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Development and Validation of a Wearable Sensing Platform for Assessment of Patients Undergoing Breast and Axillary Surgery

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October 2024

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A thesis submitted in fulfilment of the requirements of

Imperial College London

for the award of Doctor of Philosophy

To my husband and daughter ~ without whom my life would be incomplete…

To my mother ~ without whom I would never have enjoyed so many opportunities…

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STATEMENT OF ORIGINALITY

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ABSTRACT

Patient-reported outcomes are commonly used to evaluate upper limb (UL) morbidities following breast cancer surgery. Although they help to gauge patients' views of their UL function, these assessments are primarily subjective and susceptible to recall or response bias. Objective outcome tools, such as goniometry, can be used to measure range of motion. Nevertheless, these measurements are prone to inter-operator variability, necessitate periodic evaluation, and can be time-consuming in clinical environments. The aim of this thesis was to develop and validate the use of wearable activity monitors (WAMs) to provide postoperative monitoring options for patients undergoing breast/axillary surgery.

This work evolved from an initial feasibility study in a healthy cohort and a breast cancer cohort undergoing breast/axillary surgery to a larger cohort of breast cancer survivors with a long-term follow-up. UL activity was assessed preoperatively, postoperatively on the inpatient ward and on discharge home for up to 2 weeks, as well as at greater than 6 months postoperatively. Activity data provided insight into patients' baseline UL activity, as well as their recovery following different types of breast surgeries. Further detailed analysis revealed that preoperative activity and the magnitude of short-term UL activity measured by WAMs may predict for longer term UL activity (>6 months). The qualitative evaluation demonstrated that patients were satisfied with this monitoring method and that the majority of patients believed that these systems could improve engagement in physiotherapy.

This thesis has made significant contributions to the field of study by developing a new WAM methodology and testing them under clinically relevant conditions. The findings of this research can be applied by researchers/clinicians aiming to employ wearable technologies for continuous and objective patient monitoring, as well as for developing personalised rehabilitation strategies. Implementing these technologies has the potential to improve the quality and cost-effectiveness of managing UL morbidities.

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ACKNOWLEDGEMENTS

The content of this thesis is the result of three years of research at the Department of Surgery and Cancer, Imperial College London, which was thoroughly challenging but also an enjoyable period in my career. This would not have been possible without the excellent supervision and help that the people around me provided.

First and foremost, I would like to thank Mr Daniel Leff for his unwavering encouragement and support. He is generous with his time and is always ready to provide guidance and leadership. He has played a crucial role in my continued growth and academic success over the years. His emphasis on how hard work will pay off, has pushed me every step of the way. He has passed on his incredibly meticulous and precise attitude to research, which will help me in my future work. I am confident that anyone who has the privilege to be under his guidance will make important contributions to science that exceed their initial expectations.

I am deeply grateful to Mr Richard Kwasnicki, who has consistently guided me throughout this thesis with positivity and reassurance. His knowledge and expertise in wearable technology provided me with an excellent platform to explore and contribute to this new and exciting field of science.

I am greatly indebted to Mr Hutan Ashrafian for his continued guidance on statistical analysis and practical aspects of the work while providing an invaluable critical appraisal of the work.

To Professor the Lord Ara Darzi for providing me with the opportunities and resources necessary to undertake this research. To Dr Ines Baptista, Dr Steve McAteer and Dr Simon Dryden for their support and patience. To Dr Ping Wu, our medical statistician for providing advice on challenging statistical questions.

To a group of medical students and BSc students (who are now doctors! – Dr Naairah Khan, Dr Omar Ghandour, Dr Manolis Giannas, Dr Luqman Tenang, Dr Zoha Imam, Dr Catharina Moenig, Dr Kieran Dhillon, Dr Tanusree Dutta and Dr Salem Elias) who helped with patient recruitment and data

collection, thank you for their hard work and dedication. I am confident that they will excel in their chosen careers.

To all Clinical Research Fellows in the Darzi and Leff groups for their camaraderie and steadfast support. In particular, Ms Scarlet Nazarian for going through this PhD journey together as we both became first time mothers and being able to see our kids grow up. To Ms Natasha Jiwa and Ms Dhurka Shanthakumar, who have continuously provided me with emotional support and a sounding board when I needed someone to talk to.

Finally, I would like to thank my friends and family for their support and belief in me, and for all the encouragement and nudging along the way. Thank you to my mother, who has always been instrumental in helping me reach my goals. To my husband, Alex, who has encouraged, questioned, and supported me throughout. And last but not least to my little princess, Arabella, for giving me cuddles and strength to complete this thesis.

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List of Abbreviations and Acronyms

ABPI	Accelerated Partial Breast Irradiation
AC	Acromioclavicular
ACCI	Age-adjusted Charlson Comorbidity Index
ACSM	American College of Sports Medicine
ADL	Activities of Daily Living
ADM	Acellular Dermal Matrices
AHA	American Heart Association
ALMANAC	Axillary Lymphatic Mapping Against Nodal Axillary Clearance
ALN	Axillary Lymph Node
ALND	Axillary Lymph Node Dissection
AMAROS	After Mapping of the Axilla: Radiotherapy Or Surgery
ARM	Axillary Reverse Mapping
ART	Breast and Axilla Radiotherapy
ASP	Arm/shoulder Problems
AWL	Axillary Web Syndrome
BCRL	Breast-Cancer Related Lymphoedema
BCS	Breast Conserving Surgery
BCT	Behaviour Change Technique
BCTOS	Breast Cancer Treatment Outcome Scale
BEAT	Better Exercise Adherence after Treatment for Cancer
BIS	Body Image Scale
BIS	bioimpedance spectroscopy
BMI	Body Mass Index
BRT	Only Breast Radiotherapy
CF-WBI	Conventionally Fractionated Whole-breast Irradiation
CI	Confidence Intervals
CINAHL	Cumulated Index in Nursing and Allied Health Literature
CON	Closure without Flap Fixation
COVID-19	Coronavirus Disease 2019
CPSP	Chronic Post-surgical Pain
CR	Conventional Radiotherapy
CSS	Constant Shoulder Score
DASH	Disabilities of the Arm, Shoulder and Hand

DEPART	iDEntification and Preservation of ARm lymphaTic system
DIEP	Deep Inferior Epigastric Perforator
DVH	Dose-Volume Histograms
EBRT	External Beam Whole Breast Radiotherapy
EORTC QLQ-C30	European Organization for Research and Treatment of Cancer core quality of life
EQ-5D-5L	EuroQol-5D-5L
ER	External Rotator
ERAS	Enhanced Recovery after Surgery
EWB	Emotional Well-Being
FACT-B	Functional Assessment of Cancer Therapy – Breast
FDA	Food and Drug Administration
FF-G	Flap Fixation using an Adhesive Tissue Glue
FFeS	Flap Fixation using Sutures
fTRAM	free Transverse Rectus Abdominis Musculocutaneous
HF-WBI	Hypofractionated Whole-breast Irradiation
HL	Healthy Limb
HRQoL	Health-Related Quality-of-Life
IBR	Implant-based Reconstruction
IDDD	Deterioration in Daily Living Activities in Dementia
IGAP	Inferior Gluteal Artery Perforator
IMU	Inertial Measurement Unit
INSEMA	Intergroup-Sentinel Mamma
IORT	Intraoperative Radiotherapy
IPAQ	International Physical Activity Questionnaire
IR	Internal Rotator
LD	Latissimus Dorsi
LE	Lymphoedema
LR	Lymphoedema Rate
LYMPHA	the LYmphatic Microsurgical Preventive Healing Approach
MARI	Marking the AxillaRy positive lymph node with an Iodine seed
MEMS	Micro-electromechanical System
METs	Metabolic Equivalent of Tasks
MRM	Modified Radical Mastectomy
MVPA	Moderate to Vigorous Physical Activity

Mx	Simple Mastectomy
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NRS	Numerical Rating Scale
NRT	No Radiotherapy
OL	Operated Limb
OMGUI	Open Movement Graphical User Interface
PA	Physical Activity
PCORI	Patient-Centered Outcomes Research Institute
PLE	Persistent Lymphoedema
PM	Partial Mastectomy
POD	Postoperative Day
PPBR	Pre-pectoral Breast Reconstruction
PPIE	Patient, public, involvement and engagement
PPSP	Persistent Postsurgical Pain
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-analyse
PROM	Patient Reported Outcome
PROSPERO	International Prospective Register of Systematic Reviews
pTRAM	pedicled Transverse Rectus Abdominis Musculocutaneous
PWB	Physical well-being
QALY	Quality-adjusted Life Year
QLQ-BR23	Breast cancer specific module
RAC	Routine Axillary Clearance
RCT	Randomised Controlled Trial
RLNR	Regional Lymph Node Radiation
RoB2	Risk of Bias 2
ROBINS-I	Risk of Bias in Non-randomised Studies - of Interventions
ROM	Range of Motion
RT	Radiotherapy
SA	Scapula Alata
SD	Standard Deviation
SDM	Shared Decision Making
SEP	Supervised Exercise Programme
SF-36	36-Item Short Form Survey
SGAP	Superior Gluteal Artery Perforator
SLNB	Sentinel Lymph Node Biopsy

SNBM	Sentinel Node-based Management
SOUND	Sentinel Node vs Observation After Axillary Ultra-Sound
SVM	Signal Vector Magnitude
SWB	Social & Family Well-being
TAP	Thoracodorsal Artery Perforator Flap
TLE	Transient Lymphoedema
TM	Total Mastectomy
TM-R	Immediate Reconstruction after Total Mastectomy
TMG	Transverse Myocutaneous Gracilis flap
TRAM	Transverse Rectus Abdominis Myocutaneous
TT	Hypofractionated Tomotherapy
TUG	Transverse Upper Gracilis
UBF	Upper Body Function
UED	Upper Extremity Disability
UK	United Kingdom
UL	Upper Limb
VAS	Visual Analogue Scale
WAM	Wearable Activity Monitor
WBI	Whole Breast Irradiation

1 INTRODUCTION

Breast cancer is the most prevalent form of cancer in the United Kingdom (UK) and has a five-year survival rate of 85%.[1] Treatments for breast cancer frequently result in long-term morbidity, such as pain, lymphoedema, and limited range of motion, which may negatively impact patient's health-related quality of life (HRQoL).[2] The impact of treatments on breast cancer survivors should be objectively documented, given the high prevalence and improved survival rates of breast cancer. Historically, there has been inadequate monitoring of upper limb morbidity.[3] The reasons for this are multifactorial, partly due to a lack of focus on survivorship. Previous studies demonstrated that increased physical activity can reduce upper limb dysfunction and is correlated with reduced breast cancer recurrence and mortality among breast cancer survivors.[4-6]

Whilst different methods for capturing postoperative morbidity have been published, the most commonly used outcome measures in clinical and research settings are patient-reported outcome measures (PROMs) and arm volume measurements.[7,8] For instance, PROMs may be vulnerable to recall or response bias,[9] which may result in inaccurate estimates of postoperative morbidity and return to functionality. They depend on patients filling out questionnaires on a regular basis, which could be burdensome.[9] Arm volume measurements, on the other hand, are susceptible to inter-operator variability and can be time-consuming to conduct.[2,8,9] Therefore, in order to determine an accurate representation of upper limb morbidity associated with breast cancer treatment, a continuous, objective assessment of upper limb activity is desirable.

1.1 Treatment of breast cancer

Breast cancer treatment includes surgery, chemotherapy, radiotherapy (RT), endocrine therapy, targeted therapy and immunotherapy.[10] Eradicating the tumour from the breast and surrounding lymph nodes and avoiding a metastatic recurrence are the primary objectives of treatment for non-metastatic breast cancer.[11] This involves breast surgery and taking a few samples or more extensive removal of axillary

lymph nodes, along with the potential for postoperative radiotherapy. Preoperative (neoadjuvant) chemotherapy may decrease the breast tumour's volume, and reducing the necessity for axillary lymph node dissection (ALND).[12] On the other hand, the principal objective in managing metastatic breast cancer is to prolong survival and alleviate symptoms. Systemic therapy (such as chemotherapy or immunotherapy) is the standard treatment for metastatic breast cancer, and surgery is available to a limited number of patients for palliation.[11,12] Depending on the subtypes of breast cancer, endocrine therapy, targeted therapy, and immunotherapy offer supplementary therapeutic options for individuals with both metastatic and non-metastatic breast cancer.[11,12] The impact of breast cancer treatment on upper limb morbidity is further discussed in chapter 2.

Surgery

Breast-conserving surgery (BCS) and mastectomy, with or without immediate reconstruction, are both well-recognised local treatments for early invasive breast cancer (defined as cancer that has not spread beyond the breast or axillary lymph nodes). BCS involves the excision of only the cancerous portion of the breast, whereas mastectomy is the complete removal of breast tissue. Breast reconstruction aims at restoring the form and shape of the breast following mastectomy.

Nesvold *et al.,*[13] demonstrated that the frequency of lymphoedema, shoulder pain, and reduced range of motion is greater in mastectomy patients compared to those undergoing breast-conserving surgery (BCS) also known as wide local excision. Mastectomy may lead to injury in the axillary region, affecting muscle, nerve, and vascular tissues, potentially resulting in muscular atrophy and a decline in upper body strength and functionality over time.[14,15] Breast reconstruction such as latissimus dorsi (LD) flap reconstruction results in significantly higher (43.2%) upper limb morbidity compared with other types of breast reconstructions.[16] This is because a significant amount of LD muscle is removed from its origin and transferred to the breast reconstruction site, resulting in a substantial reduction in muscle function.[16-21] In deep inferior epigastric perforator (DIEP) reconstruction, the muscles surrounding the shoulder joint remains intact, and the reconstructed tissue is inserted into the prepectoral space (above the pectoralis major) already created by mastectomy.[16] Even though the muscles surrounding the

shoulder joint are not sacrificed, DIEP results in shoulder morbidity in 14.1% of breast cancer patients.[16] This may be caused by weakened abdominal muscles resulting from the DIEP surgery, which could potentially lead to postural changes that affect upper limb movement.[22,23] Subpectoral implant-based reconstruction in which the implant is positioned beneath the pectoralis major muscle, increases tension on the underlying pectoralis muscle and tendon, resulting in pectoralis tightness.[16] The performance of early postoperative rehabilitation exercises may be impeded by pectoralis tightness and pain, which may modify three-dimensional scapulothoracic motion, resulting in shoulder dysfunction.[24] The detachment of the sternocostal fibre region of the pectoralis major is required, which may affect shoulder strength.[25] In comparison with prepectoral implant breast reconstruction, which involves positioning the implant above the pectoralis major muscle, subpectoral implant breast reconstruction is associated with a greater degree of upper limb functional impairment.[26]

Compared to patients receiving sentinel lymph node biopsy (SLNB), which involves less invasive surgery (sampling two to three lymph nodes to determine if cancer has spread), patients undergoing ALND (removal of >10 lymph nodes in the axilla) are more likely to experience upper limb morbidity.[27] For example, the incidence of lymphoedema following SLNB and ALND is reported to be 5.6% and 19.9% respectively.[28] ALND can significantly impact the drainage of lymph fluid following lymph node excision, hence increasing the risk of lymphoedema, which may reduce the range of motion due to swelling and stiffness. The development of scar tissue following surgery at the axillary incision site may result in pain and limitations in shoulder range of motion. Moreover, there is a potential injury (including laceration, stretching, or damage) to the nerves in the axillary area (e.g intercostobrachial nerve), which may result in numbness or tingling in the upper limb, along with reduced strength and pain.[29-33] Injury to the long thoracic nerve, which innervates the serratus anterior muscle, may result in a winged scapula and may also induce modifications to upper trapezius activity, a muscle that functions synergistically with the serratus anterior, and therefore may affect upper limb function.[34,35] It is also intriguing to observe that only a subset of women develops lymphoedema, whereas the majority do not, despite undergoing identical surgical procedures. Although the cause is not entirely understood there are a few hypotheses that could account for this phenomenon. Some individuals may develop collateral

channels that reduce the risk of lymphoedema, or there may be genetic, molecular, and physiologic characteristics that may have a lower propensity to lymphoedema.[36-38] This will be further elaborated upon on page 62-63.

Radiotherapy (RT)

Radiation therapy is often administered to a portion or the entirety of the breast, the axilla, the supraclavicular region (above the collarbone), or the internal mammary chain (behind the breastbone). A meta-analysis comparing patients who had irradiation with those who did not indicated that the former group were marginally more likely to experience lymphoedema and reduced range of motion compared to the latter.[39] In a randomised-controlled trial (RCT) comparing axillary RT or ALND, patients who had axillary RT were observed to have significantly less arm lymphoedema compared with ALND patients.[40] When comparing ALND + RT with ALND only and SLNB + RT, patients who received combination of ALND and RT demonstrated the greatest 5-year risk of lymphoedema.[41] RT typically causes fibrosis in the affected area which can cause muscle stiffness, tightness of the chest and shoulder which can lead to reduced shoulder range of motion.[42] Radiation damage to the brachial plexus can cause pain, sensory loss, and weakening of upper extremity muscles.[42] Moreover, radiation-induced damage to the pectoralis major and minor may result in diminished muscle activation over time and increase the likelihood of developing shoulder impingement syndrome and rotator cuff injuries.[42-45]

Chemotherapy

Chemotherapy can lead to peripheral neuropathy and generalised tiredness.[46] For example, Bandos *et al.,* demonstrated that docetaxel is associated with long-term peripheral neuropathy (due to nerve damage)[47] such as pain, tingling, burning and weakness of the arms, hands, legs and feet, loss of sensation, unable to pick up objects or fasten clothing as well as sudden sharp, stabbing or shocking pain sensations which may impact their upper limb function.[47-49]

Endocrine therapy

Treatment with endocrine therapy such as aromatase inhibitor can lead to pain in the joints (arthralgia) in various sites including hands and shoulders. The mechanism is not completely understood, although it is thought to be due to acute drop in oestrogen level produced by aromatase inhibition.[50] Several studies investigating the use of aromatase inhibitor in patients with early breast cancer demonstrated increased joint symptoms such as arthralgia and arthritis.[51-53] The combination of anastrozole and prior chemotherapy led to a 12·4% increase in joint symptoms compared to those taking tamoxifen without prior chemotherapy.[51]

Immunotherapy

One type of immunotherapy used to treat breast cancer is called immune checkpoint inhibitors (ICIs). There have been reports that ICIs may lead to myositis, arthralgia, and inflammatory arthritis.[54] For example, up to 40% of patients had arthralgia due to ICI therapy, potentially affecting upper limb function.[55] The joints often impacted are the shoulders, hands, fingers, and wrists.[54] The pathophysiology remains incompletely understood, nevertheless, it is probably associated with the influence of immune checkpoint inhibitors on T-cell activation, which triggers inflammatory side effects termed immune-related adverse events.[54,55]

Impact of upper limb morbidity on quality of life

It is well established that breast cancer survivors develop long-term upper limb/shoulder impairment that persist for many years following surgery and linked to poor quality of life (QoL).[56] A meta-analysis of 39 studies on the impact of upper limb morbidity on QoL showed that physical wellbeing, psychological/emotional wellbeing, and social wellbeing/function were significantly poorer in patients with upper limb morbidity compared to those without.[57] The inability to perform usual roles within home, social and work context may impact their psychological and social wellbeing. More invasive surgery such as ALND is associated with significantly more perceived disability in activities of daily living (ADLs) and worsening QoL compared with SLNB.[27]

Peri-operative assessment of upper limb activity has multiple purposes including:

- ◊ Delineating longitudinal functional recovery after breast cancer surgery
- ◊ Detecting and monitoring post-operative complications
- ◊ Informing patients and clinicians about potential recovery profiles for different breast cancer surgeries and supporting patient personalised rehabilitation strategies
- ◊ Evaluation of postoperative patient outcomes
- ◊ To be used as a long-term prognostic indicator for patient's upper limb recovery

1.2 Problem Identification

Current upper limb morbidity assessment for breast cancer has several challenges and limitations:

- ◊ The upper limb morbidity assessment for breast cancer is often based on subjective measures (e.g. questionnaires) rather than objective clinical evidence.
- ◊ The objective assessment method (e.g. volume measurement for lymphoedema) may not reliably capture the functional morbidity after breast cancer treatment.
- ◊ Physical evaluations by objective measure are frequently performed in the clinic on a single occasion or episodically, which may not be a reliable or accurate picture of the patient's function, physiological or biomechanical condition.
- ◊ Following hospital discharge, assessment of physical morbidity is intermittent or may not be assessed at all, with outpatient appointments scheduled at random intervals.
- ◊ There is no standardised service to detect other upper limb complications after breast cancer treatment.
- ◊ Early detection of upper limb complications relies on patients' self-report to their physicians.
- ◊ The inability to provide timely and real-time functional status updates to the healthcare team and patients delays the adaption of rehabilitation strategies and the detection of upper limb complications.

1.3 Proposed Solutions

In recent decades, there has been substantial progress in the field of wearable sensor technology, making it possible to measure and track physical activity effectively.[58-60] As a result, a growing corpus of research has been conducted to examine the possible application of these tools in clinical and rehabilitation settings.[59,61-63] Wearable sensors are capable of monitoring and analysing human movement, as well as providing personalised feedback that can be used to facilitate self-directed therapy.[62] There have been notable breakthroughs in the performance of wearable sensors and their pervasive application in clinical and research environments, including their use for activity identification, fall detection, and interventional-led studies that use wearable sensors to promote physical activity in patients with cancer or peripheral vascular disease, potentially improving their outcomes.[64-66] Based on qualitative research findings, patients perceived wearable sensors as potentially effective in increasing their motivation to engage in higher levels of physical exercise.[67,68] Wearable activity monitors (WAMs) have the potential to be used in the breast cancer cohort to longitudinally, measure upper limb activity and therefore be used as an objective outcome measure of upper limb function. This thesis focuses on the conceptualisation, development, and validation of WAMs for facilitating the upper limb assessment of patients having breast and axillary surgery.

1.4 Thesis Overview

HYPOTHESIS

"Assessment of upper limb activities using WAMs is objective and practical, can differentiate between different surgical procedures and provide insight into upper limb function and level of activities after breast and axillary surgery, which have the potential to be used in personalised rehabilitation after surgery."

A summary of the resulting ten-chapter thesis is illustrated below in Figure 1-1.

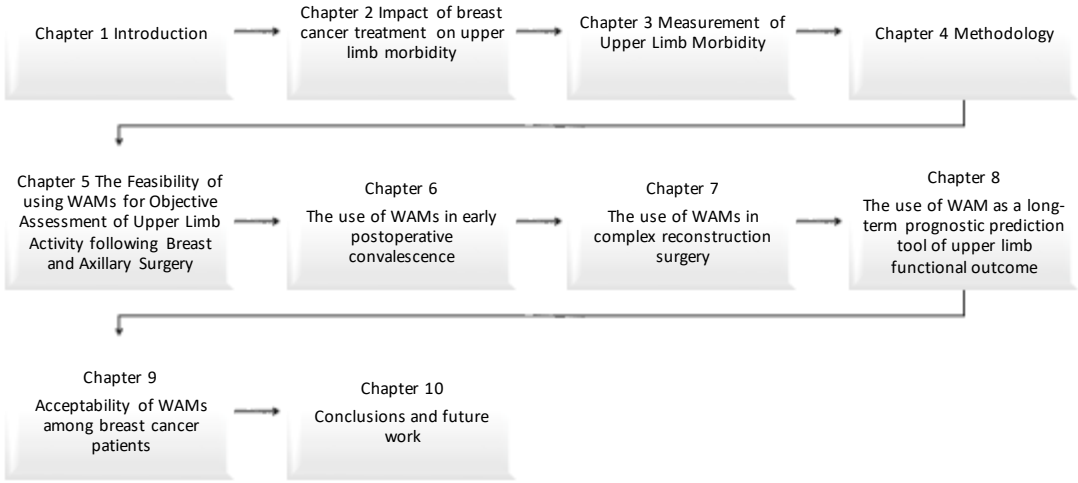


Figure 1-1 Flow diagram of thesis structure to investigate the development and validation of wearable sensing platform for assessment of patients undergoing breast and axillary surgery

Chapter 2 describes the impact of breast cancer treatment on upper limb morbidity in breast cancer patients. This is achieved through reviewing and performing meta-analyses on a selection of randomised controlled trials and observational studies to provide quantitative evidence of the impact of breast and axillary surgeries on lymphoedema, pain, range of motion, strength, upper limb function, and quality of life.

Chapter 3 describes the pathophysiology of upper limb dysfunction, current tools for measuring upper limb morbidities and different types of wearable sensors.

Chapter 4 describes the methodology used in chapter 5 to 8.

Chapter 5 focuses on a feasibility study using WAMs to achieve a continuous, objective evaluation of functional recovery through the measurement of perioperative upper limb activity. The construct validity of WAMs as an objective tool to measure upper limb function is evaluated by quantifying pre- and postoperative arm activity for surgically treated and non-surgically treated (control) sides and analysing upper limb activities in various types of surgical procedures. Expected post-operative recovery curves are produced using sensor data. Concurrent validity is measured by correlating upper limb activity with patient-reported upper limb function (disabilities of the arm, shoulder and hand (DASH) questionnaire) and quality of life (EQ-5D-5L questionnaire) scores.

Chapter 6 introduces the use of WAMs in the early postoperative convalescence. Building on the outcomes of the previous feasibility study, a further study is conducted, designed to further validate WAMs in acute postoperative setting comparing 2 different types of axillary surgical procedures (axillary lymph node dissection (ALND) and sentinel lymph node biopsy (SLNB)).

Despite the highly promising results, it is uncertain whether WAMs is appropriate for use in complex reconstruction procedures with extended follow-up periods. The use of WAMs in complex breast reconstruction surgery is explored in Chapter 7 through a prospective longitudinal cohort study in patients undergoing simple mastectomy (Mx), deep inferior epigastric perforator (DIEP) reconstruction surgery and implant-based reconstruction (IBR) surgery. The patients were followed up for more than 6 months following surgery to determine if surgery type has an impact on short- and long-term recovery.

Chapter 8 investigates the potential of WAM to serve as a prognostic prediction tool that can be used to identify patients who require additional support during their recovery and to facilitate self-directed rehabilitation. Prior data collection is extended, measuring objective long-term data at greater than 6 months postoperatively to allow characterisation of longitudinal upper limb recovery.

Chapter 9 investigates patient perceptions of wearable technology, with a focus on WAMs, and their role in surgical and rehabilitation setting. A mock-up application presenting upper limb activity data collected is shown to patients, and qualitative, semi-structured feedback interviews are used to understand how sensor technology is viewed, as well as its utility and usability within breast surgery setting and as a personalised rehabilitation adjunct.

Chapter 10 provides a concise overview of the conclusions drawn from this thesis and proposes potential future directions for investigating the use of WAMs in breast cancer surgery.

1.5 Original Contribution of the Thesis

- ◊ Investigated the use of WAMs in patients undergoing breast and axillary surgery in acute perioperative period, complex breast reconstruction surgery, and long-term follow up settings where upper limb activity was objectively measured.
- ◊ Evaluated patients' opinions and feedback about wearable technology and its utilisation in monitoring and supporting rehabilitation following breast and axillary surgery.

The contents of this thesis have resulted in the following publications and conference presentations:

- *Publication* - Che Bakri NA, Kwasnicki RM, Giannas E, Dutta T, Hunter JE, Henry FP, Wood S, Ashrafian H, Darzi A, Leff DR. Delineating upper limb longitudinal recovery after simple mastectomy, implant or autologous breast reconstruction using wearable activity monitors. J Plast Reconstr Aesthet Surg. 2025 Feb 13;104:113-122. doi: 10.1016/j.bjps.2025.02.012. Epub ahead of print. PMID: 40120218.

- *Publication* - Che Bakri NA, Kwasnicki RM, Khan N, Ghandour O, Lee A, Grant Y, Dawidziuk A, Darzi A, Ashrafian H, Leff DR. Impact of Axillary Lymph Node Dissection and Sentinel Lymph Node Biopsy on Upper Limb Morbidity in Breast Cancer Patients: A Systematic Review and Meta-Analysis. Ann Surg. 2022 Aug 10. doi: 10.1097/SLA.0000000000005671. Epub ahead of print. PMID: 35946806.

