	4	5
Frequently stopped operating and seemed unsure of next move		Demonstrated some forward planning with reasonable progression of procedure	Obviously planned course of operation with effortless flow from one move to the next	
Use of Assistants				
1	2	3	4	5
Consistently placed assistants poorly or failed to use assistants		Appropriate use of assistants most of time	Strategically used assistants to the best advantage at all times	
Knowledge of Specific Procedure				
1	2	3	4	5
Deficient knowledge. Needed specific instruction at most steps		Knew all important steps of operation	Demonstrated familiarity with all aspects of operation	

Overall impression *Please circle the number corresponding to your overall impression of the candidate's performance*				
1	2	3	4	5
Below expectation		According to expectation	Above expectation	

Appendix 6: Research Ethics Committee Approval for global survey study

The Secretariat
University of Leeds
Leeds, LS2 9JT
Tel: 0113 3431642
Email: FMHUniEthics@leeds.ac.uk

UNIVERSITY OF LEEDS

School of Medicine Research Ethics Committee (SoMREC)

Dr William Bolton
Clinical Research Fellow
Leeds Institute of Medical Research
School of Medicine
Faulty of Medicine and Health
University of Leeds
Office 7.19, Clinical Sciences Building
St James's Hospital
Beckett Street
LEEDS LS9 7TF

21 October 2019

Dear Will

Ref no: MREC 18-102

Title: Barriers and Facilitators to Innovation and Technology Evaluation in Global Surgery: A mixed methods global study

Thank you for submitting your documentation for the above project. Following review by the School of Medicine Research Ethics Committee (SoMREC) I can confirm a conditional favourable ethical opinion based on the documentation listed below, received at date of this letter *and subject to the following conditions which must be fulfilled prior to the study commencing:*

- **A statement should be added to the consent form regarding the use of anonymised direct quotations**

The study documentation must be amended as required to meet the above conditions and submitted for file and possible future audit. Once you have addressed the conditions and submitted for file/future audit, you may commence the study and further confirmation of approval is not provided.

Please note, failure to comply with the above conditions will be considered a breach of ethics approval and may result in disciplinary action.

Document Received	*Version*	*Date Received*

Barriers and Facilitators Survey Ethics UoL_V2	2.0	19/09/2019
Barriers and Facilitators Survey CF_V2	2.0	19/09/2019
Barriers and Facilitators Survey Email invitation_V2	2.0	19/09/2019
Barriers and Facilitators Survey_ethics protocol	0.5	19/09/2019
Barriers and Facilitators Survey PIS_V2	2.0	19/09/2019
Barriers and Facilitators Survey interview topic guide	1.0	19/09/2019

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 Administrator for further information FMHUniEthics@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 SoMREC takes no responsibility for you gaining access to staff, students and/or premises prior to, during or following your research activities.

You are expected to keep a record of all your approved documentation, as well as documents such as sample consent forms, risk assessments and other documents relating to the study. This should be kept in your study file, and may be subject to an audit inspection. If your project is to be audited, you will be given at least 2 weeks notice.

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.

The committee wishes you every success with your project.

Yours sincerely

Dr Naomi Quinton
Co-Chair, School of Medicine Research Ethics Committee