- *Publication* - Che Bakri NA, Kwasnicki RM, Dhillon K, Khan N, Ghandour O, Cairns A, Darzi A, Leff DR. Objective Assessment of Postoperative Morbidity After Breast Cancer Treatments with Wearable Activity Monitors: The "BRACELET" Study. Ann Surg Oncol. 2021 Oct;28(10):5597-5609. doi: 10.1245/s10434-021-10458-4. Epub 2021 Jul 26. PMID: 34309777; PMCID: PMC8312212

- *Publication* - Che Bakri NA, Kwasnicki RM, Dhillon K, Khan N, Ghandour O, Cairns A, Darzi A, Leff DR. ASO Author Reflections: Improving Management of Upper Limb Complications after Breast Cancer Treatments. Ann Surg Oncol. 2021 Aug 24. doi: 10.1245/s10434-021-10603-z. Epub ahead of print. PMID: 34431022.

- *Publication* - Che Bakri NA, Kwasnicki RM, Dhillon K, Khan N, Ghandour O, Cairns A, Darzi A, Leff DR. ASO Visual Abstract: Objective Assessment of Postoperative Morbidity Following Breast Cancer Treatments with Wearable Activity Monitors: The "BRACELET" Study. Ann Surg Oncol. 2021 Sep 9. doi: 10.1245/s10434-021-10597-8. Epub ahead of print. PMID: 34505217.

- *Publication* - Che Bakri NA, Kwasnicki RM, Giannas E, Tenang L, Khan N, Moenig C, Imam Z, Dhillon K, Ashrafian H, Darzi A, Leff DR. The Use of Wearable Activity Monitors to Measure Upper Limb Physical Activity After Axillary Lymph Node Dissection and Sentinel

Lymph Node Biopsy. Ann Surg Oncol. 2023 Nov;30(12):7036-7045. doi: 10.1245/s10434-023-13966-7. Epub 2023 Jul 28. PMID: 37507555; PMCID: PMC10562272.

- *Publication* - Che Bakri NA, Kwasnicki RM, Giannas E, Tenang L, Khan N, Moenig C, Imam Z, Dhillon K, Ashrafian H, Darzi A, Leff DR. ASO Author Reflections: Objective Outcome Measure of Upper Limb Function Following Axillary Lymph Node Dissection and Sentinel Lymph Node Biopsy. Ann Surg Oncol. 2023 Nov;30(12):7133-7134. doi: 10.1245/s10434-023-13984-5. Epub 2023 Jul 23. PMID: 37482598; PMCID: PMC10562312

- *Publication* - Che Bakri NA, Kwasnicki RM, Giannas E, Tenang L, Khan N, Moenig C, Imam Z, Dhillon K, Ashrafian H, Darzi A, Leff DR. ASO Visual Abstract: The Use of Wearable Activity Monitors to Measure the Upper Limb Physical Activity After Axillary Lymph Node Dissection and Sentinel Lymph Node Biopsy. *Ann Surg Oncol* **30**, 7144–7145 (2023). https://doi.org/10.1245/s10434-023-14112-z

- *Presentation and published abstract* - Che Bakri NA, Kwasnicki RM, Khan N, Ghandour O, Lee A, Grant Y, Darzi A, Ashrafian H, Leff DR. Impact of Axillary Lymph Node Dissection and Sentinel Lymph Node Biopsy on Upper Limb Morbidity in Breast Cancer Patients: Systematic Review and Meta-Analysis at American Breast Surgeon's Conference 2022 (Las Vegas, USA) and published abstract in Annals of Surgical Oncology.

- *Presentation and published abstract* - Che Bakri NA, Kwasnicki RM, Dhillon K, Khan N, Ghandour O, Cairns A, Darzi A, Leff DR. Objective Assessment of Postoperative Morbidity After Breast Cancer Treatments with Wearable Activity Monitors: The "BRACELET" Study. Quick shot oral presentation at American Breast Surgeon's Conference (virtual) on 29th April – 2nd May 2021 and published abstract in Annals of Surgical Oncology.

- *Presentation and published abstract*- Che Bakri NA, Kwasnicki RM, Giannas E, Tenang L, Khan N, Moenig C, Imam Z, Dhillon K, Ashrafian H, Darzi A, Leff DR. The Use of Wearable Activity Monitors to Measure the Upper Limb Physical Activity after Axillary Lymph Node Dissection and Sentinel Lymph Node Biopsy. Oral presentation (Mammary Fold Prize session) at Association of Breast Surgeon's Conference, May 2023. Published abstract in European Journal of Surgical Oncology DOI: https://doi.org/10.1016/j.ejso.2023.03.189

- *Presentation and published abstract* - Che Bakri NA, Kwasnicki RM, Moenig C, Elias S, Imam Z, Tenang L, Dhillon K, Darzi A, Leff DR. Objective Assessment of Mastectomy Only versus Deep Inferior Epigastric Perforator Reconstruction Surgery using Wearable Activity Monitors – The "BRACELET" study. Oral presentation (Mammary Fold Prize session) at Association of Breast Surgeon's Conference 2022. Published abstract in European Journal of Surgery DOI: https://doi.org/10.1016/j.ejso.2022.03.166

- *Presentation and published abstract* - Che Bakri NA, Kwasnicki RM, Dutta T, Rizk C, Giannas E, Darzi A, Ashrafian H, Hunter J, Henry F, Wood S, Leff DR. Short-term Physical Recovery After Breast Cancer Surgery Predicts Long-term Functional Outcomes presented at American Breast Surgeon's Conference 2024 (Orlando, USA) and published abstract in Annals of Surgical Oncology.

- *Presentation and conference proceedings* - Che Bakri NA, Kwasnicki R, Dhillon K, Ghandour O, Khan N, Cairns A, Ashrafian H, Darzi A, Leff DR. Objective Comparison of Post-operative Activity after Sentinel Lymph Node Biopsy versus Axillary Node Clearance Using Wearable Activity Monitors. Poster presentation at 38th Miami Breast Cancer Conference (virtual) on 4th – 7th March 2021.

- *Presentation and conference proceedings* - Che Bakri NA, Kwasnicki RM, Dhillon K, Khan N, Ghandour O, Cairns A, Ashrafian Hutan, Darzi A, Leff DR. Objective Assessment of Post-

Operative Morbidity following Breast Cancer Surgery with Wearable Activity Monitors - The BRACELET study. 14th London Surgical Symposium, Sept 2022.

- *Presentation and conference proceedings* - Che Bakri NA, Kwasnicki RM, Khan N, Ghandour O, Lee A, Grant Y, Darzi A, Ashrafian H, Leff DR. Incidence of Lymphoedema Following Axillary Lymph Node Clearance and Sentinel Lymph Node Biopsy in Breast Cancer Patients– Systematic Review and Meta-analysis. Oral presentation at Surgery and Cancer Departmental Research Afternoon 2022

- *Presentation and conference proceedings* - Che Bakri NA, Kwasnicki RM, Tenang L, Giannas, E, Moenig C, Elias S, Imam Z, Dhillon K, Darzi A, Leff DR. Deep Inferior Epigastric Perforator Reconstruction vs Mastectomy Only: Objective Assessment of Recovery after Breast Surgery using Wearable Activity Monitors. Oral presentation at American Society of Plastic Surgeons, 2022, Boston, USA

- *Presentation and conference proceedings* - Che Bakri NA, Kwasnicki RM, Tenang L, Giannas, E, Moenig C, Elias S, Imam Z, Dhillon K, Darzi A, Leff DR. Upper Limb Recovery Following Mastectomy with and without Breast Reconstruction, with Wearable Activity Monitors. Poster presentation at American Breast Surgeon's Conference, Boston, USA, April 2023.

- *Presentation and conference proceedings.* Kwasnicki RM, Che Bakri NA, Dutta T, Giannas E, Dunne J, Wood S, Leff DR. Recovery After Breast Surgery Predicts Long Term Functional Outcomes. Oral presentation at American Society of Plastic Surgeons, 2023, USA

Awards/Prizes:

- People's Choice Prize Winner at Imperial PhD Summer Showcase competition 2021

- Quick shot oral presentation at American Breast Surgeon's Conference 2021
- Oral Presentation at Mammary Fold Prize session, Association of Breast Surgeon's Conference 2022
- Oral Presentation at Mammary Fold Prize session, Association of Breast Surgeon's Conference 2023
- Top 3 abstract at Surgery and Cancer Departmental Research Afternoon 2022 (Oral presentation)
- NIHR Imperial Biomedical Research Centre (BRC) award grant £15880

2 IMPACT OF BREAST CANCER TREATMENT ON UPPER LIMB MORBIDITY – SYSTEMATIC REVIEW AND META-ANALYSIS

2.1 Abstract

This chapter acts as an introduction to the impact of breast cancer treatment on upper limb morbidity. Based on the most prevalent findings from the reviewed studies, six outcomes were extracted which includes lymphoedema, range of motion, strength, upper limb function, pain, and health-related quality of life. The meta-analysis included studies that were assessed objectively or using validated instruments.

The main body of the chapter considers the impact of breast cancer treatment at different time points (less than 12 months, between 12 and 24 months, and more than 24 months). Understanding the impact of breast cancer treatment and disparities in operative procedures on postoperative arm morbidity would identify patients who are at risk of developing complications and encourage better direct resources to the point of need. Furthermore, this systematic review concluded that there was an urgent need to develop a standardised tool that is user-friendly in both clinical and home settings, and that incorporates current technology to evaluate these morbidities to facilitate more accurate comparisons between treatments and studies.

Sections of this chapter have been previously published as: Che Bakri NA, Kwasnicki RM, Khan N, Ghandour O, Lee A, Grant Y, Dawidziuk A, Darzi A, Ashrafian H, Leff DR. Impact of Axillary Lymph Node Dissection and Sentinel Lymph Node Biopsy on Upper Limb Morbidity in Breast Cancer Patients: A Systematic Review and Meta-Analysis. Ann Surg. 2022 Aug 10. doi: 10.1097/SLA.0000000000005671. Epub ahead of print. PMID: 35946806.

2.2 Introduction

More individualised and focused therapy have led to a longitudinal improvement in survival following breast cancer treatment.[69] This results in an increase in the number of breast cancer survivors suffering from long-term side effects of treatment, such as reduced shoulder mobility, muscular strength, pain, and lymphoedema.[8] Patients with upper limb impairments are prone to experiencing limitations in their everyday activities, which can diminish their health-related quality of life (HRQoL) and hinder their ability to resume work.[8] Long term physical impairments will put additional strain on healthcare services to provide support for breast cancer survivors.[70] Consequently, it is crucial to understand the extent and severity of these complications to facilitate the planning of healthcare support and provision.

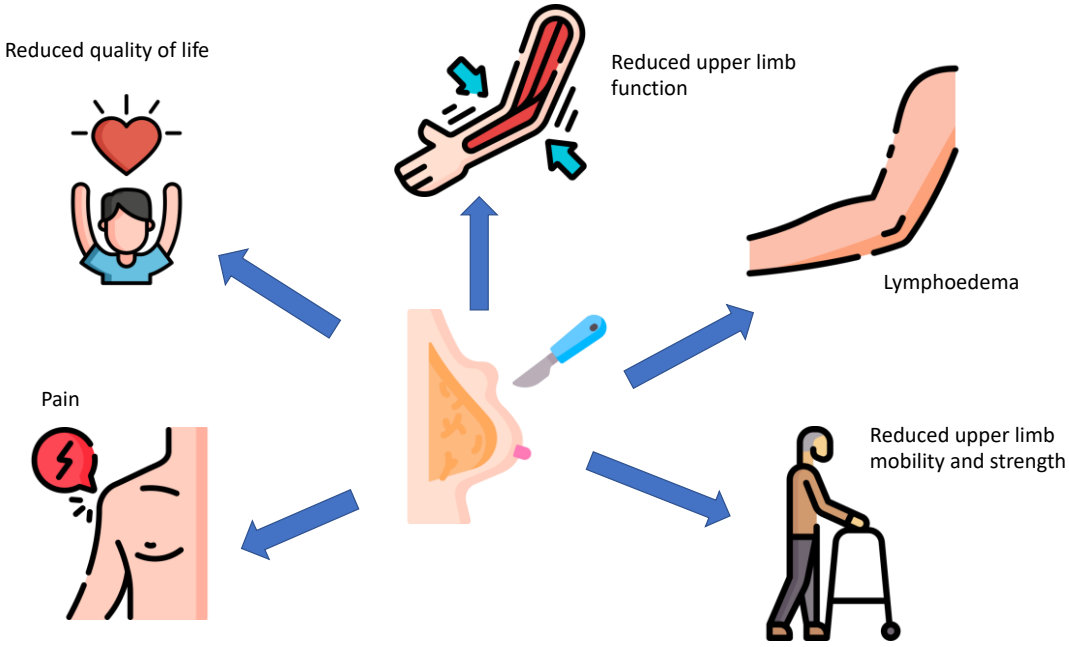


Figure 2-1 Impact of breast cancer treatment on upper limb function

There are misconceptions that upper limb morbidity will resolve over time without intervention, and this has caused inadequate monitoring of these morbidities in breast cancer survivors.[3] Long-term upper limb morbidity has been reported in research, but has been under-diagnosed and under-treated.[3] Hence, research on survivorship should be focused on reducing complications associated with breast cancer treatments and improving patients' HRQoL. As a result of growing awareness of the impact of upper

limb morbidity, an expanding body of research has been conducted to identify individuals who are more susceptible to the complications that necessitate early intervention.

The After Mapping of the Axilla: Radiotherapy Or Surgery (AMAROS) trial, which investigated patients with T1 or T2 cancer, found that those who underwent axillary lymph node dissection (ALND) experienced a higher incidence of upper limb complications compared with those who received radiotherapy (RT).[40] These morbidities can persist for two or more years[71,72] after treatment and the failure to identify these impairments may have debilitating effects on patients.[3] Previous research has also demonstrated that individuals who underwent ALND were more prone to shoulder complications in comparison with those who underwent sentinel lymph node biopsy (SLNB), which is a less invasive procedure.[73-75] Furthermore, it has been reported that RT can result in late upper limb morbidity that may persist for several years after treatment.[76,77]

Axillary radiation and ALND are well-established risk factors for the development of lymphoedema and limited upper limb range of motion. Although the advent of SLNB in the 1990s resulted in a decrease in the frequency of ALNDs, there is still a significant degree of arm morbidity related with SLNB that has yet to be quantified.[78] Axillary de-escalation is motivated by a desire to avoid harm and an increased understanding of the oncological safety of axillary preservation in breast cancer therapy.[40] If the effect of axillary surgery and various other surgical interventions on post-operative arm and shoulder morbidity were better understood, it would be possible to allocate resources more effectively and highlight the necessity of de-escalation strategies. Additionally, the impact of breast reconstruction surgery on upper limb function remains under-researched despite the extensive data on the impact of the surgery on abdominal morbidity.[16,79] It is vital to determine which procedures or treatments are linked to the highest rates of morbidity to provide clinicians with the necessary information to advise patients on strategies that will improve their HRQoL.

Since the publication of the last systematic review in 2014,[2] a number of important studies have been published investigating the adverse effects of breast cancer treatment on upper limb.[21,40,80-89] Whilst

prior systematic reviews of the literature regarding upper limb morbidity have been performed, due to multiple methodologies of data presentation, the complexity of quantitative assessment through meta-analysis was precluded.[2] Other systematic reviews focused on specific outcomes (e.g., lymphoedema),[28] or medical treatments,[88] or included non-validated outcomes.[2]

In the last decade, the quality of contemporary studies, such as randomised controlled trials (RCTs) and prospective cohort trials, have improved, which may have an impact on the findings.[40,80,81,83] In the present meta-analysis, only objective data assessed by validated instruments for lymphoedema, range of motion (ROM), and strength, or assessed using validated questionnaires for upper limb function, pain, and HRQoL, were included to achieve standardisation wherever possible. Data were appraised at an individual-study level with raw variables for preoperative to postoperative outcomes representing an internal difference metric, which could then be expanded sequentially for study group synthesis. This was made possible by applying meta-analytical outcome weighting to each study and applying inverse variance methodologies.

2.2.1 Aim

The objective of this chapter was to conduct a systematic review and meta-analysis of existing literature in order to assess the impact of breast cancer treatment on upper limb function. This meta-analysis is a critical foundation for the thesis in assessing the current methods of measuring upper limb morbidities and serves as a benchmark against which the performance of new emerging technology can be compared.

2.3 Methods

2.3.1 Literature Search

The databases of Embase, Medline, CINAHL, and PsychINFO were used to perform a systematic literature search from 1990 to March 2020 in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines.[8] The review was submitted via PROSPERO (CRD42020199311). The keywords used are listed in Appendix 1. The outlined eligibility criteria were used to screen the studies, and additional studies were identified by cross-referencing the bibliographies of the included papers and from Google Scholar.

2.3.2 Inclusion and Exclusion Criteria

Included studies focused on upper limb function in patients undergoing breast surgery +/- adjuvant treatments, and the outcomes must be assessed using instruments that had been validated (Table 2-1). Papers that satisfied the requirements for inclusion were examined using a methodological checklist.[90] Excluded papers were case reports, case series, letters, systematic reviews of the literature, unpublished or ongoing trials, research conducted before the 1990s, studies conducted in languages other than English, and post-treatment interventional studies. Studies that exclusively addressed hormone treatment or chemotherapy were excluded.

Table 2-1 Inclusion and exclusion criteria

Inclusion	**Exclusion**
Randomised-Controlled Trials and observational studies (cohort and case-control) are eligible.	Exclude case reports, case series, letters, systematic/literature reviews and opinion pieces, study protocol, in-vitro, animals or cadaveric studies, unpublished or ongoing trials
Studies assessing any upper limb functional outcome post breast and/or axillary surgery +/- additional therapies (radiotherapy, chemotherapy, hormonal therapy).	Exclude studies focusing on other therapies (i.e. chemotherapy, hormonal therapy)

Outcomes should be measured by validated tools (published)	Exclude post-treatment interventional studies
	Exclude non-English studies
	Exclude studies prior to 1990s

2.3.3 Study Selection

Independent assessment of the abstracts and titles by two investigators was carried out using Covidence (Veritas Health Innovation, Melbourne, Australia) which is a web-based screening tool and data extraction tool.[91] Full text screening was performed independently by four investigators. Any conflicts that arose during the assessment were discussed until the investigators reached a consensus or if it was not possible, a fifth investigator was consulted.

2.3.4 Data Extraction

Based on the most prevalent findings from the reviewed studies, six outcomes were extracted (Appendix 2). Outcomes that were objectively measured for lymphoedema, ROM and strength or measured using validated tools for upper limb function, pain, and HRQoL were included in the review. Adverse treatment effects were divided into three categories, according to the time point at which the data was collected: less than 12 months, between 12 and 24 months, and more than 24 months. Appendix 3 describes the various methods of outcome reporting.

2.3.5 Study Quality

Two investigators independently evaluated the risk of bias in each study using the Risk of Bias 2 (RoB2)[92] and Risk of Bias in Non-randomised Studies - of Interventions (ROBINS-I) tools[93] for RCTs and non-randomised studies, respectively. Disputes were addressed by discussion, and if required, a third investigator served as an arbitrator.

2.3.6 Statistical Analysis

Meta-analysis was performed where possible on the prevalence rates of upper limb morbidity after breast cancer treatment. The pooled prevalence was computed using a random effects model and presented with 95% Confidence Intervals (CI) using the DerSimonian & Laird method as a between-study variance estimator.[94] The I^2 statistic (<30% - low, 31-59% - moderate, >60% - high) and Cochran's Q statistic were used to evaluate heterogeneity. Stata version 15 was used to conduct analyses (Stata Corp LP, College Station, TX, USA). Probability values (p-value) ≤0.05 were deemed statistically significant. If meta-analysis was not feasible, a narrative review was performed to further assess the relevant literature.

2.4 Results

The initial search yielded 7415 articles (Figure 2-2). Nineteen additional articles were discovered through the examination of existing references, while an additional five articles were obtained from alternative sources. A total of 279 articles fulfilled the primary selection criterion. The articles were categorised based on the specific outcome measure of interest, and subsequently, the six most prevalent outcomes were identified (Appendix 2). As a result, a total of 85 studies were included in the systematic review (Appendix 4).

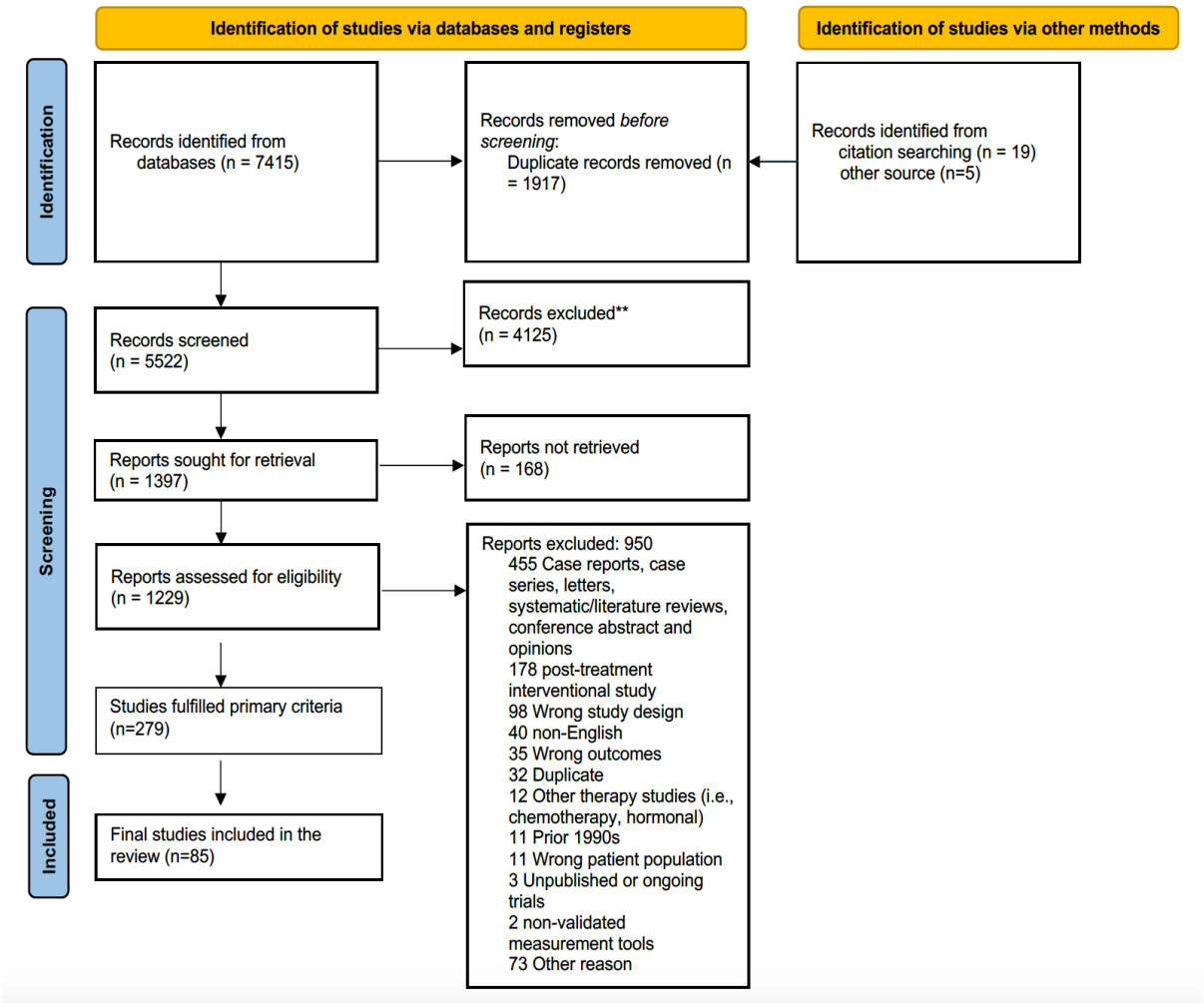


Figure 2-2 PRISMA flow diagram investigating the impact of breast cancer treatment on upper limb morbidity – systematic review and meta-analysis.

2.4.1 Lymphoedema

2.4.1.1 Rates of Lymphoedema after ALND and SLNB

Among 38 studies that reported the prevalence of lymphoedema at different time intervals, the pooled estimate for the prevalence of lymphoedema after ALND at less than 12 months,[40,80,95-108] 12-24 months,[80,95,96,99,105-107,109-113] and more than 24 months[40,80,81,95,107,114-131] was observed to be 16.5% (16 studies, n=3515, 95% CI 11-22, $I^2 = 97.1\%$, $p < 0.0005$), 24.6% (12 studies, n=1971; 95% CI 11-38, $I^2 = 98.3\%$, $p < 0.0005$) and 23.6% (23 studies, n=5288; 95% CI 16.4-30.9, $I^2 = 98.3\%$, $p < 0.0005$) respectively (Figure 2-3).

The equivalent pooled estimate for the prevalence of lymphoedema after SLNB at less than 12 months,[97,98,101-103,132,133] 12-24 months,[99,109-111,134] and more than 24 months[116-121,128,129,135] was observed to be 7.5% (6 studies, n=3866; 95% CI 4.9-10.1, $I^2 = 79.8\%$, $p < 0.0005$), 3.7% (4 studies, n=491; 95% CI 1.8-5.6, $I^2 = 70\%$, $p < 0.0005$), and 5.9% (11 studies, n=3136; 95% CI 3.6-8.1, $I^2 = 82.8\%$, $p < 0.0005$) respectively.

There was a statistically significant difference in the prevalence of lymphoedema between ALND and SLNB, as illustrated in Figure 2-3 (19 studies, n=9381; difference in pooled estimate =13.7%, 95% CI 10.5-16.8, $I^2 = 97.4\%$, $p < 0.0005$). All studies included in the meta-analysis[97-99,102,109,110,116,118-122,135] reported higher rate of lymphoedema following ALND.

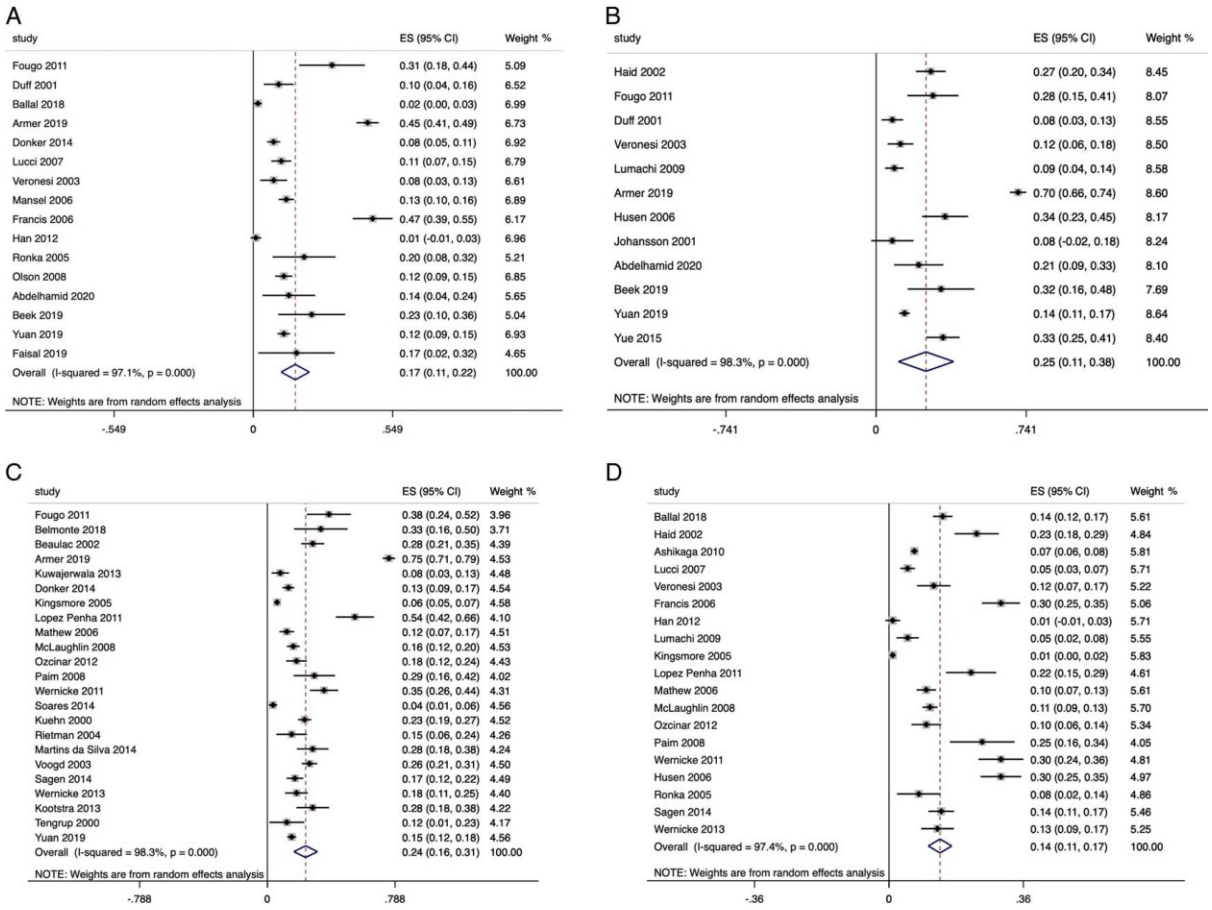


Figure 2-3 a) Prevalence of lymphoedema after ALND at <12 months. b) Prevalence of lymphoedema after ALND between 12 and 24 months. c) Prevalence of lymphoedema after ALND at more than 24 months. d) Differences of lymphoedema prevalence between ALND and SLNB. ALND, Axillary Lymph Node Dissection; SLNB, Sentinel Lymph Node Biopsy.

2.4.1.2 Rates of Lymphoedema after ALND and Axillary Reverse Mapping (ARM)

The prevalence of lymphoedema after ALND + ARM at less than 12 months[105-108] and more than 12 months[105-107,113] was observed to be 3.3% (4 studies, n=657; 95% CI 1.9-4.7, $I^2 = 0\%$, p =0.437) and 6.4% (4 studies, n=762; 95% CI 1.9-10.9, $I^2 = 72\%$, p =0.013) respectively.

2.4.1.3 Immediate versus Completion ALND

There was no significant difference in the rate of lymphoedema when comparing immediate and completion ALND particularly in the long-term follow up. At 12 and 36 months, patients who underwent immediate ALND had no significant difference in lymphoedema rate compared with completion ALND (17.8 vs 8.6%, p= 0.092;[97] 10.3% vs. 14.3%, p= 0.65).[115]

2.4.1.4 ALND and Radiotherapy

ALND conferred a higher rate of lymphoedema compared with axillary radiotherapy at 1 year (8% vs 6%, p=0.332), 3 years (10% vs 6%, p=0.08) and 5 years (13% vs 5%, p=0.0009) where the difference in lymphoedema rate was statistically significant at 5 years.[40] Similarly, another RCT observed higher rates of lymphoedema following ALND and breast irradiation (ALND-breast irradiation=22% vs ALND=12%).[131] Patients receiving ALND and regional lymph node radiation (RLNR) had the greatest 5-year risk of lymphoedema (31.2%, HR 0.613, 95% CI: 0.403–0.935, p=0.023)[41] when compared with ALND without RLNR (24.6%) and SLNB with RLNR (12.2%, HR 0.285, 95% CI: 0.149–0.545, p=0.0002). In a trial comparing radiotherapy (RT) vs. non-RT, irradiated patients had a higher rate of lymphoedema than non-irradiated (14% vs 3%, p=not significant).[136]

2.4.1.5 Breast Conserving Surgery, Mastectomy and Breast Reconstruction

Lymphoedema was observed to be more common after mastectomy than after breast conserving surgery in 2 studies (20% vs 8%, p=0.02; 6.5% vs 1%, p=0.008).[13,137] The rates of lymphoedema after breast conserving surgery or mastectomy ranged from 2.5% to 28%.[13,114,124,137,138] Additionally, the lymphoedema rate did not differ between individuals who underwent breast conserving surgery and those who received immediate breast reconstruction (18% vs 12%, p=0.66).[139]

2.4.1.6 Factors Increasing Risk of Lymphoedema

Significant predictors for lymphoedema included ALND ($p<0.0001$),[41] chemotherapy ($p<0.0001$),[41] high BMI ($p<0.0001$),[41] diabetes ($p<0.05$),[82] palpable tumour ($p<0.05$),[82] weight gain exceeding 10% of baseline value ($p<0.001$),[82] and RLNR ($p<0.0001$).[41] Lymphoedema was also associated with a higher number of metastatic axillary lymph nodes ($p<0.05$),[13] radical mastectomy ($p<0.05$),[13] advanced age ($p=0.006$),[135] the presence of seroma ($p<0.001$)[140] and the amount of time passed after the procedure ($p<0.05$).[140]

2.4.2 Pain

2.4.2.1 Rates of Pain after SLNB and ALND

According to 12 studies that reported the prevalence of pain after ALND at different time intervals, the pooled estimates at less than 12 months,[95,99,103,141-143] between 12-24 months,[95,111,121,141,144] and beyond 24 months[95,99,109,125,131,145] was 40% (6 studies, n=1335; 95% CI 23.8-56.2, $I^2 = 97.8\%$, $p < 0.0005$), 38.5% (5 studies, n=540; 95% CI 15.7-61.4, $I^2 = 96.2\%$, $p < 0.0005$), and 32.9% (6 studies, n=426; 95% CI 18.8-47, $I^2 = 90.9\%$, $p < 0.0005$), respectively (Figure 2-4).

In contrast, the pooled estimate for the prevalence of pain after SLNB at any different follow-up intervals was 21.7% (10 studies, n=1039; 95% CI 13.9-29.5, $I^2 = 91.8\%$, $p < 0.0005$).[99,103,109,111,121,141,143-145] Nine studies comparing SLNB and ALND found the latter led to greater pain, with the pooled difference estimate of 24.2% (Figure 2-4) (9 studies, n=1788; 95% CI 12.1-36.3, $I^2 = 95.7\%$, $p < 0.0005$).[99,103,109,111,121,141,143-145]

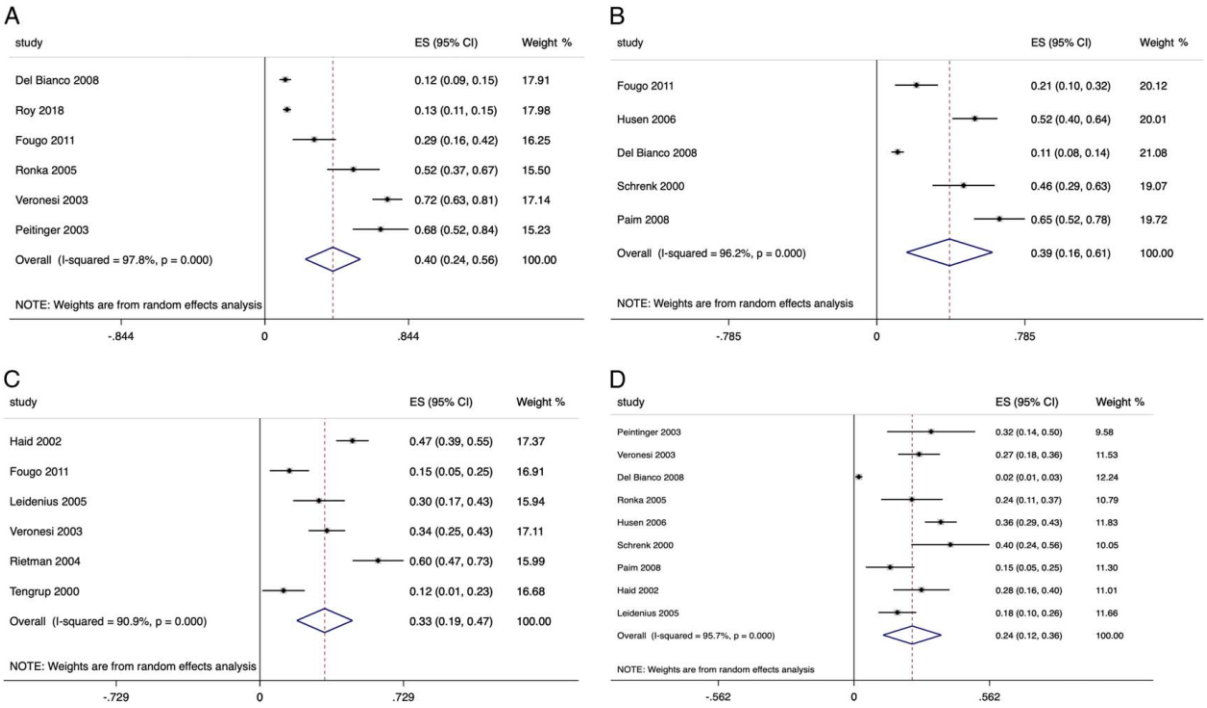


Figure 2-4 a) Prevalence of pain after ALND at <12 months. b) Prevalence of pain after ALND between 12 and 24 months. c) Prevalence of pain after ALND at more than 24 months. d) Differences of pain prevalence between SLNB and ALND. ALND, Axillary Lymph Node Dissection; SLNB, Sentinel Lymph Node Biopsy.

2.4.2.2 Variation in Pain by Procedure

When comparing acellular dermal matrices (ADM) to standard (submuscular tissue expander/implant), no disparities in pain in the immediate post-operative period (p=0.19) or pain during the expansion phase (p=0.65) were observed between the 2 groups.[146] In comparison with submuscular implants, patients with pre-pectoral breast implants experienced less postoperative pain (p<0.001).[147] In patients who underwent latissimus dorsi (LD) flap reconstruction, one study indicated an initial increase in pain at the 6-week and 6-month assessments, however, pain levels were shown to have decreased compared to preoperative assessments at the 1-year follow-up.[148]

2.4.2.3 Predictors of Post-Operative Pain

Younger age (p<0.001) and acute postoperative pain (odds ratio [OR] 1.34, 95% CI 1.12 to 1.60) were independent predictors of chronic pain at 4 months, whereas preoperative psychological robustness (OR 0.70, 95% CI 0.49 to 0.99), composed of high dispositional optimism, high positive affect, and low

emotional distress, were found to be protective.[149] At 9 months, pain persistence was predicted by younger age (p=0.002), ALND (OR 2.97, 95% CI 1.09 to 8.06), and the intensity of early postoperative pain (OR 1.17, 95% CI 1.00 to 1.37).[149]

2.4.3 Range of Motion

2.4.3.1 Prevalence of Reduced ROM and Flexion after ALND and SLNB

A greater proportion of patients experienced reduced range of motion (ROM) following ALND[97,104-106,111,112,129,131,144,150,151] compared with SLNB,[97,111,129,132,133,150] with a pooled estimate of 29.8% (11 studies, n=826, 95% CI 17.5-42, $I^2 = 98.1\%$, $p < 0.0005$) and 17.1% (6 studies, n=5809, 95% CI 11.1-23.1, $I^2 = 96\%$, $p < 0.0005$) respectively. Similarly, the pooled estimate for prevalence of reduced flexion after ALND[103,121,124,125,130,145] and SLNB[103,121,133,145] was 27.2% (6 studies, n=662, 95% CI 15.2-39.2, $I^2 = 91.4\%$, $p < 0.0005$) and 20% (4 studies, n=283, 95% CI 11.5-28.6, $I^2 = 70.8\%$, $p < 0.0005$) respectively.

2.4.3.2 Impact of Breast Reconstruction on Range of Motion

Regarding types of breast reconstruction surgeries, the LD flap group demonstrated the most common morbidity of the shoulder (43.2%) followed by the expander-implant (23.8%) and the deep inferior epigastric perforator (DIEP) (14.1%) groups.[16] Patients who underwent mastectomy and LD flap reconstruction regained a complete range of shoulder mobility 12 months after surgery as compared to pre-operative levels.[21] In another study, the range of motion between patients who underwent LD flap and those who underwent conventional breast conserving surgery was not significantly different.[152] Furthermore, another study demonstrated an initial loss of the majority of range of motion at 6 weeks post-surgery, however, at the 6-month and 1-year assessments, the ranges of motion had marginally increased relative to preoperative values.[148] In a study comparing mastectomy only and the transverse rectus abdominis myocutaneous (TRAM) flaps after mastectomy, there was no significant difference in reduced ROM (p=0.053).[153]

2.4.3.3 Impact of Mastectomy versus Breast Conserving Surgery

Individuals who underwent radical modified mastectomy had a higher rate of impaired flexion (24% vs 7%, $p<0.01$) than those who underwent breast conserving surgery.[13]

2.4.3.4 Impact of Radiation on ROM

Reduced ROM was more prevalent in patients receiving axillary, supraclavicular and/or chest wall radiotherapy compared with non-irradiated patients (52% vs 15%, $p<0.01$).[136] Similarly, a greater rate of reduced ROM was observed when combining ALND and axillary radiotherapy compared with ALND only (82% vs 28%).[154] In an RCT comparing ALND and axillary radiotherapy, ROM did not differ significantly between the two groups (1 year: $p=0.29$; 5 years: $p=0.47$).[40]

2.4.3.5 Predictors of Reduced ROM

ALND ($p<0.001$),[155] radiotherapy ($p<0.05$),[155] and hand dominance ($p<0.05$)[156] were found to be significant predictors of decreased ROM. Additionally, increased observation time ($p<0.05$),[13] advanced age ($p=0.011$),[133] radical modified mastectomy ($p<0.05$),[13] higher BMI ($p<0.05$),[13] chemotherapy ($p=0.002$),[16] presence of tumour-positive lymph nodes ($p=0.014$),[16] expander-implant ($p<0.05$)[16] and the LD flap ($p<0.0001$)[16] were significant risk factors to decreased arm/shoulder function.

2.4.4 Strength

2.4.4.1 Prevalence of Reduced Strength after SLNB and ALND

The pooled estimate of the prevalence of reduction in any strength (e.g. grip, abduction, internal rotators strength) after ALND and SLNB was 30.9% (6 studies, n=825, 95% CI 15.3-46.5, $I^2 = 96.5\%$, $p < 0.0005$)[81,121,124,125,128,130] and 15.2% (5 studies, n=437, 95% CI 5.2-25.2, $I^2 = 91.8\%$, $p < 0.0005$)[81,121,128,130,133] respectively.The ALND group experienced more strength loss than the SLNB. In both SLNB and ALND, a decrease in strength of shoulder external rotation/abduction and ROM remained 5-7 years after surgery.[81,130]

2.4.4.2 Impact of Mastectomy and Breast Reconstruction on Strength

At 3 months and 3 years post-operatively, when the LD flap was combined with radiotherapy, there were statistically significant reductions in adduction (3 months: 30.7% ($p<0.01$); 3 years: 36.4% ($p<0.001$)) and medial rotation (3 months: 25.9% ($p<0.01$); 3 years: 20.4% ($p<0.05$)).[157] In another study, patients who underwent LD flap reconstruction demonstrated a significant reduction in shoulder strength for extension ($p<0.05$), adduction ($p<0.05$), and internal rotation ($p<0.05$) on the operated side relative to the non-operated side.[158] There was no significant difference in muscle strength (forward flexion: $p=0.339$; external rotation: $p=0.100$; internal rotation: $p=0.193$; abduction: $p=0.667$) in a study comparing mastectomy only and the TRAM flaps after mastectomy.[153]

2.4.4.3 Predictors and Association with Reduced Strength

Shoulder–arm function/strength 6 weeks following surgery and age were the greatest predictors of long-term shoulder–arm function/strength.[130] Women who had surgery on their non-dominant side demonstrated a larger loss of grip strength compared with those who had surgery on their dominant side ($p=0.001$).[159] Additionally, strength loss was associated with ALND surgery ($p=0.046$) and having received physical/occupational therapy ($p=0.036$) during follow-up.[150]

2.4.5 Upper Limb Function

2.4.5.1 Prevalence of Reduced Upper Limb Function

The pooled estimate for the prevalence of reduced upper limb function after any breast cancer treatment was 34.4%% (3 studies, n=880, 95% CI 17.2-51.7, $I^2 = 91.4\%$, $p < 0.0005$).[83,133,156]

2.4.5.2 Impact of Mastectomy and Breast Reconstruction on Upper Limb Function

Most studies[18,148,158,160] on LD flap reconstruction demonstrated a reduction in upper limb function as reflected by their DASH scores and one study demonstrated that the reduced upper limb function remained 1-year post-surgery.[18] One study discovered that the LD flap surgery had a moderate effect

on upper limb function as measured by DASH (mean 29.0 (± 23.9)) and those who had LD reconstruction and ALND experienced significantly worse disability scores as measured by DASH (p=0.04).[160] There was a strong correlation between DASH scores at 3 months and long-term function up to 3 years after surgery (r=0.66, p<0.0003).[161]

2.4.5.3 Association with Worse Upper Limb Function

Post-mastectomy radiation+/-chemotherapy (p=0.0093) resulted in considerably worse upper limb function and HRQoL.[162] Women with a history of diabetes (p=0.0249), rheumatoid arthritis (p<0.0001), or shoulder pain (p=0.002), a lower income (p<0.0001), and less health literacy (p=0.0062) were associated with poorer upper limb function.[162]

2.4.6 Health-Related Quality of Life

2.4.6.1 Health-Related Quality of Life post SLNB and ALND

Studies comparing SLNB and ALND found that patients who received SLNB experienced better HRQoL than those who had ALND. Compared with global HRQoL scores pre-operatively, the global scores post-operatively measured by European Organization for Research and Treatment of Cancer core quality of life (EORTC-QLQ-C30) improved by 15% (3 studies, n=155, 95% CI 4.4-26.1, I^2 =99.9%, $p < 0.0005$) in SLNB and 6% (3 studies, n=92, 95% CI 0.7-11, I^2 =99.8%, $p < 0.0005$) in ALND.[143,163,164]

2.4.6.2 Impact of Breast Conserving Surgery, Mastectomy and Breast Reconstruction

When comparing breast conserving surgery with mastectomy + immediate breast reconstruction, one study[139] found no difference in HRQoL and satisfaction between the two groups (physical functioning, p=0.16; physical role functioning, p=0.55; emotional role functioning, p=0.44; bodily pain, p=0.48; vitality, p=0.56; mental health, p=0.95; social role functioning, p=0.94; general health perceptions, p=0.95; physical component summary, p=0.76; mental component summary, p=0.58), whereas another study discovered that the breast conserving surgery group had superior outcomes to the total mastectomy and reconstruction groups in terms of emotional function (p=0.014), social function (p=0.038), nausea/vomiting (p=0.015), financial difficulty (p=0.009), body image (p<0.001), and self-esteem (p<0.001) and sexual scale (p=0.001).[165] Furthermore, patients who underwent autologous or

implant-assisted LD flap reconstruction experienced improvement in emotional and social functioning, emotional and functional well-being, and reduction in depression, with overall improvement in quality of life at 3 years after LD reconstruction, but worsening physical function, body image, social well-being and anxiety at 2 and 3 years after LD reconstruction.[166] Patients who had autologous LD reconstruction were observed to have significantly improved sexual functioning at 3 years (p=0·003) in comparison with those who had implant-assisted LD reconstruction.[166]

2.4.6.3 Association with Health-Related Quality of Life

Factors associated with poorer level of functioning and HRQoL were stage of disease (p=0.005),[167] menopausal status (p=0.031),[167] comorbidities (p=0.032),[167] chemotherapy (p=0.009),[167] post-operative complications (p=0.02),[168] upper-body function (p<0.001),[168] greater psychological burden (p=0.001),[168] had no confidante for social and emotional support (p<0.01),[168] had unmet health care needs (p<0.001),[168] and low health self-efficacy (p<0.001).[168] Patients with "moderate/severe" arm swelling (5 years: p=0.004; 10 years: p=0.005), arm pain (5 years: p<0.001; 10 years: p<0.001), restriction of movement (5 years: p<0.001; 10 years: p<0.001) and loss of feeling in fingers (5 years: p=0.001; 10 years: p=0.013) had a substantially poorer quality of life than those with "none/little" symptoms at 5 years and 10 years respectively. Multivariable analysis demonstrated that arm pain (p<0.001) had the largest effect on HRQoL after 10 years.[169]

2.4.7 Risk of Bias Assessment

Overall, the risk of bias for included RCTs and non-randomised studies were high or serious (Figure 2-5). Risk of bias for individual studies can be found in Appendix 5 and 6.

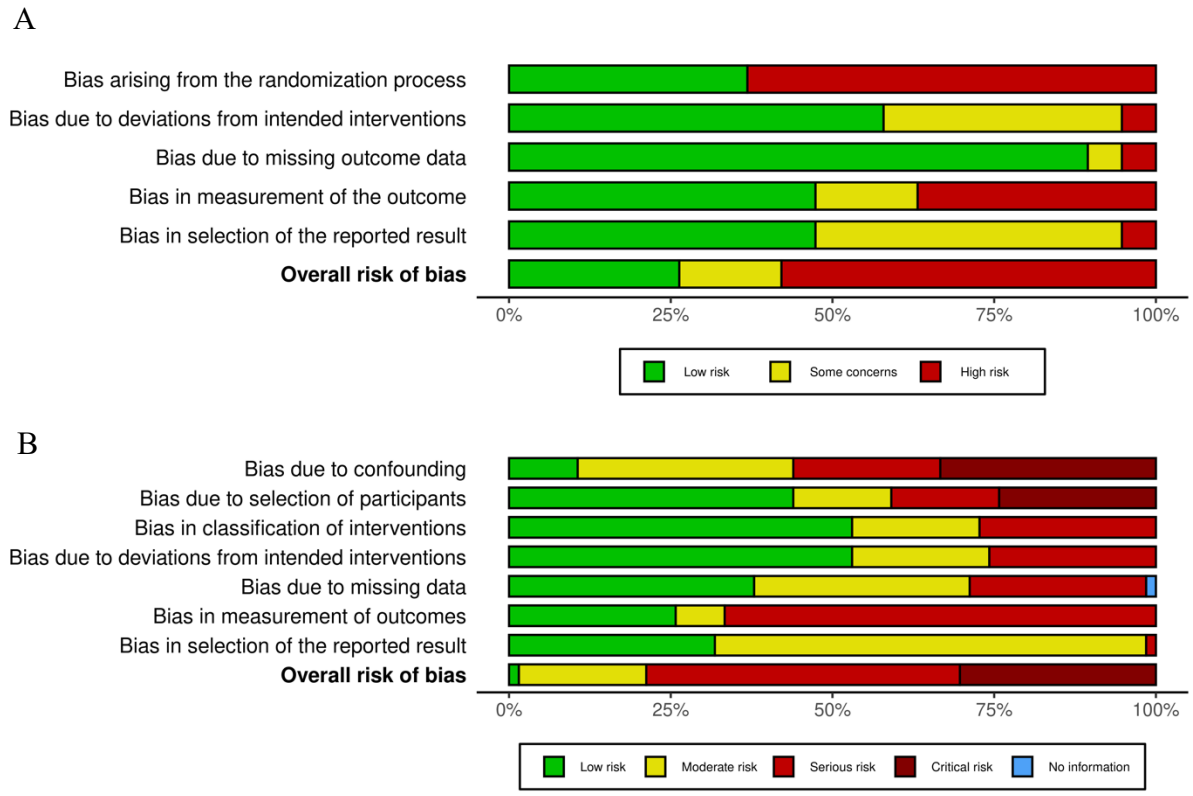


Figure 2-5 a) RoB2 tool for assessing risk of bias of randomised-controlled trials. B) ROBINS-I tool for assessing risk of bias of nonrandomised studies (The figures were created using robvis visualisation tool).[170]

2.5 Discussion

There are 4 critical findings from this systematic review and meta-analysis. Firstly, the pooled estimates for the prevalence of lymphoedema following ALND over the short- and long-term are greater than those reported in previous systematic reviews.[2,28] When compared with SLNB, ALND is observed to have higher prevalence of lymphoedema, pain, reduced strength, and ROM. Secondly, the data on upper limb function evaluated by DASH following axillary surgical procedures are scarce. Thirdly, the assessment of upper limb morbidities is not standardised, making it challenging to compare various treatments. Finally, LD flap is linked to worsening range of motion, strength, and upper limb function.

Previous systematic reviews focused on specific outcomes such as lymphoedema[28] or pain[171] and medical treatments such as radiotherapy and surgery.[88] One systematic review[2] examined all the upper limb complications related to breast cancer treatments but did not perform a meta-analysis. As far as I know, this is the first meta-analysis to better estimate the prevalence of lymphoedema, pain, reduced ROM, and reduced strength following ALND and SLNB at different time intervals where possible.

The pooled estimates of the prevalence of lymphoedema after ALND seem to rise with longer follow-up, which is consistent with the findings by Hidding *et al.*[2] Additionally, the results of the present meta-analysis are in agreement with the meta-analysis conducted by DiSipio *et al*,[28] which demonstrated that the rate of lymphoedema increased longitudinally up to two years following diagnosis or surgery, after which the rate decreased. In the long run, the prevalence of lymphoedema following ALND in the current review using objective validated outcomes is greater than the estimates by DiSipio *et al* (>24 months, 23.6% versus 18.6%).[28] Compared with ALND, it is interesting that the prevalence of lymphoedema following SLNB in the current meta-analysis decreases with time. In this instance, time may not increase the prevalence of lymphoedema; rather, the results may suggest that early lymphoedema following SLNB is more prevalent, but it can resolve with time (with or without intervention). Consistent with the meta-analysis conducted by Wang *et al*,[171] the pooled prevalence of pain in the current review decreases over time. It is interesting to note that younger age is a predictor of

chronic pain at 4 months. The reason for this is not completely understood. There are many different hypotheses as to why younger patients report more pain including greater likelihood of higher histopathological tumour grade, larger tumour size, negative oestrogen receptor status and the necessity for adjuvant treatment especially chemotherapy.[172,173] It has also been postulated that postoperative pain often diminishes with advancing age. However, it remains ambiguous whether this is attributable to a physiological alteration in the pain perception system, a modification in the subjective expression of pain and how different age groups report pain, or a variation in physical activities.[174-176] Additionally, younger individuals may have higher expectations regarding their functional recovery or have heightened central nervous system responses that make them more susceptible to pain.[177]

There is a reduction of lymphoedema rate when combining ALND and ARM approach compared with ALND only or SLNB in the first 12 months. Yuan *et al.*,[107] proposed a modified ARM technique termed iDEntification and Preservation of ARm lymphaTic system (DEPART), which allows for a full identification of the axillary lymphatic system and hence may further reduce the occurrences of lymphoedema. ALND patients have a higher rate of lymphoedema, pain, reduced strength, and range of motion compared with SLNB. Consistent with a previous systematic review, the current meta-analysis reveals that the addition of axillary radiation to ALND increases the risk of upper limb morbidity, particularly lymphoedema and impaired ROM.[88]

The goal of de-escalating axillary surgery is to minimise upper limb morbidities related to ALND and thus improve patients' HRQoL.[40] The present meta-analysis contributes further evidence to support the benefits of de-escalating axillary surgery, such as SLNB, or to perform better surgery, such as evaluating the ARM approach[105] or the LYmphatic Microsurgical Preventive Healing Approach (LYMPHA)[178] where appropriate. LYMPHA procedure involves performing prophylactic bypass of lymphatics to a nearby vein during the primary surgery to prevent lymphoedema.[179] Additionally, there is a need to inform patients and healthcare professionals on what to expect from their surgeries. Therefore, resources can be allocated at an appropriate time to address these upper limb complications.

Although DASH was a frequently used patient-reported outcome for upper limb assessment, there are few studies assessing upper limb function following ALND and SLNB. In a recent RCT, it was demonstrated that women with breast cancer who received physiotherapy-led structured exercise had better upper limb function, as assessed by DASH questionnaires one year after treatment, compared with those who received standard care, which was proven to be cost-effective.[4] The study supports the adoption of an exercise programme following breast cancer treatment, reinforcing the necessity of identifying at-risk individuals and taking prompt action.

There is growing evidence of the impact of breast reconstruction on upper limb function.[16-18,21,161] LD flap reconstruction appears to cause the most morbidity in upper limb function compared with the other types of breast reconstruction,[16] which can subsequently impact patients' HRQoL. This is explainable given that in LD reconstruction the muscle is detached from its origin, causing instability of the shoulder joint and a reduction in strength. However, it is suggested that that teres major and other muscles in the shoulder may hypertrophy and take over the function of the LD muscles.[17] Reduced mobility of the shoulder joint may also be due to scar formation and postoperative pain rather than loss of LD muscle.[17] It is noted that the outcomes and the degree of severity of morbidity after different breast reconstructions may vary in various studies due to non-standardised measurement outcomes and low-quality methodologies.[17]

The lack of standardisation in the assessment of upper limb morbidities following breast cancer treatment makes comparisons difficult and meta-analysis challenging. Numerous tools, such as questionnaires, are subjective and susceptible to recall bias.[78] To overcome the drawbacks associated with subjective outcome measures, wearable sensors have been proposed to complement the subjective outcome measure generated from the perspectives of clinicians and patients as they examine different parameters. Various applications of wearable sensors have been suggested and proposed in various disciplines, including healthcare, military, sports, and gaming.[180-183] They are non-obtrusive, offer continuous, objective measures, and are capable of remotely monitoring patient's condition in free living environment. The introduction of wearable technology may facilitate the development of personalised

rehabilitation therapy, which can offer feedback and motivate health-promoting behaviours. Prior studies found the use of wearable sensors as an assessment tool for upper limb function and activities following stroke and Parkinson's disease to be beneficial.[68,184] The wearable sensor can be implemented in breast cancer cohort to objectively assess upper limb activity following surgery and may improve the comparability of post-operative limb function outcomes data in the future. This will be further elaborated in the next few chapters of this thesis.

This systematic review and meta-analysis have several limitations that must be taken into account. Language bias might occur as only papers published in English were included. Due to the lack of a universally accepted method for documenting and quantifying shoulder morbidity, it was difficult to compare treatments and studies. The prevalence of lymphoedema, limited range of motion, and decreased strength may be underreported, as the outcomes measured by subjective tools were excluded from the review. There was a significant statistical heterogeneity in the studies included in the meta-analysis, therefore any interpretations of outcome measures require measured consideration. To mitigate these limitations, papers published from non-English speaking countries were included. To achieve standardisation whenever possible, the meta-analysis included only objective data and data assessed by validated methods. There is an urgent need to standardise the measurement of upper limb morbidities in future studies to reduce heterogeneity.

2.6 Thesis Implications

This systematic review demonstrates that the pooled estimates for the short-term and long-term prevalence of lymphoedema following ALND are greater than previously reported. Compared with SLNB, patients receiving ALND were observed to have higher rates of lymphoedema (difference in prevalence of 13.7%, $p<0.005$), pain (difference in prevalence of 24.2%, $p<0.005$), decreased strength (prevalence of SLNB: 15.2% versus prevalence of ALND: 30.9%), and range of motion (prevalence of SLNB: 17.1% versus prevalence of ALND: 29.8%). The findings support the benefit of de-escalating surgical management of the axilla, including extending the use of axillary irradiation as an alternative

to ALND in a subset of patients and exploring lymphatic microsurgery or the ARM method as viable options and adjuncts. Even though there is growing evidence regarding the impact of breast reconstruction on the upper limb function, the evidence particularly by objective means is still lacking.

To provide better support for breast cancer survivors and facilitate a more accurate comparison of treatments and studies, it is imperative to develop a standardised, technologically advanced, and clinically applicable assessment method for various upper limb morbidities. Based on prior studies, the use of wearable sensors to assess upper limb function is promising.[68,184] Therefore, it is necessary to investigate this further by exploring the use of wearable technology in the breast cancer cohort. The next steps are therefore studies with specific aims and objectives, investigating the use of wearable activity monitors (WAMs) to objectively assess and monitor upper limb activity following breast cancer surgery in the perioperative period and in the long-term.

It is hypothesised that an assessment of upper limb activities using WAMs is objective and practical, can differentiate between different surgical procedures and provide insight into upper limb function and level of activities after breast and axillary surgery, which have the potential to be used in personalised rehabilitation after surgery.

Therefore, the aim of the thesis are as follows:

- ◊ To identify different types of validated outcome measures of upper limb function following breast cancer surgery
- ◊ To identify potential wearable sensors to be used for assessment of upper limb function
- ◊ To investigate the feasibility of using WAMs, develop and validate the use of WAM as an objective assessment tool for measurement of upper limb activity in the perioperative period following breast cancer surgery
- ◊ To investigate the use of WAMs in the early postoperative convalescence comparing the impact of sentinel lymph node biopsy and axillary lymph node dissection

- ◊ To investigate the use of WAMs in complex breast reconstruction procedures and quantify the degree of upper limb activity in patients undergoing simple mastectomy, deep inferior epigastric perforator (DIEP) reconstruction and implant-based reconstruction (IBR) in the short-term postoperative period and at greater than 6 months follow up
- ◊ To investigate the potential of short-term upper limb activity levels measured by WAMs to serve as a predictor of upper limb activity in the long-term
- ◊ To ascertain the views of breast cancer patients on the use of WAMs in the context of patient monitoring and personalised rehabilitation programme

The following chapter delves into the first two objectives of the thesis, offering a comprehensive overview of the current methods of evaluating upper limb morbidity and the various types of wearable technology that could be employed as an objective instrument to measure upper limb recovery.

3 MEASUREMENT OF UPPER LIMB MORBIDITY POST-BREAST CANCER TREATMENT

3.1 Introduction

The prior systematic review and meta-analysis highlighted the impact of breast cancer treatment on upper limb function including lymphoedema, pain, restricted range of motion, reduced upper limb function and changes to HRQoL. However, the comparison between treatment and studies is difficult due to the absence of a standardised technique for measuring upper limb morbidities. Furthermore, the current methods of assessing upper limb function is mostly subjective including the disabilities of the arm, shoulder and hand (DASH)[185] questionnaire and EuroQol-5D-5L (EQ-5D-5L)[186] questionnaire which, can provide information from patients' perspectives, such as their wellbeing and overall quality of life.[9] While these outcome measures may include valuable information, it is important to note that they may not consistently capture the extent of functional impairment and may not provide sufficient grounds for comparing patients.[9] Previous research has also indicated that questionnaires are susceptible to recall bias.[187] Objective outcome measure such as the use of tape measurements for assessing lymphoedema and goniometry for evaluating range of motion, on the other hand have a great value in surgical research as they can measure outcome objectively. However, they may present some limitations in terms of practicality due to their time-consuming nature and susceptibility to operator bias.[9]

The nature, intensity, or duration of physical activity may abruptly change when an individual becomes acutely ill, or gradually decrease over time due to chronic problems, frequently before a formal diagnosis or identification of the illness takes place. Physical activity may return to its normal baseline levels as patients recover. Nevertheless, this may require a significant amount of time and may not result in a complete return to baseline levels, as it is dependent upon other factors such as the presence of other comorbidities or previous mobility issues. When a breast cancer patient develops upper limb complications, they may have reduced upper limb activity due to restricted range of motion, pain, reduced strength, and lymphoedema.[188] In addition, their overall physical activity may also decrease as a result of their disease.[189] Mason *et al.,*[190] reported that, compared with physical activity levels one

month prior to breast cancer diagnosis, women on average experienced a 23% reduction in weekly moderate-intensity physical activity at 4–12 months post-diagnosis, with an additional decline in physical activity observed between five to ten years post-diagnosis. Notably, nearly 20% of women classified as sufficiently active at the five-year follow-up were deemed insufficiently active at the ten-year follow-up.[190] Some cancer patients may have concerns that physical activity could adversely affect their condition or exacerbate their symptoms, stemming from a lack of awareness of the benefits of exercise.[191] There are many factors or barriers to participation in physical activity reported by cancer patients including coping mechanism, fatigue, treatment and disease-related side effects, severe pain, time pressures, lack of exercise partner, lack of exercise facilities, fear of injury, lack of motivation or interest and lack of equipment.[192-197] Many cancer patients also reported that insufficient access to information regarding appropriate exercises and exercise modalities contributed to their lack of physical activity engagement.[197] The American College of Sports Medicine (ACSM) and the American Heart Association (AHA) emphasise the positive benefits of physical activity by recommending moderate-intensity aerobic activity for thirty minutes on five days per week, vigorous intensity aerobic activity for 75 minutes per week or combination of both to promote and maintain health, as well as reduce the likelihood of chronic disease and premature death.[198] Physical activity plays a crucial role in the prevention of various diseases, such as cancer, cardiovascular disease, and chronic renal disease, both in primary and secondary settings.[199] Physical activity results in breast cancer prevention, with the greatest reduction seen in pre-menopausal women who engage in vigorous activity.[200-203] The UK biobank study demonstrated that very active women had a 23% lower risk of pre-menopausal breast cancer and a 17% lower risk of post-menopausal breast cancer.[201] Additionally, physical activity is associated with a reduced risk of mortality by approximately 40% in individuals with a breast cancer diagnosis[5,6] and a reduced risk of breast cancer recurrence by approximately 20-30%.[5,6] There is also evidence of a dose-response curve for physical activity, indicating that an increase in physical activity is related with a reduction in all-cause mortality.[204-206]

Wearable sensors have been the subject of investigation in various specialised fields, including the evaluation of physical activity in patients with cancer, stroke, Parkinson's disease, and those undergoing

orthopaedic surgery.[207-210] Sensing technologies facilitate the acquisition of functional and activity data, thereby offering novel perspectives on postoperative recovery and supporting tailored interventions.[211] WAMs have the capability to non-obtrusively capture and document arm activity during the peri-operative period. The utilisation of WAMs has been motivated by the need to improve outcomes and quality of life by measuring, monitoring, and offering feedback on levels of physical activity, hence promoting the process of recovery.[212,213]

This chapter focuses on discussing the current methods of assessing upper limb morbidities and different types of wearable technology that could be used to assess upper limb function and morbidity.

3.1.1 Anatomy of Shoulder Joint

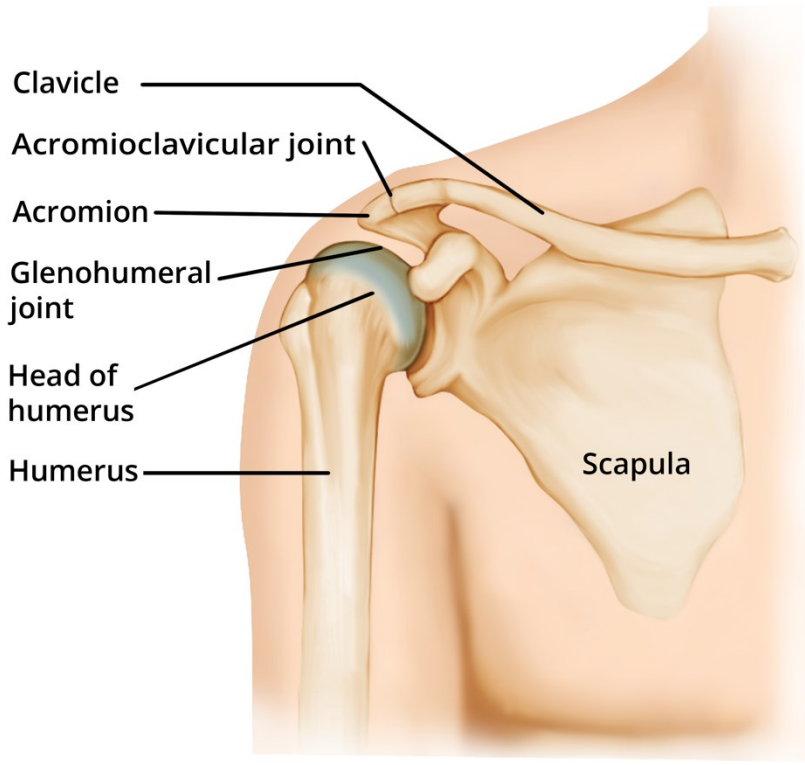


Figure 3-1 Anatomy of shoulder joint. Shoulder joint is composed of glenohumeral joint, acromioclavicular joint, sternoclavicular joint and scapulothoracic joint. (The figure was created by Mohesh Mohan, used with permission)

The shoulder joint is composed of the clavicle and scapula which articulates with the proximal humerus of the upper limb (Figure 3-1). It encompasses of the glenohumeral joint, acromioclavicular joint (AC), sternoclavicular joint, and scapulothoracic joint.[214] The shoulder joint is widely recognised as one of the most mobile regions inside the human anatomy. Nevertheless, as a result of its extensive range of motion, it is sensitive to diminished joint stability and susceptible to injury and dislocation. The shoulder joint exhibits various movements, including abduction and adduction, which involve the lateral and medial rotation of the upper arm along the sagittal plane, flexion and extension movements as well as internal and external rotation.[214]

The sternoclavicular joint is classified as a synovial saddle joint, facilitating the connection between the manubrium of the sternum and the clavicle. It is the only joint that connects the upper limb to the axial skeleton.[214] The AC joint articulates the lateral extremity of the clavicle and the acromion, which protrudes anteriorly off the scapula. The AC joint plays a crucial role in providing both stability and mobility to the shoulder complex.[214] The scapulothoracic joint is not a true anatomical joint as it does not possess the typical characteristics of a real anatomic joint, such as being formed by fibrous, cartilaginous, or synovial tissues. It refers to the articulation of the scapula with the thorax where the scapula glides over the posterior thoracic cage.[214] Finally, the glenohumeral joint is anatomically classified as a ball-and-socket joint, and functionally categorised as a diarthrodial, multiaxial joint. The glenohumeral joint is formed by the articulation of the humeral head and the glenoid cavity of the scapula.[214] This joint serves as the primary articulation of the shoulder girdle and allows and extreme range of motion in multiple planes.[214]

3.1.2 Pathophysiology of Upper Limb Dysfunction

As discussed in chapter 1 and 2, breast cancer treatment can lead to upper limb dysfunction includes reduced shoulder range of motion, pain, and reduced strength. Following a surgical procedure, patients may experience formation of scar tissue, fibrosis, and contraction of soft tissues in the anterior thoracic and axillary regions.[215] These physiological changes can result in a range of functional impairments, including reduced range of movement and strength. For instance, mastectomy can alter the orientation

and positioning of the scapula, leading to modifications in the shoulder joint and thus increasing the susceptibility to shoulder impingement and rotator cuff pathology.[216,217]

A combination of angiogenesis and chronic inflammatory changes leads to development of local and regional pain syndromes.[217] Many patients in this cohort commonly undergo radiation, which can induce cellular apoptosis accompanied by the production of inflammatory cytokines, tissue injury, and fibrosis.[216] These effects contribute substantially to increasing chronic shoulder dysfunction and pain over an extended period.[216,218] Furthermore, it is important to note that surgical procedures, such as ALND, might potentially result in nerve injury, which in turn may cause abnormal sensations in the post-operative region.[219-221] Additionally, individuals experiencing paraesthesia exhibit a higher propensity for chronic pain.[219] Patients who develop these complications are prone to worsening physical function and reduced quality of life.[27] For example, they may have difficulties doing their own shopping, vacuuming, or performing other common daily activities.[222] Breast cancer survivors may lack knowledge regarding the possible complications that can arise and therefore may not communicate their symptoms, leaving them underreported in the clinical setting.[223] Consequently, this can result in a delay in seeking medical attention and treatment, ultimately increasing the probability of sustaining long-term dysfunction. Johnson *et al.,*[224] reported that although 51% of patients experienced significant shoulder dysfunction following breast cancer treatment, only 28% reported access to rehabilitation, highlighting the necessity to optimise the rehabilitation pathway and establish a system for the early identification of upper limb complications.

3.1.3 Pathophysiology of Breast Cancer-Related Lymphoedema

Breast Cancer-Related Lymphoedema (BCRL) is a chronic condition due to an abnormal accumulation of protein-rich fluid in the interstitial space because of inadequate lymphatic drainage, yet the aetiology is not completely understood.[36] It can develop anytime from 6 months to many years post-treatment, with about 30% of breast cancer survivors developing lymphoedema by 18 months after surgery.[225] The previous chapter extensively discussed the various causes of BCRL in breast cancer survivors, including

surgery and radiotherapy. Several notable risk factors associated with the development of lymphoedema include high body mass index (BMI), undergoing a mastectomy procedure, the extent of lymph node removal (the more nodes removed, the greater the risk), axillary radiotherapy, having radiation therapy together with ALND as well as infections in the area after breast surgery.[27,28,119,226-228]

In a normal state, lymphatic system transport water, lipids, and proteins from the interstitium to the intravascular space. In breast cancer, the lymphatic transport capacity is reduced or obstructed because of excision of lymph nodes.[229] This results in accumulation of interstitial fluid which leads to lymphoedema. However, the pathophysiology seems to be more complex and multifactorial and may not be explained by the theory above.

It is interesting to note that only some women develop BCRL, and majority do not, and the reason is not completely understood. In patients who develop BCRL, the oedema may be localised rather than affecting the entire arm.[229] Moreover, BCRL may not appear clinically until years after surgery or radiotherapy. A possible explanation is that some individuals may establish lymphatic collateral channels that lower the risk of BCRL or that patient factors such as genetic, molecular, and physiologic characteristics have a lower propensity for oedema development.[36-38] For example, individuals who do not develop BRCL may establish alternate mechanisms for protein removal by redirecting lymph into lympholymphatic or lymphovenous channels, and/or by increasing protein transport directly into local blood vessels.[36,38,230]

Moreover, the majority of patients do not experience BRCL, likely due to the implementation of less invasive surgical procedures, such as SLNB instead of ALND, which greatly lowers the risk of lymphoedema by three to four times.[27] Advancements in surgical procedures, such as the ARM method, for mapping and preserving axillary lymphatics during surgery may potentially decrease the occurrence of post-surgical lymphoedema in patients.[105,107,108] The LYMPHA procedure on the other hand establishes lymphatic-venous anastomoses between the arm lymphatics and a collateral branch of the axillary vein during axillary surgery in order to avoid lymphoedema.[231] Furthermore, appropriate

post-operative care, including arm exercises and compression garments, might mitigate the risk of lymphoedema onset.[232]

Breast cancer survivors with lymphoedema experience an array of symptoms including swelling, tightness, heaviness, pain/ache, tingling, numbness, stiffness, upper limb weakness and fatigue as well as reduced of motion of the arm and fingers.[233-236]

3.1.4 Management of Shoulder Dysfunction and Lymphoedema

In the UK, recommendations for non-reconstructive breast surgery support the gradual rehabilitation of upper limb movement, with physiotherapy being indicated if issues arise.[4,237,238] In our unit, all breast cancer patients are given a standard leaflet from Breast Cancer Care Now (Appendix 7) +/- a visit from a physiotherapist if needed as an in-patient as part of our routine care. The therapies being implemented in clinical practice and in research are passive mobilisation to restore joint mobility or prevent muscular shortening,[239] myofascial techniques to relieve painful muscular trigger points,[3] manual stretching and transverse strain to prevent tightness of the pectoral muscles[43] and active or active/assisted mobilisation exercise to restore arm strength and prevent reduction of activities of daily living.[240,241] However, there is some concern that physical therapy may lengthen the time it takes for a wound to drain, may interfere with regeneration of lymphatic channels damaged by the surgery,[242] and it can also result in seroma production and delayed wound healing. As such, it is important to carefully consider the timing and intensity of these activities.[240,243,244]

Three systematic reviews[240,241,243,245] were conducted to examine the evidence of post-operative physical therapy for upper limb impairments after breast cancer treatment. However, the data is limited, with many low-quality trials and short-term follow up and many high-risk patients were excluded. These systematic reviews[240,243,246] demonstrated good benefits of early rehabilitation, but no specific recommendations for the type of exercise or protocol that might support and improve the management of upper limb morbidities were provided. A recent RCT[4] was conducted to address these challenges particularly in high-risk patients. Prior studies showed that patients who had planned axillary lymph node dissection, planned radiotherapy to the axilla or supraclavicular fossa, high body mass index (≥30),

and existing shoulder problems are at high risk of developing upper limb complications.[27,39,149] The patients were randomly allocated to usual care only (with written information leaflets recommending postoperative exercises and generic postoperative advice from the UK charity Breast Cancer Care) or usual care plus structured exercise programme with a defined protocol introduced within 7-10 days after surgery. At 12 months post-surgery, the mean DASH score in the intervention group was significantly better in terms of activity limitations, participation restrictions and impairment compared with the standard care. There were also fewer disability symptoms measured by The Functional Assessment of Cancer Therapy – Breast (FACT-B) questionnaire at both 6 months and 12 months for the former compared to the latter.[4] Physical health related quality of life scores were higher after exercise compared with usual care at 6 and 12 months and patients were more confident in their ability to return to usual activities and regular physical activity compared with usual care participants at all time points.[4] However, there were no differences in self-reported activity of walking or strenuous activity between treatment groups.[4] The implementation of this structured exercise programme was also found to be more cost-effective compared with usual care and did not increase neuropathic pain, lymphoedema or wound-related complications.[4]

Prior to the early 2000s, breast cancer related lymphoedema patients were advised to avoid doing exercise on the affected arm as it was deemed to be unsafe, may lead to the development of new lymphoedema, and may exacerbate the signs and symptoms of an existing lymphoedema.[247,248] However, Harris and Niesen-Vertommen publicly challenged this belief.[247] Subsequently, many research studies including well-designed randomised-controlled trials were conducted and indicated that there is no adverse effect from doing upper body exercise.[249] A meta-analysis of 6 studies showed a significant reduction of lymphoedema and a significant improvement in muscular strength following resistance exercise.[249] Due to its effectiveness, exercise has been added to the standard treatment of lymphoedema alongside the complete decongestive therapy consisting of manual drainage, bandaging, compression, and skin care.[250]

3.1.5 Measurement of Upper Limb Activity

As previously outlined in chapter 2, breast and axillary surgery may result in upper limb morbidity, including lymphoedema, pain, reduced range of motion, decreased strength, and impaired upper limb function, all of which can adversely affect the patient's quality of life. In order to monitor and improve long-term upper limb function post-breast cancer treatment, the first step is to enable assessment of upper limb function during postoperative period. Upper limb dysfunction or impairment is predominantly evaluated by subjective patient-reported outcome measures (PROMs), such as the Disabilities of the Arm, Shoulder, and Hand Questionnaire (DASH). However, subjective measurement of upper limb function is susceptible to recall or response bias, which will be discussed in detail in section 3.1.7.

To develop a quantitative upper limb functional outcome for clinical screening and research, there is a need for low-cost tools that can measure upper limb morbidity outside laboratory settings. Prior studies showed a correlation between upper limb morbidity evaluated through clinical assessments and upper limb activity measured by accelerometers.[251-253] Upper limb activity assessment can work as a surrogate marker for upper limb morbidity, providing objective metrics of function and activity that are correlated with clinical deficits.[254] In particular, the functional capacity of the affected upper limb may be reflected in upper limb activity. It concentrates on activities of daily living, such as cleaning, dressing, and cooking, and offers a more objective evaluation of upper limb functional outcome.

Lymphoedema, for instance, can markedly reduce upper limb activity due to oedema and stiffness, complicating movement of the affected arm.[255] Likewise, pain and weakness in the upper limbs might hinder patients' ability to engage in everyday activities, resulting in diminished range of motion and activity levels.[256] Measuring upper limb activity is a helpful way to track how the disease is progressing, how well someone is recovering, and how effective interventions are, all without needing any invasive tests.

One way to measure upper limb activity objectively is using wearable sensors such as accelerometers. This will be further elucidated upon in section 3.1.8. The sensor data is easy to collect and analyse outside of the laboratory, rendering it appropriate for inpatient and home-based monitoring.[257] They provide a more comprehensive understanding of upper limb functional outcome when combined with conventional clinical evaluations. Nonetheless, surrogate markers have inherent limitations, as association does not imply causation. Measurements of upper limb activity should be regarded as indicators of impairment rather than replacements for clinical evaluation. Moreover, measurement of upper limb activity will not be equally sensitive for all individuals with upper limb impairment, as there are individual variations. For example, wearable sensors are not going to recognise the presence of lymphoedema in patients who only experience arm heaviness (which is one of the initial symptoms) and maintain normal upper limb activity. Additionally, the shoulder is a complex joint, where posture can influence upper limb functionality, thus may be affecting upper limb activity.[258,259] Certain postures can induce muscle imbalances, resulting in some muscles being hyperactive while others weaken, hence impairing performance in activities necessitating coordination and strength in the upper limbs.[260] Suboptimal posture, including hunching or slouching, can lead to muscle fatigue and tension, potentially affecting range of motion and activity level.[259]

3.1.6 Enhanced Recovery After Surgery

Enhanced Recovery After Surgery (ERAS) is a comprehensive evidence-based approach to perioperative management that involves multiple disciplines and modalities involving the surgeons, anaesthetists, nurses and physiotherapists.[261] Since it was first described by Kehlet *et al.,* in 1999,[262] the ERAS guideline has been implemented in numerous major surgical operations, including bariatric, gastrointestinal, orthopaedic, vascular, breast or breast reconstruction surgery. This implementation has resulted in decreased postoperative complications and a shorter hospital stay.[263-267]

For example, The ERAS Society published the ERAS guideline specifically for breast reconstruction surgery in 2017 which described 18 care elements in the pre-, peri- and postoperative periods,[268]

following the first ERAS landmark study that demonstrated a decrease in opioid consumption and duration of hospital stay.[269] The implementation of ERAS in the breast reconstruction cohort has been the subject of numerous studies since then. Pierzachajlo *et al.,*[270] conducted a systematic review and meta-analysis that examined 14 studies with a total combined of 2102 patients. The review concluded that the ERAS pathway in DIEP breast reconstruction is consistently linked with shorter hospital stays, reduced opioid use, and lower patient expenditures. Furthermore, in appropriately selected patients, discharge within 24–48 hours is safe after undergoing DIEP reconstruction surgery.[271]

Table 3-1 illustrated an ERAS recovery protocol that is implemented after breast reconstruction surgery in Imperial College Healthcare National Health Service (NHS) trust. Continuous innovation is necessary to improve processes as ERAS principles are implemented in all surgical specialities. Although the advantages of ERAS are widely acknowledged, a significant criticism is that the implementation of ERAS programme is challenging, necessitates a substantial time investment for complete implementation, and it can be difficult to consistently adhere to the required standards.[270] One significant component of the ERAS protocol is the early mobilisation and postoperative exercises, which are essential for improving recovery. As part of the NHS long-term care plan, the NHS has taken deliberate measures towards a new model of care that emphasises prevention and community-based care management.[272] This transition has progressively positioned patients at the forefront of their own care, facilitated and empowered by technology. A technologically advanced and objective instrument can be utilised to monitor and evaluate the progress of patients' recovery.[272] This tool can be incorporated as a supplementary component of the ERAS protocol, with the aim of monitoring and encouraging patients to perform the recommended postoperative exercises. It is imperative to conduct research on the more efficient implementation of the ERAS protocols in order to further improve hospitals' readiness to adopt the protocol and to continue optimising patient outcomes.

Day 1	Day 2	Day 3	Day 4
Post-operative bloods	Trial without catheter am	Offer suppository/enema if not opening bowels	Home with drains if still not discharged
Oxygen off	Mobilise as tolerated	Aim home with or without drains	
IV fluids down	Bra on		
Seen by physiotherapist and sit out for lunch	Shower if able		
Arm exercises			
Bair hugger off pm			
Flowtrons off			
Remove drains <30ml/24h			

Table 3-1 ERAS protocol for breast reconstruction surgery at Imperial College Healthcare NHS Trust

3.1.7 Outline of Clinical Problem and Potential Solution

Based on the meta-analysis in chapter 2, the current methods (Table 3-2) of assessing upper limb morbidities are not standardised and many of the validated tools are mainly subjective and the results can be inconsistent.[27,273] The frequently used patient-reported outcome measure (PROMs) in breast surgery includes DASH[185] questionnaire to assess upper limb function, BREAST-Q[274] to assess the satisfaction and quality of life after breast surgery and The European Organisation of Research and Treatment of Cancer's Quality of Life Questionnaire (EORTC QLQ)[275] to assess quality of life. PROMs are a well-known instrument for collecting data that objective measurements had previously overlooked.[9] Ultimately, PROMs allow patients to assess the impact and the effectiveness of the intervention. This is in contrast to objective metrics, which are derived without account for the patient experience in an unbiased manner.[9] However, the use of PROMs might result in a low response rate,

which can result in response bias since some patients may not recognise the advantages of their involvement. A systematic review demonstrated that response rates in trials using BREAST-Q varied from 32% to 100%.[276] Due to the subjective nature of PROMs, there are concerns about the validity of the results. Some patients may purposely over-report or under-report their symptoms making the assessment more challenging. Recall bias may influence the validity of PROMs if the recall period chosen is too long for respondents to correctly recall their experience. On the other hand, a recall period that is too brief could not provide enough time for a meaningful outcome to develop or resolve.[277,278] Some patients may also experience "telescoping," in which they mistakenly recall a significant event that might be more important to them than minor symptoms, which could potentially introduce recall bias.[278] PROMs could also be influenced by patients' backgrounds and their level of education.[277] Furthermore, based on a scoping review, only 45.5% of the studies reviewed used a PROM that was specifically validated for the country and/or language of administration, which limits the utility of these studies among populations in low- and middle-income countries who do not speak English.[279]

There are various methods of measuring lymphoedema including tape measurement, bioimpedance spectroscopy, volumetry, perometer, tonometry and MoistureMeter.[8,27] According to a systematic review conducted by Hidding *et al.,*[8] the first four methods are recommended for use in a clinical setting since they have demonstrated good reliability and validity. During the initial phases of lymphoedema (stage 0- early stage 2), bioimpedance spectroscopy is more effective than volumetric measurement devices at detecting changes in the amount of extracellular fluid before swelling becomes apparent.[8] However, for later stages of lymphoedema, volumetry and tonometry are the most suitable options.[8] Although these metrics are beneficial for assessing lymphoedema, they do not reflect functional morbidities. Furthermore, bioimpedance spectroscopy is costly, and the volumeter requires major storage capacity.[8]

Goniometry and inclinometer are the most frequently used methods for measuring range of motion, while dynamometers are often used to assess upper body strength. Goniometry for example is reported to be reliable and repeatable and measures the range of motion in degrees (flexion, abduction, external

rotation and internal rotation).[280] The shoulder is a complex joint, comprising a system of interconnected joints, including the glenohumeral, sternoclavicular, scapulothoracic, and acromioclavicular joints. This complexity makes precise geometric measurement difficult, as isolating the motion of a single joint for measurement proves challenging, particularly with conventional geometric techniques.[281] Geometric measurements might also be user-dependent and do not always account for patient's premorbid function.[2,8] These assessments are also difficult to perform in clinical setting and need to be done by someone who is specially trained.[8] Whenever feasible, it is advisable to have the same therapist do the assessments, use standardised method with the same measurement tool and assessed at the same time of day in order to improve the accuracy of the measurements.[282,283] However, achieving this target within the NHS context presents challenges. Additionally, when using these instruments, the impact of hand dominance is rarely taken into consideration.[284] Moreover, existing measurements depend on patients presenting with upper limb dysfunction symptoms in order to identify the condition, causing an underestimate of the true number of patients affected.

Other methods of assessing upper limb function includes self- report and structured interviews which are truly subjective based on patient's experiences. While it is easy to collect self-report data at clinic appointments, similar to questionnaires, patients may either exaggerate symptoms to amplify their symptoms or underreport the severity or frequency of the symptoms to minimise their problems. It is suggested that some patients may under-report their symptoms than warranted in order to appear socially desirable.[285] This is because they are often driven by a desire to avoid embarrassment and the potential consequences of sharing confidential information.[286] While structured interviews encourage consistency in the questions asked, interviewers may influence the answer through using tone of voice and body language.[287]

The visual analogue scale (VAS) is defined by Food and Drug Administration (FDA) as "a line of fixed length (usually 100 mm) with words that anchor the scale at the extreme ends and no words describing intermediate positions".[288] The VAS has been used either independently or in conjunction with other assessment tools to evaluate pain. It is used for the first time in 1921 by Hayes and Patterson and is

commonly used to assess pain in healthcare setting, helping in the management of pain.[289] The VAS is easy to use and do not need specific training to complete. Nevertheless, the evaluation of VAS remains highly subjective and is conducted either through traditional paper and pencil methods or digitally. Consequently, it is not possible to administer it verbally or over the phone.[290] Hence, some people may not be able to use it due to visual or physical impairment.[291]

Functional or social measure is another important indicator of recovery after breast cancer treatment. The ability to return to work is affected by multifactorial factors such as level of education, ethnicity, stage of breast cancer, type of surgery, radiotherapy, chemotherapy, complications related to treatment (upper limb morbidity, fatigue, pain, cognitive impairment nausea and vomiting) or work-related factors including work-place accommodation or discrimination and job type.[292-297] Schmidt *et al.*,[298] reported that in 135 breast cancer survivors, 22% were not working at 1 year after surgery. In those who returned to work, majority of the women had reduced working time and only 27% of the survivors were working full time 5 years after surgery.[298] In another study in Germany of 577 patients, 35.2% did not return to work 40 weeks after surgery.[299] Even though return to work is a good marker of patient's performance status, it is difficult to establish the causality (i.e. to what extent upper limb morbidity is a cause of cessation of work).[299]

Table 3-2 Measures used for assessment of upper limb morbidity following breast and axillary surgery

Measure of Morbidity	**Studies**
Questionnaire Consisting of multiple assessment items to determine patient reported outcome measures (PROMs) related to quality of life, or specific to body function or a clinical condition. (e.g. DASH, BREAST-Q, EORTC QLQC-30, EORTC QLQBR23, SF-36, FACT B+4)	*Arraras[163], Atisha[300], Assis[301], Beaulac[114], Belmonte[81], Bogusevicius[164], Button[161], Blackburn[160], Cattelani[147], Chrischilles[162], Del Bianco[141]. DiSipio[168], Freitas-Silva[139], Hau[169], Hopwood[302], Jassim[167], Koehler[83], Kopec[156], Mansel[100], da Silva[126], Paim[121], Peintinger[143], Perez[159], Rietman[155], Sun[165], Tengrup[131], van Huizum[158], Winters[166], Yang[303], Zhou[152]*

Tape Measurement Used to determine values of arm volume by arm circumference measurements for lymphoedema assessment.	*Abdelhamid[105], Armer[80], Ashikaga[135], Ballal[97], Beek[106], De Groef[133], Del Bianco[141], Devoogdt[151], Donker[40], Duff[96], Faisal[108], Fougo[95], Francis[101], Freitas-Silva[139], Gosselink[138], Golshan[134], Haid[109], Han[102], Hojris[136], Kim[304], Kootstra[130], Kuehn[124], Kuwajerwala[115], Leidenius[145], Lucci[98], Lumachi[110], Mansel[100], da Silva[126], McDuff[41], McLaughlin[119], Nagel[154], Nesvold[13], Olson[104], Ozcinar[120], Paim[121], Paiva[140], Perez[159], Rietman[125], Ronka[103], Sagen[128], Soares[123], Veronesi[99], Voogd[127], Wernicke[122], Wetzig[82], Yue[113]*
Other Lymphoedema Assessment Alternative methods have emerged for better measurement to improve the traditional tape measurement method. (For example bioimpedance spectroscopy, tonometry, volumetry, perometer)	*Beaulac[114], Johansson[112], Koehler[83], Kopec[156], Lopez Penha[117], Yuan[107]*
Range of motion Conducted in the outpatient or emergency setting appointments with various adjuncts to ascertain estimates of mobility, often with repeated measurement over time. (e.g Goniometer, inclinometer, motion capture)	*Abdelhamid[105], Ashikaga[135], Ballal[97], Beaulac[114], Beek[106], Belmonte[81], De Groef[133], Devoogdt[151], Duff[96], Eyjolfsdottir[21], Freitas-Silva[139], Gosselink[138], Johansson[112], Koehler[83], Kootstra[130], Kopec[156], Kuehn[124], Leidenius[145], Lorek[137], da Silva[126], Miaskowski[305], Nagel[154], Nesvold[13], Olson[104], Paim[121], Peintinger[143], Rietman[125], Ronka[103], Sagen[128], Soares[123], Sowa[157], Tengrup[131], Voogd[127], Woo[16], Zhou[152]*
Strength e.g. Dynamometer	*Beaulac[114], Belmonte[81], De Groef[133], Eyjolfsdottir[21], Johansson[112], Kootstra[130], Monleon[150], Miaskowski[305], Perez[159], Rietman[125], Sagen[128], Sowa[157], van Huizum[158]*

Self-report Documentation of problems/outcomes reported by patients in follow up appointments.	*Roy*[142], *Burak*[306], *Lauridsen*[307], *Liljegren*[308], *Veronesi*[99], *Isaksson*[309]
Structured Interview Qualitative assessment of outcomes in devised sessions by healthcare professionals, usually with a pre-set guide of questions addressing various psychological, social and physical parameters. (e,g face-to-face, telephone interview)	*Husen*[111], *Toledano*[310], *Fehlauer*[311], *Yen*[312], *Ruddy*[313]
Pain Subjective assessment of pain e.g Visual Analogue Scale (VAS) or Numerical Rating Scale (NRS)	*Bruce*[149], *De Groef*[133], *Del Bianco*[141], *Devoogdt*[151], *Eyjolfsdottir*[21], *Gosselink*[138], *Koehler*[83], *Leidenius*[145], *Lee*[153], *McCarthy*[146], *Miaskowski*[305], *Nagel*[154], *Rietman*[125], *Rietman*[155], *Ronka*[103], *Sagen*[128], *Tengrup*[131]
Functional/Social Measure Assessment of ability to conduct everyday tasks and activities. (e.g ability to carry out activities of daily living, ability to return to wok)	*Johnsson*[314], *Musti*[315], *Soderman*[316], *Ballance*[222], *De-Santo Madeya*[317], *Hurria*[318], *Repetto*[319], *Ogce*[320], *Johnsson*[297], *Molina*[321]

Currently, the responsibility for identifying upper limb impairment early lies with the patient, who must directly communicate their needs to their surgeons. As a result of this reactive strategy, a significant number of patients are not receiving the essential survivorship care they need following their treatment. Prior research study demonstrated that approximately 90% of individuals undergoing treatment for breast cancer necessitate some degree of physical rehabilitation. However, unfortunately less than 30% of these patients actually receive the necessary treatment.[322]

To help fulfil the clinical challenges above, the system should be scalable (available to large patient cohorts), adaptable (flexible protocols that account for case-specific differences), resource-efficient

(cost and time), applicable in both clinical and community settings, and holistic, integrating both subjective and objective data. Furthermore, in order to implement intervention early, the system should be able to identify patients who are at risk or are developing complications in real-time.

This can be achieved by using WAMs where objective assessment of upper limb activity can be measured in a non-obtrusive manner and in free living conditions. An objective, longitudinal assessment of upper limb activity across the post-operative period using WAMS, would allow for both patient and surgeon to have better insight into the upper limb recovery associated with their surgery. Objective assessment would also give the opportunity to highlight vulnerable patients that would benefit from early exercise intervention or physiotherapy. Ultimately, the development of a personalised rehabilitation programme based on a patient's surgery type and individual objective assessment could then follow.

3.1.8 Wearable Sensor-Based Assessment

Technological advancements and high-quality research are transforming healthcare norms. As patient expectations rise, the public expects access to cutting-edge treatments. As the population grows and healthcare demands increase, it is crucial to develop sustainable healthcare technologies and policies. The ability to safely relocate appropriate healthcare services to the community environment is critical, allowing patients to take a more active part in their own management.[272] Furthermore, continuous patient monitoring strategies are likely to improve conventional episodic clinic-based recordings of patient's physiology.

Undergoing a period of functional rehabilitation is crucial after surgery or hospital stay.[4] The goal is to ensure that patient will resume their standard activities of daily living and restore their optimum quality of life. Following a surgical procedure, patients are generally instructed to perform exercise or rehabilitation activities in their own homes. It is plausible that a structured and timely recovery to a high functional level will reduce the time off work and prevent future complications and healthcare

expenditures. An accurate objective assessment of function may facilitate a more rapid recovery and enable the identification of patients who require additional assistance.

There are different types of WAMs that can measure parameters of human body movement using different mechanisms:

- ◊ Goniometer
- ◊ Gyroscope
- ◊ Accelerometer
- ◊ Pedometer
- ◊ Magnetometer
- ◊ Inertial measurement units (IMUs)
- ◊ Kirigami-based sensor (Strain sensor)
- ◊ Motion capture

Goniometer

A goniometer measures the range of motion in a joint and it needs to be done by a trained clinician. It is usually used to measure the range of motion of the shoulder, knee, ankle and wrist.[282] Physical therapists have been measuring range of motion with the traditional universal goniometer tool for many years. However, goniometry presents several limitations, such as inter-rater reliability influenced by discrepancies in experience and techniques, the requirement for two-handed operation and stabilisation complicating precise alignment, subjective visual estimation susceptible to error, and the incapacity to measure certain type of movements due to the complexities of the shoulder joint.[323-326] The goniometer has been incorporated into wearable technologies and smartphone applications such as the Dr. Goniometer and Simple Goniometer app. For example, Ishida *et al.,*[327] developed a wearable goniometer sensor controlled by a mobile application. They reported that this wearable is a valid and reliable tool for measuring knee flexion angle during gait especially during the stance phase.[327] However, it is limited by its bulky size and is attached to the lateral side of the knee using double-sided

tape and elastic tape. Tognetti *et al.,*[328] developed a wearable goniometer using e-textiles and low-cost inertial sensing. Similar to the former study, the bulkiness and tightness of the sensing material used may increase the risk of lower compliance in the patient population.

Gyroscope

A gyroscope detects the angular velocity of an object where it determines its tilt or lateral orientation.[329] A rotor, which is a disk that freely rotates, is positioned on a spinning axis in the centre of a bigger and more stable wheel.[330] As the axis rotates, the rotor remains fixed to represent the gravitational attraction at the centre and, thus determine which direction is "down." Angular velocity is the change in the rotational angle of an object per unit of time (measured in degrees per second).[330] Nevertheless, the measurement accuracy is compromised by elevated temperature and electronic noise.[330] The progressive accumulation of error, which is frequently referred to as drift, is the result of the integration of these faulty signals.[331] Najafi *et al.,*[332] demonstrated that the gyroscope sensor is a promising instrument for assessing the risk of falls in the elderly. The study, which conducted a comparison between two groups of elderly people categorised by their fall-risk levels, found a significant correlation between the computed parameters and the risk of falling.[332]

Accelerometer

Accelerometers are wearable sensors that detect the accelerations along reference axes of objects in motion. Accelerometers have been investigated to measure upper limb activity in patient population such as stroke and multiple sclerosis.[333,334] Typically, acceleration is expressed in terms of two or three axis-vector components, which comprise the sum/net acceleration. The accelerometers can work in 3 different ways:

- Piezoelectric effect – it employs tiny crystal formations that are stressed as a result of accelerative pressures. The stress causes these crystals to generate a voltage, which the accelerometer analyses to measure velocity and direction.[335,336]

- Piezoresistive sensor – there are silicon resistors that change their electrical resistance when subjected to a mechanical load. This generates an electrical potential that is directly proportional to both the magnitude and frequency of the acceleration.[337,338]
- Capacitance sensor – the capacitor has a mobile plate sandwiched between two stationary plates. The centre plate undergoes deflection as a result of acceleration, which in turn causes a change in the capacitance. Therefore, the acceleration may be determined.[339]

Pedometer

A pedometer is an activity monitor that counts each step a person takes by detecting movement along the long axis of the body.[340] Recently, these wearable activity trackers have gained popularity for encouraging people to be more active and tracking activity among those with a variety of chronic conditions, such as diabetes and musculoskeletal disease.[341,342] The gadgets are simple, reasonably priced and easy to use. It employs a spring-loaded mass or other switch mechanism to detect impacts caused by steps during locomotion, allowing the number of steps to be recorded to determine the distance travelled and the energy expenditure.[343] However, a major disadvantage is that it is unable to determine the intensity of movement, making it unable to precisely measure energy expenditure.[344,345] It is also not sensitive to non-ambulant activity such as cycling or swimming.[346] Pedometers are used in many fitness trackers such as FitBit and smartphones, enabling step count measurement and could be used to motivate physical activity.

Magnetometer

Magnetometers determine an absolute position in relation to magnetic north by measuring the local magnetic field. However, the presence of ferromagnetic materials, such as iron in close proximity to the sensor will disrupt the local magnetic field and thus result in significant inaccuracies in the estimated orientation.[347,348]

Inertial measurement units (IMUs)

Inertial measurement units (IMUs) use a variety of systems, including accelerometers, gyroscopes, and occasionally magnetometers,[349] to report the angular rate and particular force/acceleration experienced by the object they are attached to. Multiple sensors are typically placed in similar or different body parts.[63] The IMU sensors may also incorporate 3 different sensors into one system.[63] The combination of sensors improves the accuracy of readings compared with utilising a single sensor.[349] This system may require assessment within the lab settings and the camera systems are costly.[350]

Kirigami-based sensor (Strain sensor)

Smart textile systems are becoming an increasingly important wearable technology in different fields, including healthcare, the military, and aerospace.[351,352] A newly-invented sensor that is based on closed-shape, planar, rotationally symmetric kirigami sheets where strain sensors can be placed on the alternating local curvature enable quantification of shoulder joint movement.[353] Evke *et al.,*[353] demonstrated that symmetric kirigami structures can closely conform to surfaces with complex 3D curvature. The strategically positioned sensors inside these structures (cross-referenced by a camera motion tracking system) may be able to effectively track and monitor the movement of a complex shoulder joint.[353]

Motion capture

Motion capture is an emerging new method used to assess the range of motion in human joints.[354] It is a more efficient method for assessing human range of motion than the conventional goniometer. There are marker-based motion capture systems with reflective skin markers to significantly improve measurement accuracy. Nevertheless, the marker-based motion capture systems are subject to a number of limitations, such as the requirement for a controlled environment and ample space, interference with participant movement, and the inconvenience of marker attachment.[355,356] Markerless motion capture systems have been developed as alternatives for conventional methods. For example, the Microsoft Kinect employs camera systems that integrate a red, green and blue (RGB) sensor for recording colour images and a depth sensor, capable of producing detailed three-dimensional (3D) representations of the

environment and may correctly identifying joint positions and measuring shoulder kinematics.[354,357,358] A systematic study and meta-analysis conducted by Beshara *et al.,* revealed moderate to good intra- and inter-rater reliability for assessing shoulder range of motion.[357]

3.1.9 Accelerometers

As previously discussed in section 3.1.5, upper limb activity was chosen as a surrogate marker for assessment of upper limb impairment. The primary goal of this research study is to quantify the activity levels of the upper limbs. IMU sensors measure the angles, velocity, and orientation of the upper limb's movement. Therefore, for the purpose of this thesis, accelerometers were chosen over IMU sensors, as they are the simplest devices to achieve the goal of the study, which is detecting upper limb activity levels without the need for extra sensors such as gyroscopes and magnetometers. When the scientific research question or rehabilitation intervention is targeted at modifying the general upper limb performance in daily life, such as the amount of upper limb activity performed and the involvement of bilateral upper limbs in daily activity, the accelerometer will be the most effective tool.[359] Furthermore, IMUs may also need placements of multiple sensors at different locations, which may affect patient compliance.[63,360] Some of the IMU sensors may also require analysis in the laboratory settings.[360] There are also significant challenges in developing algorithms that can accurately estimate shoulder joint angles based on IMU measurements of acceleration and angular velocity.[360] Many commercial IMU systems do not have robust sensor synchronisation between all the sensors, causing problems with long, free-living data collections.[360] Tri-axial accelerometers, on the other hand, are appropriate for inpatient and home monitoring due to their compact size and the use of a single sensor. They have previously been validated in evaluating performance of upper limb activity in neurologically intact adults and in stroke patients.[361-363] It is crucial to acknowledge, however, that it does not provide information regarding the quality of movement or the specific activities that are carried out during the wearing period.[359] Over the years, advancements in wearable technology have led to the development of numerous low-cost, compact IMU sensors with integrated systems that could be used in future studies.

Accelerometery allows for the assessment of upper limb activity in real-world settings, capturing individuals' actual activities outside of clinical or laboratory settings, rather than merely their potential capabilities.[251] The primary output of an accelerometer is quantitative data, which can determine the frequency, duration, and intensity of an activity. Accelerometers record mechanical movement (acceleration changes due to body movement). They were first studied in the 1950s,[364] and their popularity increased in the 1970s[365] as a result of the development of micro-electromechanical system (MEMS) technology, which decreased the cost, improved sensor performance, made it available in smaller forms and decreased power consumption. Modern accelerometers use relatively small current, allowing data to be continually logged for days, weeks, or even months.[366] This approach has the advantage of being able to monitor upper limb activity in daily life over an extended period, which may offer a more reliable indicator of the degree of upper limb activity than a single time point clinical examination.

There were many studies investigating the use of accelerometers in stroke patients and those with neurology deficits.[361,367-370] For example, Bezuidenhout *et al.,*[334] demonstrated that accelerometer-based assessment is a valid method in distinguishing upper limb activity between healthy controls and individuals post stroke. Even among those who did not perceive any issues with upper-limb activity in daily life, the study showed that individuals post-stroke used their paretic arm less frequently than their non-paretic arm.[334] This suggests that the evaluation of upper limb activity using accelerometers was able to identify discrepancies in arm function that were not detected by clinical assessment or self-perceived ability. Accelerometery data has also demonstrated convergent validity, where there was an agreement between accelerometery activity and standardised measures of upper limb function, such as the Fugl-Meyer Assessment of Upper-Limb Function and the Action Research Arm Test.[371-373] Additionally, a study investigating patients with multiple sclerosis found that there was a decline in upper limb activity as the level of impairment worsened. This was supported by a significant association between the raw accelerometric counts and the Expanded Disability Status Scale score.[333]

The majority of the research mentioned above have positioned their accelerometers on both wrists (affected and non-affected arms). Accurate positioning of the WAMs is crucial in order to generate reliable data for the location being examined. The location of the accelerometers, its orientation, the subject's posture, and the activity being performed are the four parameters that affect the data generated from the accelerometer.[374,375] Accelerometery measurements of upper limb activity during everyday routines in a hospital or at home have the potential to provide additional insight into breast cancer surgery recovery.

3.1.10 Wearable Activity Monitor Placement

The placement of the WAMs on different parts of human body depends on the movement being studied (Figure 3-2). The practicability of WAM placement in a clinical study is an essential factor.[376] In order to improve compliance and that the WAMs are worn continuously, they must be in a position that is comfortable and allows for reproducibility within and between participants.[377] It should also be positioned to account for gravity and other noises caused by external movements. Numerous studies have combined numerous accelerometers at various positions on the body to improve the reading and contextual information.[376] Commonly, the sensors are placed on the sternum, lower back, or waist to monitor whole-body movement. Gjoreski *et al.,*[378] found that using 2 accelerometers (chest and waist) was more accurate than using 1 alone for recognising posture by over 90%, but using 3 or 4 instead of 2 made only a small difference in accuracy. However, increasing the number of sensors may influence data collection due to compliance issues. It can also increase the complexity of the classification problem.[376]

For these reasons, further research is being conducted to determine which position on the body gives the most relevant information to measure specific activities using a single accelerometer. Accelerometers worn at the waist may detect a variety of fundamental everyday activities, including walking, activity transitions, and postures.[379] Ankle-mounted accelerometers can monitor steps, distance, velocity, and energy expenditure.[380] Research on gait detection for limb impairment indicates that the optimal sensor placement may not correspond to the location of the symptoms or abnormalities

being assessed.[208,381] Head-worn sensors provided the best position for gait feature recognition rather than placement on the legs. For example, the e-AR sensor is worn behind the ear to measure gait, both in healthy individuals and in individuals who have had knee surgery.[208,381] This location was chosen because the head moves when people walk, but it moves less than the limbs because the neck and trunk provide stability. Hence, it is more representative of the human gait.[382] Attalah *et al.,*[383] investigated ideal sensor location for a given group of activities. Activities such as housework involving wiping tables and vacuuming are best detected by chest or wrist sensors where as high level activities such as walking, cycling and running can be picked up by ear-worn, arm and knee sensors.[383] Nevertheless, some studies[376,384,385] showed that the position of the WAM did not significantly affect its finding. Heil *et al.,*[385] studied three sites for WAM placement (ankle, hip, wrist) and reported that they offer comparable physical activity outcome measurements.

Wrist-worn tri-axial accelerometers have been validated to measure upper limb activities in previous studies.[386-391] For this reason, accelerometers worn on the wrist are selected to assess upper limb activity. Whilst the sensors are located on the wrist, it does not only measure wrist movement. They also capture gross arm and forearm movements.[392] In theory, the wrist movement almost always require movement of the muscles of the forearm attached to the humerus. A previous study demonstrated that there was a good correlation between the activity data measured by accelerometers positioned on the upper arm and on the wrist.[393] Moreover, data suggests patients are more likely to adhere to wrist-worn WAMs if they are positioned on the wrist akin to wearing a watch.[394] Therefore, a wrist-worn tri-axial accelerometer was chosen for my PhD study.

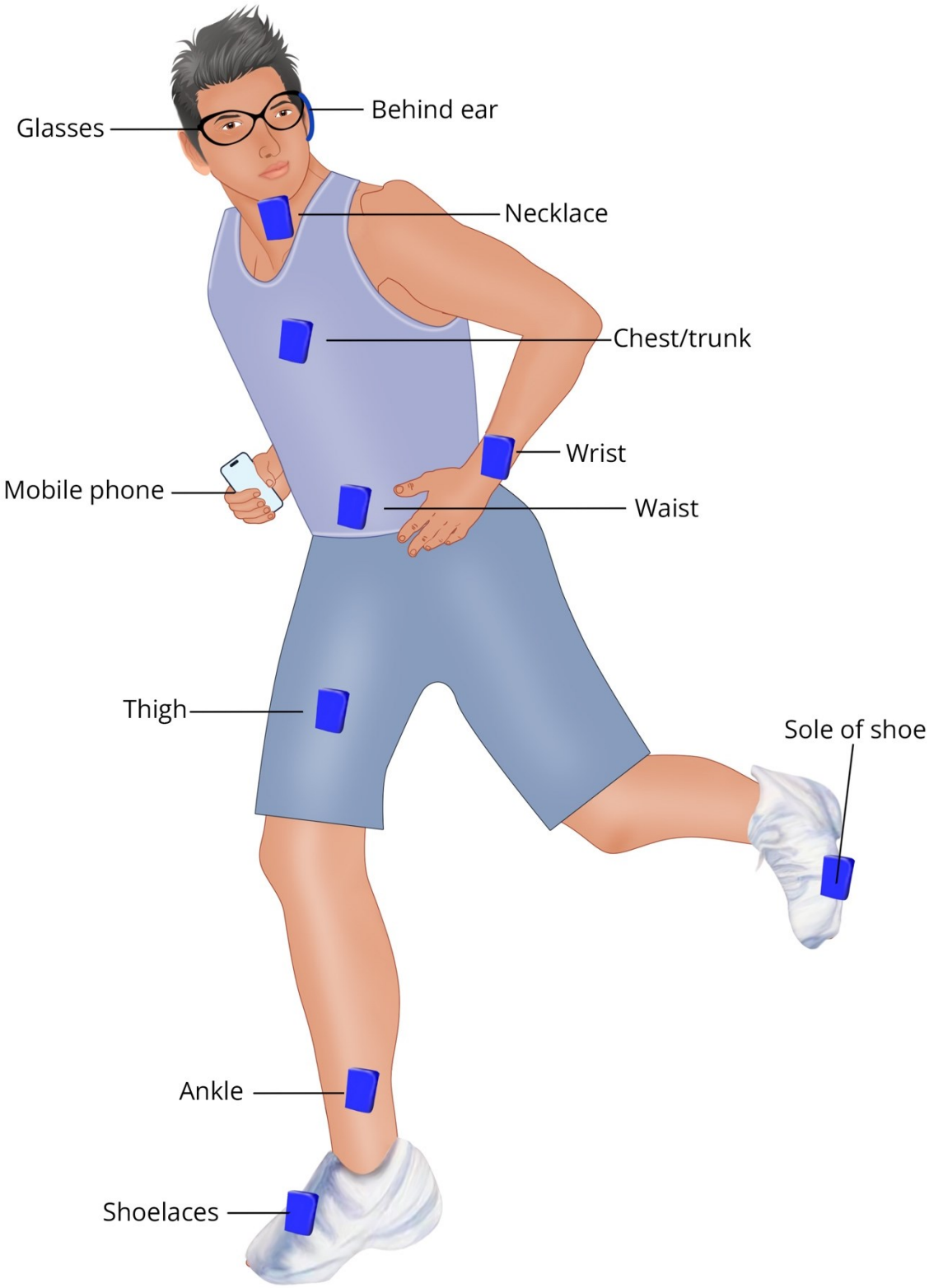


Figure 3-2 Wearable sensor placement – e.g. glasses, behind ear, necklace, chest/trunk, wrist, mobile phone, waist, thigh, sole of shoe, ankle, shoelaces (The figure was created by Mohesh Mohan, used with permission)

3.1.11 Acceleration Signal

Accelerometers quantify the movement of the upper limb by measuring its acceleration. Acceleration is the rate at which an object's speed changes over time. Acceleration is commonly quantified using gravitational acceleration units (g), where 1 g is equal to 9.8 m/s2. The measured accelerations are dependent on the activity being performed.[395] Accelerometery data can also be measured as counts.[395]

An accelerometer's output when the subject is at rest is based on how it is oriented with respect to the gravitational vector. If the accelerometer's orientation in relation to the subject is known, it can be used to determine the subject's orientation in relation to the vertical direction (gravity). When the subject is in motion, the resulting signal is a composite of the subject's orientation and movements.[395] The signal is influenced by various factors, including the movement of the body itself (which is the primary contributor) and the movement of soft tissues or external vibrations (e.g travelling in a motor vehicle). The presence of these artefact signals can be reduced by strategically positioning the instruments and implementing signal filtering techniques with a cut off frequency between 0.1 and 0.5 Hz.[395-397]

Sampling frequency is defined as the rate at which data are collected.[359] A sampling frequency of 100Hz indicates that 100 measurements of acceleration are recorded each second. A higher frequency results in a higher number of data points being collected, and often, a higher sampling frequency is used to allow detailed capture of movement, especially for rapid or high-frequency motion. The sampling frequency also affects battery life. There is an inverse relationship between sampling rates and recording time on the device - greater sample rates result in lesser recording duration, and vice versa.[398]

Once the data has been captured, the sensor output is subjected to filtration using a band pass filter. Band pass filtering selectively permits frequencies within a predetermined range, bounded by a lower and upper frequency limit, to pass through, while suppressing or reducing the amplitude of all other frequencies.[399] An excessively broad bandwidth might permit the inclusion of non-physiologically related noises (e.g external vibrations or electrical noise) in the signals. Conversely, a narrow bandwidth may result in insufficient data collection of the activities of interest.[399] Therefore, a decision must be

made regarding the appropriate sampling frequency and bandwidth filters to be used in accordance with the duration of the recording and the nature of the activities being monitored.

3.1.12 Acceleration Output and Data Analysis

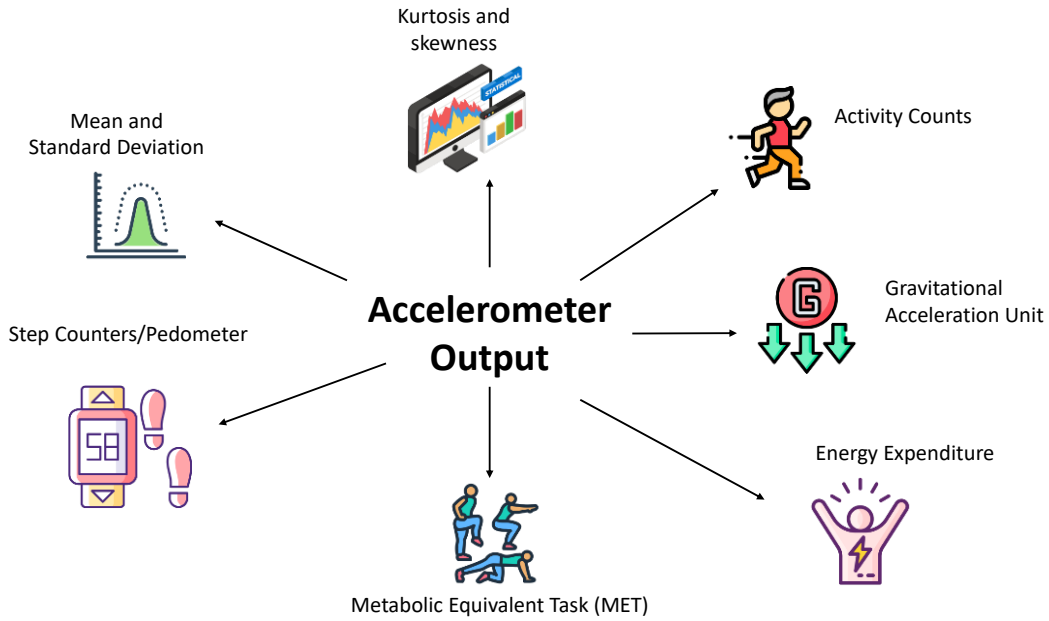


Figure 3-3 Accelerometer output and data analysis

The raw accelerometer data can be converted in a variety of ways to provide useful outputs for measuring physical activity (Figure 3-3). Each of them has advantages and disadvantages, and the best metric for a specific study must be selected to support the objectives of that investigation.

One simple way to analyse accelerometer data is by measuring the mean and standard deviation which can distinguish the static state and the dynamic state.[400,401] Other techniques include kurtosis, which measures how much a distribution is peaked at its centre, and skewness, which measures the degree of asymmetry in the acceleration data distribution. They may be able to discriminate between various physical activities such as sitting, standing, running, walking, and lying supine, although they are not always sufficient on their own for accurate activity recognition.[400,401]

As previously discussed, the raw outputs of accelerometer data can be analysed as activity counts or as a gravitational equivalent. The gravitational equivalent (raw data) analyses are conducted using open-source software, resulting in increased transparency and improved comparability among studies.[402] When analysing counts, accelerometery sensors show bidirectional behaviour, meaning they can produce both positive and negative values. The voltage signal is first filtered and amplified, and then it is sampled at a predetermined frequency by the device to transform it into a digital series of numbers, known as "raw counts."[399] The sum of each digitised signal is calculated over a user-specified time interval (epoch), such as 60 seconds. Therefore, the average physical activity counts per minute can be used to express activity counts, which is a measure of acceleration over time.[403] Nevertheless, it is challenging to make a direct comparison between count numbers obtained from various accelerometer brands due to the fact that manufacturers use different undisclosed algorithms to determine the acceleration outputs.[404]

Everyday activities often necessitate movement across numerous axes simultaneously, rather than just a single axis. Consequently, information from two or three axes can be merged to form a vector magnitude, a single measurement that quantifies the amount of acceleration that took place at a specific moment, regardless of its direction. The most common equation to transform reading from multiple axes to a single signal vector magnitude (SVM) is SVM = : $\sqrt{(x^2 + y^2 + z^2)} - 1$.[395]

Another way of analysing the accelerometery data is the amount of time spent at different intensity level bordered by cut points (count thresholds) to enable the frequency of sedentary, light, moderate and vigorous activity to be recorded. These thresholds are derived from metabolic equivalent (MET) expenditure or maximum volume of oxygen (VO2) in a lab setting that reflect thresholds for specified levels of physical activity.[405-407] There are different cut point thresholds for different population based on their age (e.g adult, adolescents, older adults).

Furthermore, energy expenditure (EE) is the amount of energy expended during physical activity and is an important indicator of the physical activity level.[408] A recent meta-analysis conducted by Wu *et*

al.,[408] has concluded that Actigraph tri-axial accelerometers are a reliable alternative for indirect calorimetry, which is the gold standard for measuring EE. Nevertheless, the precision of energy expenditure measurement can vary based on the type of activity and the specific algorithm applied to interpret the data.[344,408] Additionally, the use of accelerometers to assess EE was inaccurate for obese/overweight individuals.[409] Various equations are used to estimate EE, and these equations are tailored for diverse populations based on their unique characteristics during physical activities.[408,410,411]

Step counters or pedometers are another output of accelerometers that have increased in popularity over the last decade due to commercially available sensors such as FitBit and AppleWatch. A recent systematic review and meta-analysis found that interventions using wearable activity trackers led to significant improvements in physical activity compared with control groups. On average, these interventions resulted in an additional 1800 steps per day, 40 minutes more of walking per day, and a 6-minute increase in moderate to vigorous physical activity (MVPA) per day.[412] While walking or running, there is a regular pattern of acceleration that conforms to a sinusoidal waveform. This pattern encompasses both positive and negative accelerations, which manifest at different phases of the ambulatory cycle which are then used to estimate the total number of steps taken.[413]

3.1.13 Wearable Activity Monitors Used in Surgical Setting

WAMs have been increasingly used to monitor post-operative patients in surgical specialties such as orthopaedics, vascular and colorectal surgeries.[64,381,414] The motivation for their use is to improve the quality of life and outcomes by measuring, monitoring, and providing feedback on levels of physical activity in order to enhance recovery.[187,212]

WAMs have the potential to predict 30-day readmission rates as well as the length of hospital stay. Kane *et al.,*[414] conducted a study on 94 patients who had undergone major colorectal surgery and found that physical activity, measured using wearable technology, can be used to predict 30-day readmission. They observed that a 10% increase in the return to baseline percentage of physical activity was associated with a 40% decrease in the risk of 30-day readmission.[414] Furthermore, Daskivich *et al.,*[415]

examined the relationship between daily ambulation measured by wearable activity monitors and the length of stay among patients undergoing major surgery (e.g gastric bypass, hip replacement, robotic cystectomy, lung lobectomy and abdominal hysterectomy). The findings indicated that a higher step count up to 1000 steps on the first day after surgery, was linked to a reduced likelihood of an extended hospital stay.[415]

Another study investigated the correlation between postoperative complications and physical activity following hepatectomy by using accelerometers.[416] In patients whose activity level increased (upward slope) after surgery had a very low rate of complications (4.5%) whereas patients who demonstrated a pattern of initially increasing and then decreasing activity levels (resembling a bell curve) had a higher likelihood of experiencing complications (76.9%), such as refractory pleural effusion or ascites, as well as surgical site infection.[416] On the other hand, patients whose activity levels did not increase after surgery (displaying a flat pattern) were more prone to developing surgical site infection and pneumonia.[416] Similarly, Yehonatan *et al.,*[417] showed that patients undergoing major abdominal surgery who wore ankle pedometers were more likely to experience severe complications if they took fewer steps on the second postoperative day. The findings from these two studies suggest that wearable technology may be used to predict patients who are at higher risk of developing complications post-surgery.[417]

Moreover, WAMs have the potential to be used as part of a personalised treatment plan. An RCT was conducted to assess the effectiveness of using WAMs in patients with intermittent claudication. Participants were assigned randomly to either the intervention group, which received WAMs along with supervised exercise programmes (SEP), or the control group, which simply received SEP.[64] The findings demonstrated that individuals in the intervention group showed substantial improvement in their maximum walking distance at 3, 6, and 12 months in comparison to the control group.[64] WAMs can be used as an adjunct tool to monitor and motivate patients to improve their physical activity. This is possible because WAMs provide tangible data on the frequency with which patients meet their activity goals, in keeping with personalised treatment strategies.[64] The effectiveness of WAMs in

promoting increased physical activity is also influenced by the patient's own behaviour and motivations, which will be further elaborated upon in chapter 9.

In breast cancer survivors, step counts and general daily activities have been the main focus of the majority of studies on WAMs.[207] Previous investigations have demonstrated that lymphoedema and inadequate arm mobility are often linked to inadequate physical activity levels.[418,419] To the best of my knowledge, WAMs have never been used to objectively measure upper limb recovery following breast or axillary surgery, especially monitoring upper limb activities. Objective assessment of upper limb activity is important so that patients and surgeons can have a better understanding of the upper limb activity associated with different types of surgery. This will facilitate the identification of vulnerable patients who could benefit from early interventions, such as physiotherapy, and eventually enable the development of a personalised rehabilitation programme tailored to the specific type of surgery and individual objective assessment. The next chapter will discuss the methodology used in clinical studies described in chapter 5 to 8.

4 METHODOLOGY

This chapter describes the methods used in chapters 5 to 8. The WAMs used in the study are commercially available light-weight (16g), wrist-worn sensors (AX3, Axivity, York, UK) designed by Open Lab, Newcastle University. They are tri-axial Micro-Electro-Mechanical-Systems accelerometer (ADXL345) that measure acceleration of an object along three references axes.

The UK Biobank study[420] collected accelerometery data using AX3 from over 100,000 participants to detect associations of physical activity and health outcomes. This study proves that these WAMs are acceptable to be used in large cohort of participants with high compliance rate and good data completeness. The AX3 tri-axial accelerometer was also used in older population[421] to measure physical activity of participants with a spectrum of mobility. Considering that most breast cancer patients are elderly women, tri-axial accelerometers may be appropriate for this demographic, as they are user-friendly and may be utilised immediately by patients upon receiving them, removing the necessity for device setup. Additionally, as previously discussed tri-axial accelerometers have previously been investigated to evaluate the activities of the upper limbs in stroke patients and those with neurological conditions.[333,334] Consequently, the WAMs have the potential to be employed in a breast cancer cohort to quantify upper limb activities following breast cancer treatment.

The sampling frequency refers to the rate at which the sensor records data, measured in the number of time points captured per second. Table 4.1 illustrates the impact of sample rate on battery longevity and the application of variable sensitivity in various scenarios. The selected sample rate must effectively capture upper limb activity post-breast surgery during daily activities (eg. washing dishes, setting a table, getting dressed) while minimising data storage to prolong battery life. Previous research in stroke populations and patients who underwent arm surgery indicated that a sample rate of approximately 30 Hz is adequate for the detection of the aforementioned activities.[251,334,422] Therefore, the tri-axial accelerometer is configured to 25 Hz in order to provide sufficient detection of upper limb activity post-breast surgery and provide 34 days of battery life for pre- and postoperative monitoring.

High-intensity activities, such as boxing, typically include accelerations of approximately +/-16g, whereas less physically demanding activities, such as painting, usually involve accelerations of approximately +/-2g. In order to be able to capture fine motor movements, low-intensity post-surgical activities and activities of daily living, such as lifting a cup, reaching movement (shoulder elevation) or performing light exercises as patients recover during postoperative recovery, +/-2g was used. This is based on prior studies of patients who are recovering from stroke or engaging in upper limb rehabilitation exercise.[422,423] The selected configurations were deemed suitable given the demographic of the breast cancer population and their potential daily activities after surgery.

A bandpass filter of 0.5-20 Hz[424] was employed to isolate the movement of interest of upper limb activities and eliminate any noise present in the accelerometer signal. This process eliminates irrelevant low-frequency drift that is not considered active movement and high-frequency noise that does not represent actual movement, such as vibrations or sensor artefacts.

Table 4-1 Sample rate and sensitivity

Sample Rate (Hz)	**Typical Battery Life (Days)**	**Low Power Battery Life (days)**
400	5	5
200	9	10
100	14	18
50	21	31
25	34	47

Sensitivity	**Example Use Case**
+/-2g	Fine movements such as painting
+/-4g	Mild activities such as walking
+/-8g	Moderate activities such as sprinting and jumping
+/-16g	Severe activities such as boxing

g: acceleration due to gravity or ~9.81 ms^{-2}

4.1 Methods

4.1.1 Outline

WAMs were used to continually assess breast cancer patients pre-operatively and up to 2 weeks after surgery. In order to determine the patients' long-term upper limb activity, those who were recruited in chapters 7 and 8 were also monitored at greater than 6 months following surgery.

Additionally, 10 healthy participants were recruited as a control for the feasibility study discussed in chapter 5. The data collected from breast cancer patients were analysed in relation to that of healthy controls.

4.1.2 Conducting Prospective Observational Studies

Ethical approval

Before starting data collection, ethical approval was granted by the National Research Ethics Committee London – City Road (Ref: 15/LO/1038) (Appendix 8).

Registration

The study methods were submitted to the ClinicalTrial.gov registry (NCT03635723). The study was registered under 'The Step Home Trial: Utilising Physical Activity Data in the Acute Post-Operative Setting'.

Recruitment and eligibility

Patients scheduled for breast surgery with or without axillary surgery, including wide local excision (breast conserving surgery), simple mastectomy, implant or autologous reconstruction, axillary lymph node dissection and sentinel lymph node biopsy, were eligible for recruitment at Imperial College Healthcare NHS Trust between April 2019 and May 2022. The study was halted from March 2020 to July 2020 due to the COVID-19 pandemic.

They were identified and assessed in line with study eligibility criteria (Table 4-2). There was no restriction placed on age. Patients who had a movement disorder (e.g. Parkinson's disease) or those using a mobility device or aids were excluded, as the results would be confounded by the abnormal movements. Those who could not understand the paperwork provided (after attempted translation/explanation via staff or family members) or could not provide appropriate informed consent were also excluded from the study. Patients who had undergone any additional surgical procedures or had new medical diagnoses that might have a substantial impact on their mobility subsequent to their initial operation were excluded from the long-term data collection discussed in chapters 7 and 8.

Healthy subjects were recruited for the feasibility study in chapter 5 to determine an estimate of natural variation between right and left arm activity in healthy individuals. This may indicate an appropriation of the natural disparity in arms. Any individual who did not have a history of upper limb injuries or surgery were considered suitable for inclusion in the study. The WAMs were worn on both wrists for a 24-hour period.

Table 4-2 Inclusion and exclusion criteria

Inclusion	**Exclusion**
Breast cancer patients undergoing any form of breast surgery +/- axillary surgery*	Patients with a movement disorder (e.g. Parkinson's Disease)
All age groups	Patient using mobility device or aids
	Patient who is not able to understand the paperwork or unable to provide appropriate informed consent**
	Patients had undergone any additional operations or received new diagnoses since their initial operation that would significantly affect their mobility***

* To include wide local excision, mastectomy, implant or autologous reconstruction, axillary lymph node dissection and sentinel lymph node biopsy

** After attempted translation/explanation via staff or family members

*** Additional exclusion criteria discussed in chapters 7 and 8

Data collection

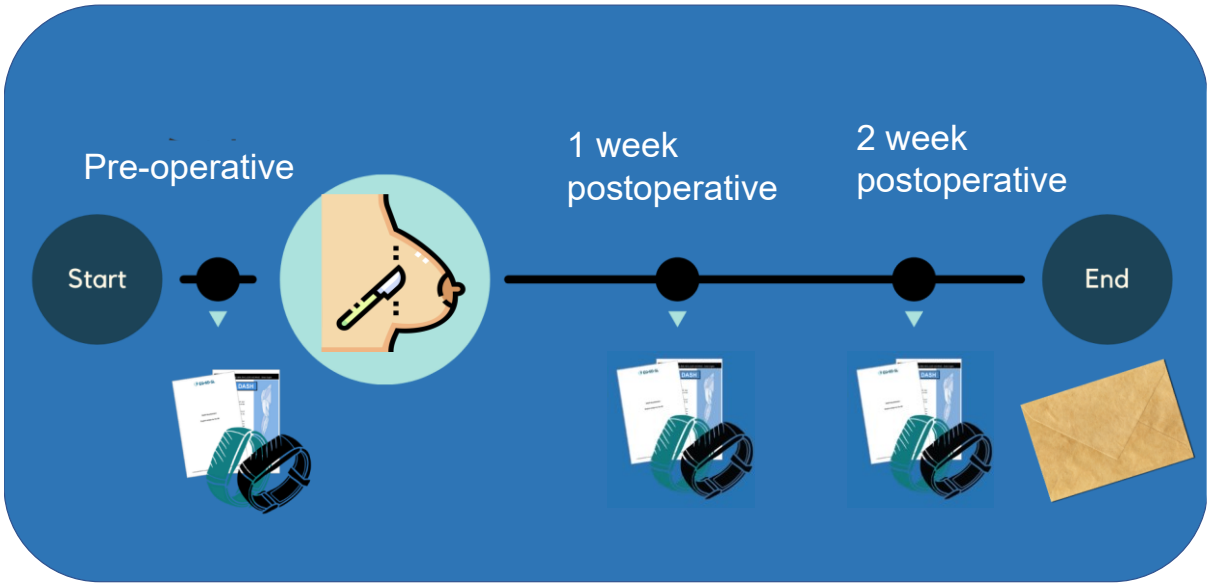


Figure 4-1 Study protocol

The protocol of the study was validated and published.[78] The patients were provided with information regarding the research study by the healthcare team in the outpatient clinics. Patients who met the eligibility criteria were contacted. Following the patient's verbal consent and statement of interest, they were provided with a research information sheet and the protocol was subsequently explained to them. The participants of the study gave their written informed consent.

The patents wore WAMs for 3 days (on average) on both wrists daily before the surgery and again for up to 2 weeks following surgery. Prior studies demonstrated that a minimum of 3 days is required for an accurate assessment of daily physical activity.[388,425,426] They were instructed to wear the WAMs 24 hours a day but were permitted to remove them for sleeping and showering/bathing if necessary. Patients who were recruited in chapters 7 and 8 were also followed up at greater than 6 months following surgery, during which they were instructed to wear the WAMs for 3 days (Figure 4-1). Wristbands were colour coordinated in terms of laterality; black for the left wrist and green/blue for the right wrist. The patients were informed that the WAMs measured arm activity, but no exercise targets were provided. Nevertheless, it is usual practise in our unit to offer all patients with standard postoperative arm mobility

instructions and a Breast Cancer Care brochure on postoperative exercises. The leaflet may be found at [www.breastcancernow.org] (Appendix 7). The patients were recommended to begin arm mobilisation the day after surgery, if possible, and to continue doing so gradually until they were able to regain their preoperative range of motion. If they developed seroma, wound infection/healing issues, or pain that worsened or continued during or after these activities, they were encouraged to stop the activity immediately or contact a doctor.

Patients who had ALND are not required to proactively wear a compression sleeve. Breast cancer survivors who develop lymphoedema or decreased range of motion are referred to a lymphoedema specialist nurse or physiotherapist. Patients undergoing IBR and DIEP procedures in our unit were encouraged mobilisation during the early postoperative period. According to our DIEP protocol, patients who had DIEP surgery were seen by a physiotherapist on the first day after the operation and they were advised to increase their mobility starting from day 1. However, patients are advised against heavy lifting, driving or gym for 6 weeks postoperatively. Drains were usually removed on day 1 and beyond as long as the drain output was less than 30 ml in 24 hours. All patients were advised to maintain their regular mobility despite the presence of drains. No monetary compensation was offered for participation.

Healthy subjects who were recruited in chapter 5 wore activity sensors on both wrists for a continuous duration of 24 hours.

Questionnaires and WAMs were returned at the follow-up clinic or in pre-paid envelopes once the study observations were completed. Commercially available tri-axial accelerometer wrist-worn sensors (AX3; Axivity Ltd,, Newcastle upon Tyne, UK) allow for manual calibration (e.g., data collection frequency and sensitivity), complete data download, and analysis using a bespoke software. The Open Movement Graphical User Interface (OMGUI®) (version 1.0.0.37, Axivity Ltd., Newcastle upon Tyne, UK) was used for calibration and calculations of activity levels using signal vector magnitude (SVM),

a well-established method for merging tri-axial accelerometer data to produce a measurable activity level.[427,428]

All patients were interviewed after (or during) the duration of data collection so they could report any technical difficulties encountered or if the WAMs were removed for any period of time. The patients were asked to complete the validated DASH and EuroQol-5D-5L (EQ-5D-5L)[186] questionnaires before (at the time of recruitment) and after surgery (week 1 and 2 +/- at greater than 6 months postoperatively). The upper limb function is evaluated using 30 questions on the DASH questionnaire, with scores ranging from 0 to 100. The lesser the disability, the lower the DASH score.[185] The validated EQ-5D-5L questionnaire, which includes a descriptive section and a visual analogue scale (VAS) was used to assess health-related quality of life (QoL).[186] The EQ-5D-5L index score was calculated using the EQ-5D-5L Crosswalk Index Value Calculator.[429] Demographic data were collected from the patient's electronic medical records, including age, ethnicity, type of surgery, site of surgery, body mass index (BMI), stage of cancer and neoadjuvant and adjuvant therapy. Patients were asked if they were right- or left-handed or ambidextrous.

4.1.3 Data Processing

The downloaded data were processed using OMGUI® (version 1.0.0.37, Axivity Ltd., Newcastle upon Tyne, UK) to determine the SVM. The SVM is defined as the magnitude of acceleration in three planes (x, y and z).[427,428] This generates a measure of upper limb activity and is calculated using this equation: $\sqrt{(x^2 + y^2 + z^2)} - 1$.[395,427,428] The SVM option was selected for the SVM conversion and 60-second epochs (windows) default filter/mode was used.[427,428] The conversion enabled the calculation of the average activity per minute based on the specific day and time when the patient was observed.

The data were organised into spreadsheets using Microsoft Excel® for Mac (Version 16.28, Microsoft Corporation, Redmond, WA, USA) to facilitate further analysis. A spreadsheet was created to calculate the sum of the left and right values of SVM for each patient daily. A spreadsheet was created to collate

all patient SVM computations, and the numbers were organised in a way suitable for entry into Statistical Package for Social Sciences (SPSS) for Mac (Version 26, IBM, Armonk, NY, USA).

The pre-operative level of SVM was obtained by calculating the mean SVM value throughout the days preceding the surgical procedure. The upper limb activity of the ipsilateral treated side was measured to determine the activity level of the arm on the surgically treated side. The upper limb activity of the contralateral side was measured to determine the activity level of the arm on the non-surgically treated side (control). The SVM for left and right arm were combined to determine the gross upper limb activity levels. The upper limb activity was determined for each postoperative day (POD) by calculating the percentage of the average preoperative SVM level (SVM for each postoperative day/mean preoperative SVM x 100).[78]

For data analysis in chapter 5, the mean percentage difference (± standard deviation) between arms (right and left) in the population was estimated along with a "hand activity ratio" and comparisons across surgical treatments. The hand activity ratio was calculated by dividing the quantity of activity in one arm by the sum of both arms' activities. The hand ratio of 0.5 for each arm indicates an equal distribution of arm activity between the right and left arms. A hand ratio greater than 0.5 indicates an increase in activity in that arm, and vice versa. A patient who is right-handed will have a right-hand ratio greater than 0.5. Bilateral surgery was considered as two independent procedures. A parallel study was conducted to establish an understanding of the natural variation between right and left arm activity in 10 healthy volunteers.



Figure 4-2 a) Wearable activity monitors (Axivity AX3, designed by Open Lab, Newcastle University) worn on both wrists; b) The front of AX3 Axivity sensors with their coded sensor ID (e.g. "AX3 18-70902"); c) The back of the AX3 Axivity sensors, labelled according to Participant ID (e.g. LT8) and laterality (e.g. L); d) Signal Vector Magnitude (SVM) calculation.*

For data analysis in chapter 6, participants' time spent in each of the four different types of activity levels (sedentary, light, moderate, and vigorous) were also quantified. By monitoring the types of activity levels, healthcare professionals can objectively assess patients' upper limb activity levels and give further insight on how they change after axillary surgeries. The time spent in each specific intensity of upper limb activity is reported by cut-point analysis, which is based on the units of metabolic equivalent of tasks (Table 4-3).[427] For the cut points analysis, 'Cut Points' option was selected on OMGUI® (version 1.0.0.37, Axivity Ltd., Newcastle upon Tyne, UK) software for the chosen file, which then converted the files into CSV format giving different bands of activity level for the patient (sedentary, light, moderate, vigorous).[427] One MET is equivalent to the rate of energy produced per unit surface area by an average person seated at rest.

Table 4-3 Activity type and corresponding Metabolic Equivalent of Tasks (METs)

Activity type	**METs**
Sedentary	<1.5
Light	1.5-4
Moderate	4-7
Vigorous	>7

Missing data

After consulting with our study statistician on the missing data, a complete-case analysis was chosen due to the limited final sample size and the data structure as well as to minimise potentially unverifiable assumptions. Multiple imputation is a robust technique to handle missing data, particularly if data are missing at random (MAR). Whilst it can produce less biased parameter estimates than complete-case analysis under certain assumptions, it also relies on the plausibility of the imputation model and the structure of the missing data mechanism. Therefore, with a modest sample size in each study, each imputation run could introduce additional uncertainty or risk of overfitting, especially if the proportion of missing data is substantial in key variables. Multiple imputation is worth exploring in future trials with larger cohorts.

4.1.4 Statistical Analysis

The data were analysed using SPSS for Mac (Version 26, IBM, Armonk, NY, USA). Shapiro-Wilk test results indicated that the data were non-normally distributed, hence nonparametric statistical tests of significance were performed.

For statistical analysis in chapter 5, The Wilcoxon signed-rank test was used to analyse group differences in longitudinal regain-of-function data. The Mann-Whitney U test was used to analyse differences in upper limb activity between two surgical procedures and between surgically treated and control sides. Concurrent validity was determined by analysing the Spearman's correlation coefficient between the upper limb activity data and the DASH and EQ-5D-5L questionnaires. Spearman correlation was also performed to determine the correlation between activity data measured by WAMs and postoperative pain score.

For statistical analysis in chapter 6, the Mann–Whitney U test was used to assess differences in upper limb activity between SLNB and ALND groups. The Friedman test with Bonferroni correction was performed to analyse the intensity reduction from preoperative to postoperative level. A sensitivity analysis was performed matching breast and/or reconstructive surgery across different axillary

procedures. Spearman correlation was performed to determine the correlation between the upper limb activity data and the DASH and EQ-5D-5L questionnaires. Spearman correlation was also performed to determine the correlation between activity data measured by WAMs and postoperative pain score.

For statistical analysis in chapter 7, the Kruskal-Wallis test was used to assess differences in combined upper limb activity, surgically treated and control side across surgical procedures. Post hoc analysis was performed using the Dunn's test. Subgroup analyses were performed to measure 'Mx versus IBR versus DIEP' with different combinations of axillary surgeries. Univariate analysis was carried out to identify an association between age, body mass index (BMI), comorbidity score, stage, operation type, neoadjuvant/adjuvant treatments, and upper limb activity levels. Multivariate regression analysis was performed to determine factors that independently affect upper limb activity levels. A Spearman correlation analysis was conducted to examine the relationship between the activity data and the pain score.

For statistical analysis in chapter 8, The Wilcoxon signed-rank test was used to assess longitudinal regain-of-function. Univariate analysis was carried out to identify an association between age, BMI, comorbidity score, upper limb activity at 2 weeks, DASH score at 1 week, surgery type and adjuvant/neoadjuvant therapies with upper limb activity and DASH score (>6 months postoperatively). Comorbidities were scored according to Age-Adjusted Charlson Comorbidity Index (ACCI).[430,431] Multivariable regression analyses were performed to determine predictors of long-term recovery. Spearman's rank correlation test was used to assess correlations between DASH score and upper limb activity levels with EQ-5D-5L score.

All statistical tests were 2 sided and the p-value threshold for significance was set at p=0.05.

4.1.5 Data Quality Assessment

The primary focus of data quality assessment was to identify particular days when patients were considered unlikely to have worn the sensors. This factor has the potential to impact the findings of the

results. A minimum threshold of 10.0g per day was established for the combined SVM value based on the feasibility study in chapter 5[78] in order to assess the extent of non-compliance with wearing sensors together with verbal confirmation from patients about their non-wearing period. These data were subsequently excluded from the dataset.

A flow diagram of the participants recruited into clinical studies discussed in chapter 5 to 8 was described below:

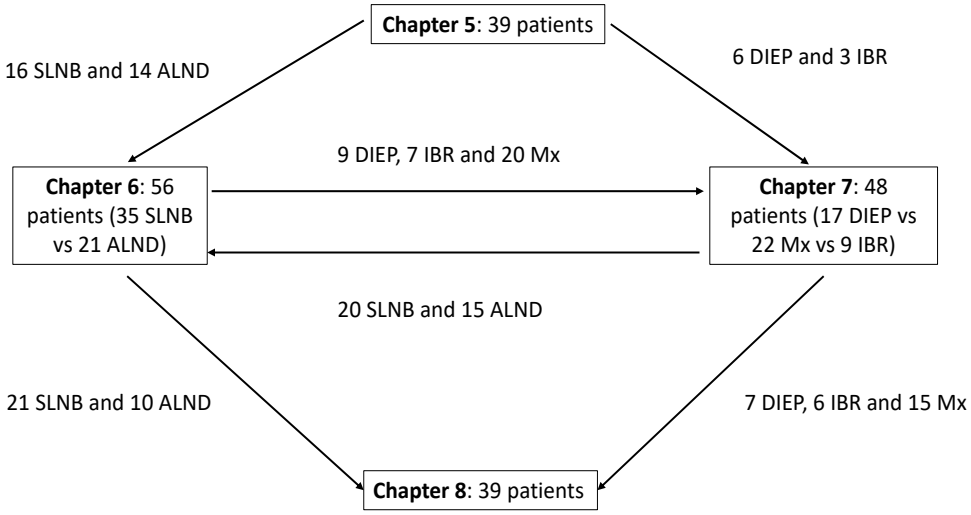


Figure 4-3 Flow diagram of participant recruited into clinical studies described in chapter 5 to 8. SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection; Mx, simple mastectomy; DIEP, deep inferior epigastric perforator; IBR, implant-based reconstruction

The study recruitment was suspended between March 2020 and July 2020 due to the COVID-19 pandemic. The number of patients recruited based on their surgery dates from April 2019 to May 2022 is illustrated in Appendix 9.

The objective of the next chapter is to evaluate the feasibility of utilising WAMs to measure the upper limb activity following breast and axillary surgery. It is hypothesised that WAMs can achieve a continuous, objective assessment and provide insight into upper limb activities after breast and axillary surgery.

5 THE FEASIBILITY OF USING WEARABLE ACTVITIY MONITORS FOR OBJECTIVE ASSESSMENT OF UPPER LIMB ACTIVITY FOLLOWING BREAST AND AXILLARY SURGERY

5.1 Abstract

Background. Current validated tools to measure upper limb dysfunction after breast cancer treatment, such as questionnaires, are prone to recall bias and do not enable comparisons between patients. This study aimed to test the feasibility of wearable activity monitors (WAMs) for achieving a continuous, objective assessment of functional recovery by measuring peri-operative upper limb activity.

Methods. A prospective, single-centre, non-randomised, observational study was conducted from April 2019 to December 2020. Patients undergoing breast and axillary surgery were invited to wear WAMs on both wrists in the perioperative period and then complete upper limb function (DASH) and quality-of-life (EQ-5D-5L) questionnaires. Statistical analyses were performed to determine the construct validity and concurrent validity of WAMs.

Results. The analysis included 39 patients with a mean age of 55 ± 13.2 years. Regain of function on the surgically treated side was observed to be an increase of upper limb activity as a percentage of preoperative levels, with the greatest increase observed between postoperative days 1 and 2. The upper limb activity was significantly greater on the side not treated by surgery than on the surgically treated side after week 1 (mean, 75.8% vs. 62.3%; $p<0.0005$) and week 2 (mean, 91.6% vs. 77.4%; $p<0.005$). Subgroup analyses showed differences in recovery trends between different surgical procedures. Concurrent validity was demonstrated by a significant negative moderate correlation between the upper limb activity and DASH questionnaires ($R=-0.506$; $p<0.05$).

Conclusion. This study demonstrated the feasibility and validity of WAMs to objectively measure postoperative upper limb activity after breast surgery, providing a starting point for personalised rehabilitation through early detection of upper limb morbidity.

Sections of this chapter have been previously published as: Che Bakri NA, Kwasnicki RM, Dhillon K, Khan N, Ghandour O, Cairns A, Darzi A, Leff DR. Objective Assessment of Postoperative Morbidity After Breast Cancer Treatments with Wearable Activity Monitors: The "BRACELET" Study. Ann Surg Oncol. 2021 Oct;28(10):5597-5609. doi: 10.1245/s10434-021-10458-4. Epub 2021 Jul 26. PMID: 34309777; PMCID: PMC8312212

5.2 Introduction

5.2.1 Wearable Activity Monitors Used in Breast Surgery Cohort

Higher levels of physical activity are linked to decreased morbidity, lower recurrence rates, and reduced mortality in individuals with breast cancer.[432,433] Nevertheless, prior studies have shown that individuals diagnosed with breast cancer tend to decrease their physical activity levels, and these effects are more pronounced in those who are treated with radiotherapy and chemotherapy.[434] Physical exercise has emerged as a crucial topic of research in breast cancer survivorship due to its potential to improve patient outcomes.[5,6,201] Thus, the majority of trials conducted in the breast surgery group primarily focused on measuring step counts and overall physical activities.[435]

Biskup *et al.,*[436] conducted a study in which they measured the physical activity levels of 135 female breast cancer survivors and compared the objectively measured physical activity using an accelerometer with the subjective measures taken using the International Physical Activity Questionnaire (IPAQ). The results suggest that the breast cancer survivors were more likely to avoid engaging in vigorous physical activity, regardless of the method of measurement.[436] The findings also demonstrated that subjective outcome-measured physical activity values were overestimated in comparison to the accelerometery data, illustrating the limitations of self-assessed physical activity measurements.[436]

Furthermore, WAMs were used as a means of encouraging patients to participate in physical exercise. An RCT conducted by Matthews *et al.,*[437] demonstrated that early breast cancer patients who had intervention with pedometer and supervised exercise programme had a significantly higher level of walking activity than the usual care group.[437] WAMs were also used as an objective tool to measure outcomes in clinical trials. Rogers *et al.,*[438] conducted a randomised study involving 222 breast cancer survivors who had completed their primary treatment. The participants were divided into two groups: an intervention group (Better Exercise Adherence after Treatment for Cancer (BEAT Cancer)) and a control group. The intervention group received a 3-month programme consisting of supervised exercise, face-to-face counselling, and group discussions, with a gradual transition to home-based exercise.[438]

The control group, on the other hand, received printed materials from the American Cancer Society that provided recommendations for physical activity in cancer survivors. The researchers measured the primary outcome of physical activity and adherence to the intervention using an accelerometer. The results suggest that the BEAT Cancer group experienced significant improvements in physical activity, fitness, and quality of life, with the benefits persisting for three months following the intervention.[438] Despite this, the authors focused on general activities, such as walking, rather than specifically on upper limb activity which is the focus of the current thesis.

Systematic review and meta-analysis in chapter 2 demonstrated that breast cancer treatment can lead to upper limb impairment such as lymphoedema, pain, reduced range of motion, reduced strength and upper limb function which can negatively impact patient's HRQoL. In a prior study, it was demonstrated that structured upper-limb exercise programmes can reduce upper-limb disabilities in patients who are susceptible to treatment-related complications.[4] As previously discussed, upper limb activity assessment can be used as a surrogate marker to assess patient's upper limb function. Nevertheless, there is a lack of research on upper limb activity monitored using wearable technology, despite the advantages of a supervised upper limb exercise plan in preventing upper limb morbidity after breast cancer treatment. Therefore, the objective of this chapter is to investigate the feasibility of using WAMs in the assessment of upper limb activity in patients undergoing breast surgery. The methodology used in this study was described in chapter 4. I conducted the patient recruitment with Dr Naairah Khan and Dr Omar Ghandour.

5.3 Hypothesis

- ◊ *Wearable activity monitors (WAMs) can achieve a continuous, objective assessment and provide insight into upper limb activities after breast and axillary surgery.*

5.3.1 Outcomes

The primary outcome of the study was the construct validity of WAMs as an objective tool for measuring upper limb activity by quantifying pre- and postoperative arm activity for surgically treated and non-surgically treated (control) sides and by characterising the upper limb activities in various types of surgical procedures. The secondary outcome was concurrent validity determined by correlating upper limb activity with patient-reported upper limb morbidity (DASH) and QoL (EQ-5D-5L) scores.

5.4 Results

5.4.1 Study Participants

From April 2019 to December 2020, 86 patients (Figure 5-1) treated at Imperial College Healthcare NHS Trust were identified as potentially eligible based on their medical data. Due to the COVID-19 pandemic, the study was suspended from March to July of 2020. The study excluded 5 patients who did not fulfil the inclusion and exclusion criteria, 25 patients who declined to participate for different reasons (such as stress associated to a cancer diagnosis, lack of response, and concurrent studies), and 7 patients whose procedures were postponed or cancelled. Thirty-nine patients were available for analysis following consideration of other factors including late postage (n=2), technical issues (battery life, faulty sensors) (n=2), and personal reasons leading to withdrawal (i.e., local discomfort, compliance) (n=6) (Table 5-1). No patients in in the current study had any additional relevant histories, such as traumatic injury to the shoulder or other shoulder impairments. Furthermore, 10 healthy subjects were recruited into the study (Table 5-2). The list of patients' comorbidities is presented in Appendix 10.

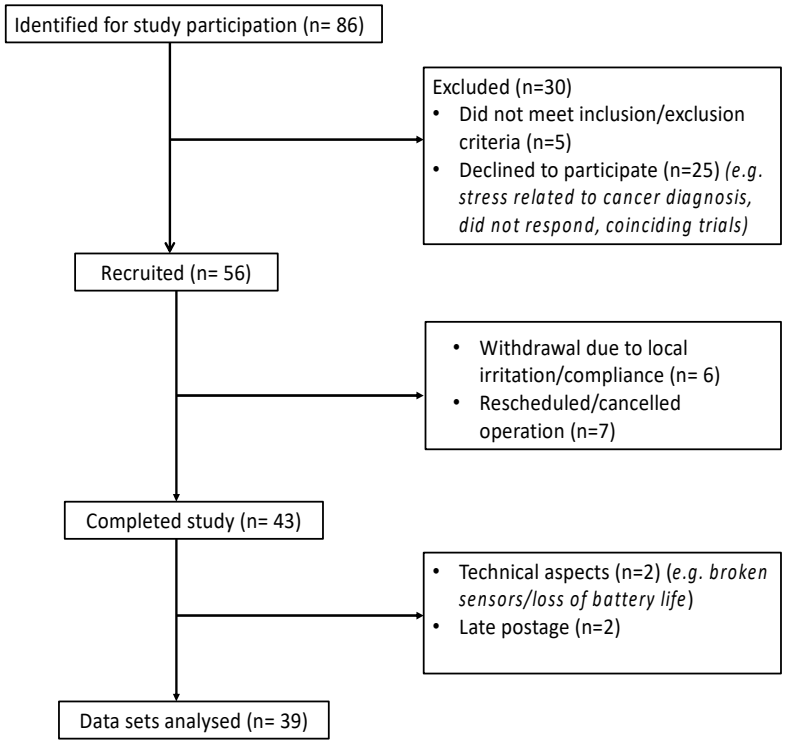


Figure 5-1 Flow diagram of participants investigating the feasibility and validity of WAMs to objectively measure postoperative recovery of upper limb function after breast and axillary surgery. WAM, Wearable Activity Monitor.

Table 5-1 Baseline demographics of study population (means presented with standard deviations and numbers presented with whole number percentage of total population).

Characteristics	**Total (n=39)**
Mean Age, (yrs.) (SD)	55 (13.2)
Sex Ratio (M:F)	1: 38
Comorbidities: n (%)	28 (71.8)
Mean BMI (SD)	27.9 (6.7)
Handedness Ratio (R:L:BL)	37:1:1
Race/ethnicity: n (%)	
White British	9 (23.1)
White Irish	2 (5.1)
White and any other White background	2 (5.1)
Asian – any other Asian background	3 (7.7)
Black or Black British African	3 (7.7)
Black or Black British Caribbean	1 (2.6)
Black or any other Black background	1 (2.6)
Mixed – White and Black Caribbean	1 (2.6)
Other – any other ethnic group	4 (10.3)
Other – not stated	13 (33.3)
Clinical and pathological characteristics	
Stage of Cancer: n (%)	
Stage 0	7 (17.9)
Stage 1	10 (25.6)
Stage IIA and IIB	11 (28.2)
Stage IIIA-IV	6 (15.4)
Cancer Type: n (%)	
Ductal Carcinoma In-situ	6 (15.4)
Invasive Ductal Carcinoma	24 (61.5)
Invasive Lobular Carcinoma	4 (10.3)
Invasive Mucinous Carcinoma	1 (2.6)
Invasive Micropapillary Carcinoma	1 (2.6)
Previous Breast Surgery: n (%)	8 (20.5)
Patients with drain (n,%)	21 (53.8)
Drain in situ in axilla/breast: Mean days (SD)	8.6 (5.3)
Length of Stay: Days (SD)	1.7 (2.2)
Advice about exercise: n (%)	39 (100)

Compliance to analgesia: n (%)	39 (100)
Treatment received	
Type of Breast Surgery: n (%)	
Wide local excision (Breast conserving surgery)	13 (33.3)
Mastectomy	13 (33.3)
Immediate Breast Reconstruction:	12 (30.8)
-Implant-based	3 (7.7)
-DIEP	6 (15.4)
-TUG	1 (2.6)
-TRAM	2 (5.1)
***Type of Axillary Surgery: n (%)**	
Sentinel Lymph Node Biopsy	16 (41)
Axillary Lymph Node Dissection	14 (35.9)
Completion of ALND after positive nodes from SLNB	0 (0)
Re-excision after positive margin from wide local excision (breast conserving surgery)	1 (2.6)
Operation Laterality Ratio (R:L:BL)	22:15:2
Neoadjuvant Therapy (n,%):	
Radiotherapy	1 (2.6)
Chemotherapy	8 (20.5)
Hormone therapy	6 (15.4)
Adjuvant Therapy Whilst Wearing WAMs (n,%):	
Radiotherapy	0
Chemotherapy	0
Hormone therapy	8 (20.5)

*Total percentages (%) will not equal to 100 as patients will have combination of different breast +/- axillary surgeries. DIEP, Deep Inferior Epigastric Perforators; TUG, Transverse Upper Gracilis; TRAM, Transverse Rectus Abdominus Muscle; SLNB; Sentinel Lymph Node Biopsy, ALND; Axillary Lymph Node Dissection

Table 5-2 Baseline demographics of healthy participants (means presented with standard deviations)

Characteristics	**Total (n=10)**
Mean Age, (yrs.) (SD)	23 (0.7)
Sex Ratio (M:F)	2:8
Comorbidities: n (%)	0
Mean BMI (SD)	21.4 (1.2)
Handedness Ratio (R:L:BL)	9:1:0

5.4.2 Adherence of Patients to Wearable Activity Monitors (WAMs)

Five hundred and forty-six (39 patients x 14 days) data points in the postoperative period could have been captured from all the patients recruited in the study. Out of 546 data points, only 59 were not captured, the majority of which were concentrated around days 12 to 14 after surgery. Therefore, the overall adherence to the WAM application protocol was 89.2%.

5.4.3 Main findings

5.4.3.1 Regain of Function: Postoperative Upper Limb Activity on the Surgically Treated Side

Upper limb activity reduced postoperatively from 100% to 45.3% and regain of function was gradually observed on the surgically treated side through the increase in upper limb activity as a percentage of preoperative levels during the postoperative period. The greatest upper limb activity increase (mean, 45.3% vs. 56%; $p<0.05$) was observed between PODs 1 and 2 (Figure 5-2). The recovery plateau (64.7% ± 27.9%), the point at which no subsequent significant increase in activity was observed (from day 7 to day 14) was identified on day 7.

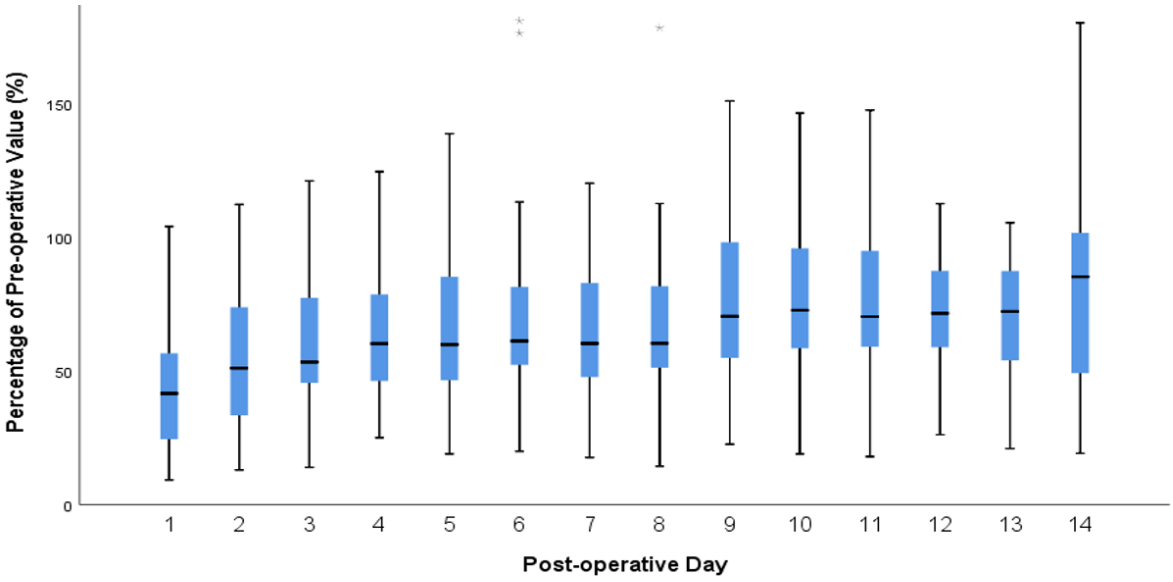


Figure 5-2 All operated sides: Percentage of pre-operative value (%) across a 14-day post-operative period

5.4.3.2 Surgically Treated Side Versus Control Side Activity

Overall, greater regain of function, represented by greater activity, was observed on the control side (non-surgically treated) than on the surgically treated side after week 1 (mean, 75.8% vs. 62.3%; $p<0.0005$) and week 2 (mean, 91.6% vs. 77.4%; $p<0.005$) (Figure 5-3). The pattern was maintained throughout for PODs 1 to 3 (mean, 66.4% vs. 55.3%; $p<0.05$), PODs 4 to 6 (mean, 83.7% vs. 68.5%; $p<0.005$), PODs 7 to 9 (mean, 86.4% vs. 71.4%; $p<0.05$), and PODs 10 to 12 (mean, 91.8% vs. 76.9%; $p<0.05$) (Figure 5-3). Intergroup comparison between the surgically treated and control sides during the 2 weeks demonstrated a statistically significant difference ($p<0.005$), with a mean disparity of 13.9% ± 2.3% between the two sides. This is higher than the data from 10 healthy volunteers, which demonstrated an average differential activity of 8% ± 5.2%, indicating iatrogenic morbidity from surgery.

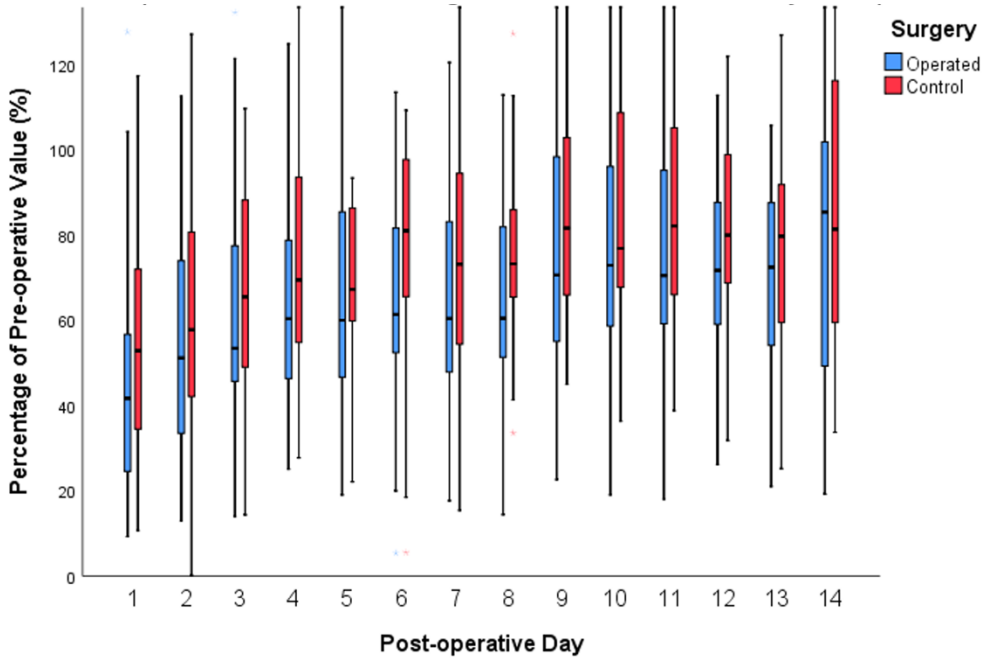


Figure 5-3 Disparity between recovery in operated vs control upper limb activity over 2 weeks postoperatively. (N.B: All patients were right handed except for 1 left handed and 1 ambidextrous, 22:15:2 R:L:BL operations). R, right; L, left; BL, bilateral.

5.4.3.3 Hand Activity Ratio and Handedness

The majority of the patients were right-handed, with 1 left-handed patient and 1 ambidextrous patient. Figure 5-4 illustrates the hand activity ratio of a patient who was right-handed and had a left wide local excision and SLNB. Patient A, who was right hand-dominant had a higher right-hand activity (0.540) preoperatively, as depicted in Figure 5-4a. The right-hand activity (non-surgically treated side) increased postoperatively up to 0.867 and gradually returned to the preoperative hand activity level on POD 11.

Similarly, patient B Figure 5-4b who was right-handed with a preoperative hand ratio of 0.533 and had a left ALND increased right-hand activity (non-surgically treated side) postoperatively up to a ratio of 0.648 and returned to preoperative hand activity level on POD 14.

Overall, the hand activity of the surgically treated side was reduced from 0.513 to 0.472 and did not return to baseline even on POD 14.

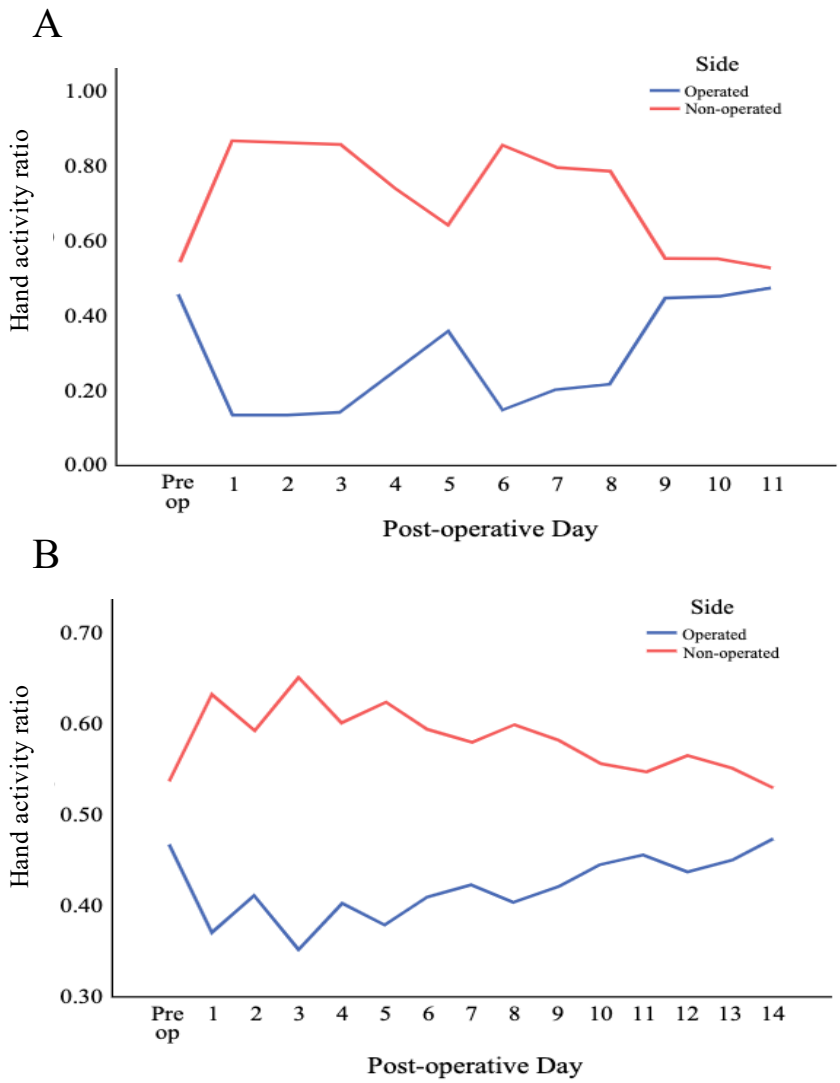


Figure 5-4 a) Patient A (right-hand dominant), who underwent left wide local excision and SLNB, had a greater right-hand activity (0.540) preoperatively. The right-hand activity (non-surgically treated side) increased postoperatively up to 0.867 and gradually returned to the preoperative hand activity level on day 11. b) Patient B (right-hand dominant), who underwent left ALND had a preoperative hand ratio of 0.533, increased right-hand activity (non-surgically treated side) postoperatively up to a ratio of 0.648 and returned to preoperative hand activity level on day 14. SLNB, Sentinel Lymph Node Biopsy; ALND, Axillary Lymph Node Dissection.

5.4.3.4 Comparison of Surgery Types and the Presence of Drains

Subgroup analyses were performed to compare SLNB with ALND, mastectomy alone with deep inferior epigastric perforators (DIEP) flap reconstruction, and the presence of drains with their absence. The patients receiving ALND (n=14) demonstrated a reduced upper limb activity than the SLNB patients (n=16) after week 1 (mean, 58.4% vs. 63.2%; p=0.165) and week 2 (mean, 68.5% vs.

75.1%; $p < 0.05$). Compared with mastectomy alone (n=12), significantly reduced upper limb activity was observed in DIEP reconstruction (n=8) across PODs 1 to 3 (mean, 62.5% vs. 44.1%; $p<0.05$) and after week 1 (mean, 66.9% vs. 56.9%; $p<0.05$). After week 1, the ALND patients who had drains in situ were observed to have significantly less upper limb activity (57%) than those without drains (64%) ($p<0.05$).

5.4.3.5 Correlation with DASH and EQ-5D Questionnaires

Comparisons were made between postoperative activity for week 1 (activity in both arms) with DASH scores and EQ-5D-5L scores. There was a moderate negative correlation between postoperative DASH scores and the upper limb activity level across week 1 (R=−0.506; $p<0.05$). The EQ-5D-5L scores had a weak correlation with the upper limb activity level across week 1 (R=0.231; p=0.313) (Figure 5-5).

5.4.3.6 Correlation with Pain Score

There was a weak negative correlation between the upper limb activity data and the upper limb pain scores (R=-0.362; p=0.082). Additionally, there was a moderate negative correlation between the upper limb activity (R=-0.43; p=0.05) and the pain levels when performing specific activity (Figure 5-5).

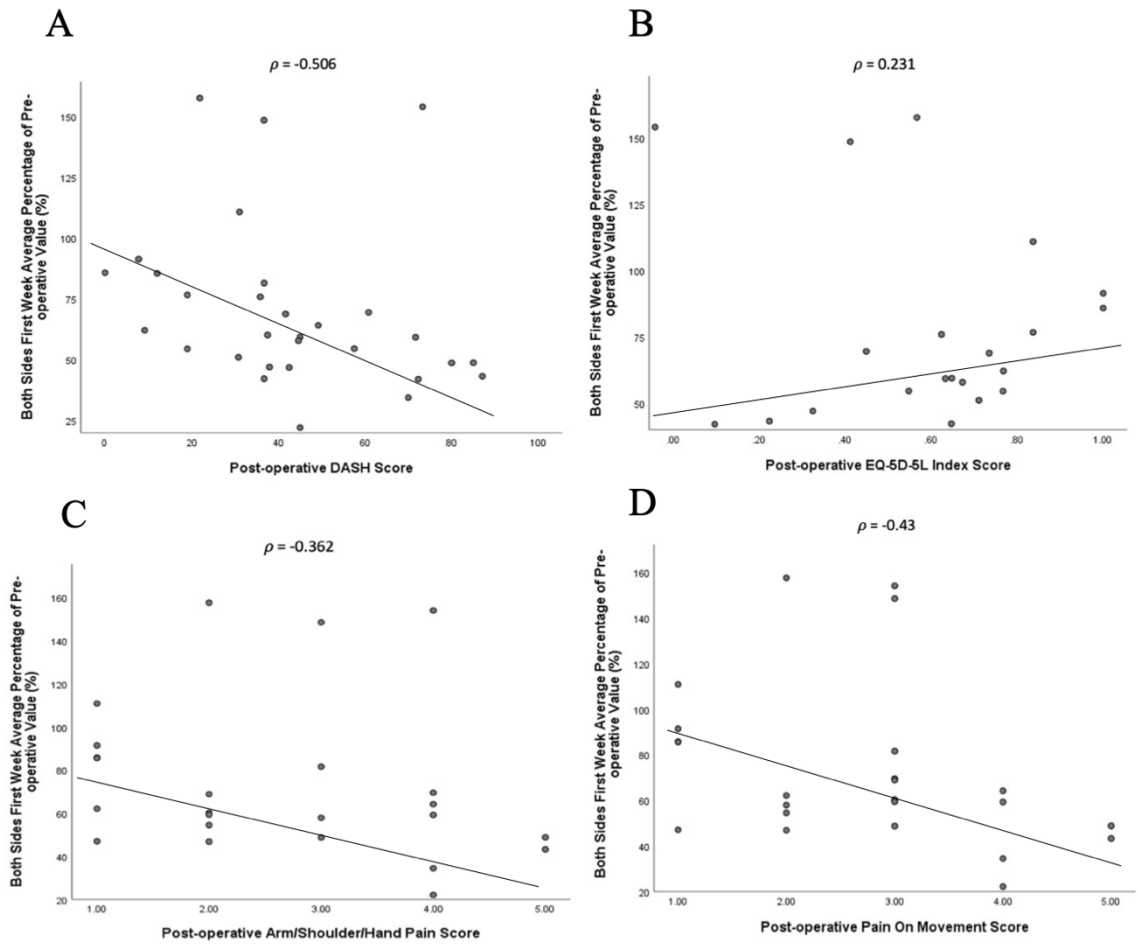


Figure 5-5 a) Spearman correlation test between the post-operative DASH score and the activity data measured by WAMs. b) Spearman correlation test between the post-operative EQ-5D-5L score and the activity data measured by WAMs. c) Spearman correlation test between the post-operative pain score and the activity data measured by WAMs. d) Spearman correlation test between the post-operative score when performing specific activity and the activity data measured by WAMs, WAM, Wearable Activity Monitor; DASH, Disabilities of the Arm, Shoulder and Hand.

5.5 Discussion

This is the first feasibility study to adopt WAMs for an objective measurement specifically focusing on upper limb activity following breast and axillary surgery. WAMs permitted assessment of pre- and postoperative activity to characterise the recovery curve, examine the difference between surgically treated and untreated sides, and compare various types of breast surgery. The results demonstrated a significant decrease in upper limb activity on the surgically treated side and a gradual recovery of activity between PODs 1 and 14, with the greatest statistical increase in activity occurring during the first 7 PODs. During the two-week postoperative period, the non-surgically treated side remained more active than the surgically treated side. Furthermore, the hand activity ratio did not return to baseline two weeks after surgery, consistent with prior studies, indicating that the effects of surgery on the surgically treated side may persist beyond the study duration.[2,3,56,439]

Even though it was less severe than in the operated arm, it is nevertheless fascinating to observe that the activity level in the control (contralateral arm) also decreased in the first 2 weeks following surgery. This finding is similar to a study by Adriaenssens *et al.,* which indicated that patients undergoing unilateral breast surgery and radiation experienced loss of abduction in both ipsilateral and contralateral arms, along with changes in arm volume for both sides.[440] Haines *et al.,* similarly observed that patients who underwent unilateral breast cancer surgery showed a 10% or more absolute volume rise in both ipsilateral and contralateral arms in 35% and 32% of cases, respectively.[441] The reason behind this remains unclear. It is hypothesised that axillary surgery can cause systemic effect which increase lymph flow on the contralateral side, potentially leading to lymphoedema on the contralateral side due to the chronically elevated lymph load opposing increased lymphatic outflow resistance, ultimately resulting in lymphatic pump failure.[441-443] The decreased activity of the contralateral arm may be attributed to post-surgery modifications in body posture at rest or during arm elevation, misalignment of the shoulder girdle, and changes in scapular kinematics due to overcompensating mechanism.[444-447]

Upper limb activity differed significantly postoperatively between the surgically treated side and the control side, and the difference was significantly greater than the natural variation observed in the

healthy cohort. In comparison with the preoperative data, the hand activity ratio of the non-surgically treated side increased, mirrored by a decrease in the activity of the surgically treated side after surgery, and the ratio did not return to baseline by POD 14. This indicated that the observed variation was unlikely to be solely due to handedness because the system was calibrated to hand activity preoperatively.

As previously discussed, there are objective physical evaluations of upper limb morbidity in breast cancer survivors, such as tape measurement/arm volume and goniometry, however, they are time-consuming, difficult to conduct in clinical settings, and are operator-dependent.[2,8] The effects of hand dominance in relation to side of treatment in assessment of physical function are rarely taken into account when these tools are used.[448] On the other hand, WAMs allow for a standard objective measurement in free-living conditions. They can be calibrated for hand dominance and are easy to use. Moreover, they are acceptable to be used by clinicians and patients.[67,449,450]

Lymphoedema is one of the most prevalent and persistent complications of breast cancer treatment.[27] The evaluation of lymphoedema is complex, and numerous factors must be considered.[451] It is essential to note that the pathologies of lymphoedema may be reflected in the activity of the affected arm.[188] WAMs may be used to measure the upper limb activity of patients with lymphoedema, and other upper limb impairments linked to breast cancer treatment, such as reduced range of motion, reduced muscular strength, and pain, as discussed in chapter 3.

In this study, activity levels correlated well with the functional (DASH) questionnaires, implying the concurrent validity of WAMs. Although DASH questionnaires may provide useful information on recovery, the measurements become invalid if used daily due to recall bias.[187,452-454] Additionally, patients may overestimate or underestimate the function of their upper limbs, making questionnaire-based assessments challenging.[285] Interestingly, there was a weak correlation between the WAMs-measured activities and the QoL (EQ-5D-5L) questionnaire scores. The results of this study concur with those of Hayes *et al.*,[284] who similarly found a weak correlation between objective and subjective measures in their study. Together, these data imply that WAMs and EQ-5D-5L evaluate various

components of upper limb dysfunction, and it is important to take this into account when designing a measurement tool. Lymphoedema also has morbidity that goes beyond only restricting movement, which may help to explain why there is not a strong association between objective and subjective score. Apart from mobility, self-care, and usual activities assessment, pain/discomfort and anxiety/depression were also included in the EQ-5D-5L survey. An effective approach may involve integrating objective sensor data with patient-reported outcomes, such as pain scores or their activities of daily living.[451,455]

In the current study, all patients were provided with pain medications. According to the patient interviews and medical data, all were compliant with their medications. There was a moderate negative correlation between the pain score during a specific activity and the WAMs measurement of the activity, suggesting that the upper limb activity could be partly influenced by pain.

To provide a holistic assessment of breast cancer survivors, it is important to establish a multidisciplinary approach and collaborate with physiotherapists, engineers, and patients to develop an assessment or screening tool (combination of objective WAMs data and patient-reported outcome). Activity monitoring is the only continuous measure of recovery available, which might facilitate real-time patient and clinician feedback. The findings of other studies that incorporated measures such as DASH scores and range-of-motion measurements are consistent with our findings. The greatest functional morbidity is in the initial postoperative period, particularly during the first week, and the apparent onset of the recovery phase happens shortly thereafter, with the majority of patients returning to their preoperative baseline at 1 month.[456,457]

The findings of the study were discussed with consultant surgeons and physiotherapists in our unit. They suggested that reduced upper limb activity in these individuals might be a reflection of upper limb morbidity following breast and axillary surgery, such as decreased strength, pain, and stiffness. As discussed in in chapter 3, prior studies showed a correlation between upper limb morbidity evaluated through clinical assessments and upper limb activity measured by accelerometers.[251-253] WAMs have the potential of measuring upper limb activity as a surrogate marker for upper limb morbidity. The reduction of upper limb activity postoperatively in the current study may indicate face validity, as

indicated by the subjective assessments of consultant surgeons and physiotherapists regarding the tool's ability to measure its intended outcome. Construct validity has been demonstrated because the trend of postoperative upper limb activity is as expected (i.e., postoperative decline followed by a gradual return to baseline). In addition, the upper limb activity data can differentiate between various surgical procedures, providing more support for this claim.

In accordance with the literature,[100,132] subgroup analysis in this feasibility study showed a greater decrease in postoperative upper limb activity in the ALND compared with the SLNB cohort. Similarly, the subgroup analysis of the DIEP patients revealed a larger reduction in postoperative upper limb activities compared with the simple mastectomy only patients, demonstrating a possible iatrogenic morbidity related with breast reconstruction. Previous research has demonstrated that autologous breast reconstruction surgery can reduce patient's strength, shoulder mobility, and function, which may impact their ability to return to work and engage in everyday activities.[16,160] Using the current methodology, WAMs may play a role in answering specific concerns concerning morbidity associated with various surgical procedures, and thereby facilitate patients and clinicians in making informed decision. This will be further elaborated in chapters 6 and 7.

A further application of the technology is to support feedback-enabled rehabilitation strategies. This may be achieved, with future studies expanding on these data in conjunction with input from engineering specialists and physiotherapists. Postoperative upper limb activity data act to keep track of personalised activity goals, such as those already implemented in many ERAS protocols,[268] that may empower and motivate patients to take control of their care. Continuation of data collection in the home environment may provide early indicators of complications and make health care professionals aware of patients needing further support, thereby improving their postoperative outcomes.[438,458]

It is important to note that the wrist-worn tri-axial accelerometers have been validated to measure upper limb activities in previous studies.[386,387,390,459] Despite the increasing evidence of their accuracy in measuring upper limb activity in a real-world environment, it is important to consider several challenges. The first challenge is the difficulty of distinguishing between intentional and unintentional

activity (i.e., upper limb movement to do a specific activity vs. upper limb swing during locomotion) as the accelerometers record all movement without regard to purpose or quality.[392] The difficulty in distinguishing between the former and the latter means wrist-worn accelerometers may overestimate intentional upper limb activity.[392] This issue can be addressed, as reflected in the current analysis, by measuring upper limb activity as a ratio.[388,392] It is also possible to develop machine learning algorithms that differentiate intentional and unintentional activity of the upper limb from the accelerometer data.[257] However, this may require individuals to wear wrist accelerometers in addition to an extra accelerometer on their leg (hip, thigh, or ankle). It may be difficult as patients may not adhere to the study protocol due to the presence of an additional accelerometer. Another obstacle is the inability of wrist-worn accelerometers to assess the quality of movement. Simply put, they are unable to differentiate between a reaching movement that has appropriate shoulder and elbow biomechanics and one that has modified shoulder and elbow biomechanics.[392] There are many debates regarding the goal of rehabilitation within stroke settings – whether the goal is to restore normal movement patterns or to restore function by whatever means possible.[254,460] Nevertheless, quantifying any voluntary upper limb activity is beneficial to understand general upper limb function post-breast cancer treatment. Another obstacle is the conversion of the accelerometer data (i.e., numerical values representing accelerations) into information that has clinical relevance. This will be discussed further in chapter 9 of this thesis based on the experience of breast cancer survivors who have viewed their activity data. Finally, WAMs may underestimate the upper limb activity as they may not capture very fine finger movements. Nevertheless, the accuracy of activity recognition and detection of the upper limb activities will be improved in the future with further development of this technology.

Although these results are interesting, they should be interpreted with caution owing to the limitations of the study design; 1) selection bias in favour of younger patients who are more technologically savvy and those who speak English as their first language; 2) attrition bias that might have occurred because more patients with arm complications, patients who were re-admitted or experienced discomfort while wearing the WAMs withdrew; 3) potential confounding factors, such as compliance with analgesia, anaesthesia effect and neoadjuvant/adjuvant therapies; 4) natural variation in habitual upper limb

activity and handedness, 5) the activity data of the 'affected' arm was compared to the contralateral arm to interpret results but there was evidence that contralateral arm may also be affected post-treatment;[461] 6) device malfunction; and 7) the small number of patients in subgroup analyses is likely to be underpowered, increases the probability of false-negative results (type II error).[462,463] When performing subgroup analyses, there is also a risk of multiplicity, resulting in an increased likelihood of obtaining a false positive result (i.e., incorrectly detecting a significant difference between compared groups when none actually exists, when multiple comparisons are performed).[462,463]

To mitigate these limitations, interpreters were used when available and the WAMs used in this study was easy to use and require minimal patient interaction. The baseline characteristics of the patients who withdrew or could not be included due to broken sensors or delays/cancellations after recruitment (n = 17) were demographically similar to those of the study patients, limiting the attrition bias. Furthermore, data were collected from healthy subjects for calculation of the normal variation in upper limb activity. Preoperative activity data were collected, and the hand activity ratio throughout the pre- and postoperative periods was analysed to allow individualised calibration of postoperative measurements, limiting the effect of handedness and the possible effect from the contralateral arm. Recruiting patients who had non-breast cancer surgery (such as ear, nose and throat surgery) in future study would better enable control for the general effects of pain and anaesthesia on upper limb activity.

Attempts to collect data were unsuccessful in 5% of cases due to device error. By doing routine inspections of the WAMs before distributing them to patients in the future, potential malfunction may be prevented. In order to increase adherence and wearability, patient's feedback was collected, and a slight modification was made to the WAMs throughout the trial (such as adding an extra loop to the wristbands).

5.6 Clinical Implications

In conclusion, this pilot study demonstrated the feasibility and validity of WAMs toward longitudinal objective monitoring of upper limb activity after breast and axillary surgery. This facilitates more objective profiling of the morbidity from breast cancer treatments. The results highlight a decline in

upper limb activity on the surgically treated side and a gradual recovery that does not return to baseline at 2 weeks after surgery. The current work will improve the protocols and usability of WAMs for future studies with more defined scientific hypotheses, which will be discussed in the next few chapters. In the following chapter, longitudinal recovery following ALND and SLNB procedures will be tracked with WAMs in the acute post-operative setting in a larger cohort of patients.

6 THE USE OF WEARABLE ACTIVITY MONITORS (WAMS) IN ACUTE POSTOPERATIVE SETTING – COMPARISON STUDY BETWEEN AXILLARY LYMPH NODE DISSECTION AND SENTINEL LYMPH NODE BIOPSY USING VALIDATED WAMS

6.1 Abstract

Background. The upper limb morbidity associated with both sentinel lymph node biopsy (SLNB) and axillary lymph node dissection (ALND) is believed to have been inadequately evaluated to date. Current methodologies are subjective and susceptible to bias. Objective assessment using wearable activity monitors (WAMs) would allow quantitative analysis of recovery by measuring upper limb activity and could provide evidence for axillary de-escalation.

Methods. A prospective, single-centre, observational study was conducted from February 2020 to May 2022. Consecutive patients undergoing breast and/or reconstructive surgery and axillary surgeries were identified from the operating schedules. Patients wore WAMs for an average of 3 days prior to surgery and up to 2 weeks following surgery. In total, 56 patients with breast cancer were recruited, of whom 35 underwent SLNB and 21 ALND.

Results. Patients who underwent ALND experienced a significantly worse upper limb activity compared with those who underwent SLNB in week 2 (median 66.4% versus 72.7%, p=0.015). Subgroup analysis revealed a significantly reduced upper limb activity in simple mastectomy (Mx)-ALND versus Mx-SLNB (median 70.5% versus 90.3%, p=0.015) in week 2. The upper limb activity for SLNB did not return to baseline at 2 weeks after surgery.

Conclusions. Compared with SLNB, ALND results in a reduced upper limb activity level in week 2. The findings also indicate that SLNB has a protracted effect on upper limb activity levels, which extend to 2 weeks postoperatively. Monitoring upper limb recovery objectively following breast cancer surgery

provides patients and surgeons with more information regarding the predicted outcomes of their surgery, which can drive the development of a personalised rehabilitation programme.

Sections of this chapter have been previously published as: Che Bakri NA, Kwasnicki RM, Giannas E, Tenang L, Khan N, Moenig C, Imam Z, Dhillon K, Ashrafian H, Darzi A, Leff DR. The Use of Wearable Activity Monitors to Measure Upper Limb Physical Activity After Axillary Lymph Node Dissection and Sentinel Lymph Node Biopsy. Ann Surg Oncol. 2023 Nov;30(12):7036-7045. doi: 10.1245/s10434-023-13966-7. Epub 2023 Jul 28. PMID: 37507555; PMCID: PMC10562272

6.2 Introduction

ALND has historically been performed routinely to treat metastases of the primary lymphatics of the breast, which is widely recognised as a significant prognostic factor for survival and recurrence.[464] The advent of SLNB using a radio-guided technique for staging of the axilla has led to a reduction in postoperative morbidity due to fewer ALND procedures (Figure 6-1).[135,465] A negative SLNB is a favourable prognostic factor because it increases the likelihood that the lymph nodes remaining in the axillary basin are cancer-free.[466]

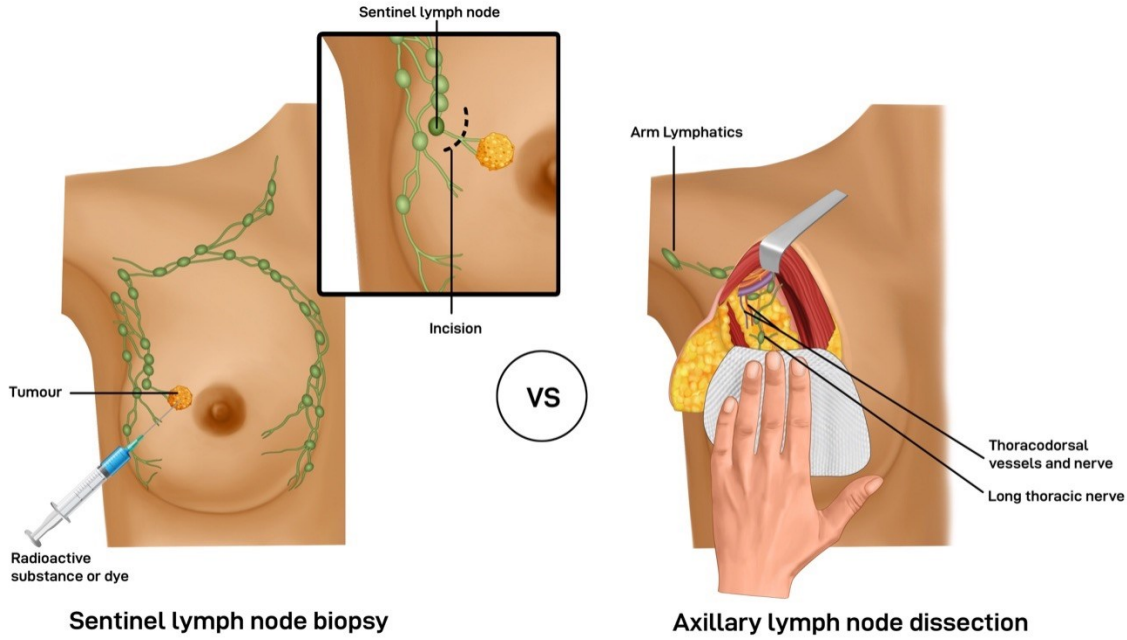


Figure 6-1 Sentinel lymph node biopsy versus axillary lymph node dissection (The figure was created by Mohesh Mohan, used with permission)

6.2.1 Sentinel Lymph Node Biopsy (SLNB)

Sentinel node is the first lymph node that collects the lymphatic flow from the tumour. SLNB is performed by injecting a combination of dye (e.g patent blue, isosulfan blue dye, and methylene blue dye) and radioisotope to identify sentinel nodes and reduce the false negative rate.[466] However, the isosulfan blue dye and patent blue dyes are associated with allergic reactions (0.1%-3%), some of which could be life threatening.[467] On the other hand, radioisotopes present challenges in terms of administration logistics, as well as the regulations for the manipulation and disposal of radioactive materials.[468] Some new tracers were developed including indocyanine green that is cheaper and no

radiation exposure. Meta-analysis showed that indocyanine green is as good as radioisotopes at detecting sentinel node and is therefore a good alternative method or could be an addition to the standard technique.[469] Furthermore, a magnetic tracer is available for SN detection, nonetheless, skin staining and possible artefacts in postoperative MRI have been the major concerns.[468] This technique appears to be comparable to the traditional technique in terms of identification rate.[468]

6.2.2 Axillary Lymph Node Dissection (ALND)

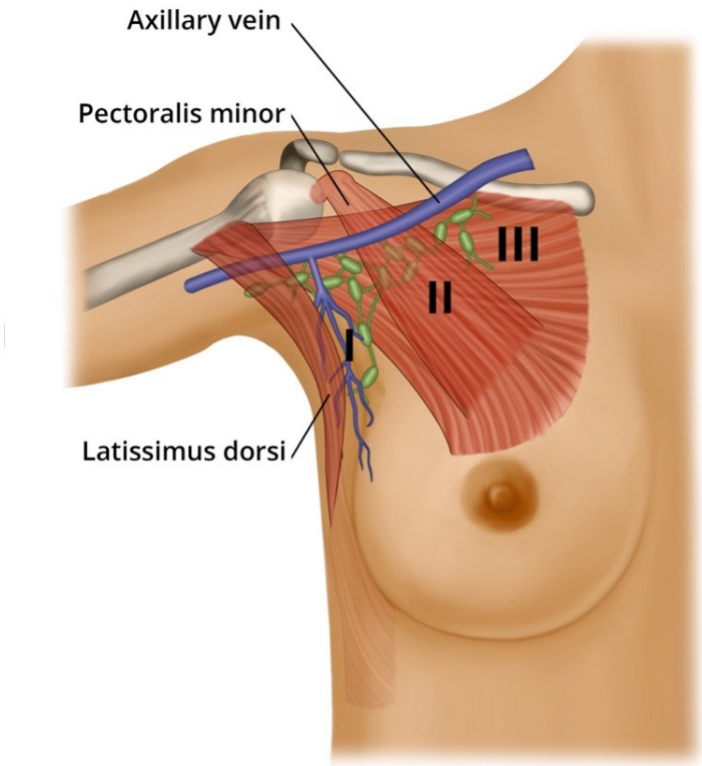


Figure 6-2 Three levels of lymph nodes, level I, below the lower margin of pectoralis minor muscle, level II: located underneath pectoralis minor muscle, level III: located above pectoralis minor muscle (The figure was created by Mohesh Mohan, used with permission)

ALND involves the removal of lymph nodes from the axilla. There are three levels of lymph nodes (Figure 6-2): level I is located below the lower margin of the pectoralis minor muscle, level II is located underneath the pectoralis minor muscle, and level III is located above the pectoralis minor muscle. Traditionally, ALND is performed by removing levels I and II lymph nodes. It is performed when there

is positive disease in the axilla.[470] This is typically done to determine the extent of the disease within the axilla, which is critical for staging. The staging of cancer will then determine if individuals require additional adjuvant treatments such as chemotherapy and radiotherapy.[470] According to the NICE guidelines, ALND should be offered to patients with invasive breast cancer who have a preoperative ultrasound-guided needle biopsy with pathologically proven lymph node metastases (1 or more sentinel lymph node macrometastases).[238]

6.2.3 Complications of Axillary Surgeries

As previously discussed in chapter 2, axillary surgeries can result in an array of post-operative complications including lymphoedema, pain, reduced strength and reduced ROM.[2,27] These complications frequently affect patients years after surgery, significantly reducing HRQoL, and limiting upper limb function.[27] In comparison to SLNB, ALND has a greater risk of developing upper limb morbidities.[27,97,99,103,121,130]

6.2.4 De-escalation of Axillary Surgery

Multiple trials were conducted to investigate the de-escalation of axillary surgery, including the NSABP-B32 trial[135] in which patients with clinically negative lymph nodes were randomised to sentinel node resection or conventional ALND. The results demonstrated that SLNB can successfully replace ALND with comparable survival and regional control as well as less morbidity.[471,472] Furthermore, ALND can be safely omitted in patients who undergo breast-conserving surgery and adjuvant therapy if there are up to two positive lymph nodes detected during SLNB. This was demonstrated by a few trials by Donker *et al.,* Galimberti *et al.*, and Giuliano *et al.*[40,473-475] Following the publication of the ACOSOG Z0011 trial results in 2011,[474] the rates of ALND declined from 32% in 2004 to 16% in 2014, with the largest decline occurring between 2010 and 2011.[476] Consequently, trials such as the Intergroup-Sentinel Mamma (INSEMA)[477] and BOOG 2013-08,[478] investigates whether it is safe to omit SLNB altogether in node-negative patients.

In patients with clinically positive lymph nodes, de-escalation of axillary surgery is also investigated by increasing the use of neoadjuvant systemic therapy. This will reduce the extent of the primary tumour, making breast-conserving surgery more feasible.[479] However, there is still a lack of consensus regarding the de-escalation of clinically positive lymph nodes in patients, as it is unclear whether it is safe to omit ALND entirely and what the long-term prognosis will be.

6.2.5 Clinical Problem and Potential Solution

The morbidity associated with SLNB and ALND has not been adequately examined using current methods, which are predominantly subjective and prone to bias (Chapter 3).[2,27] The Axillary Lymphatic Mapping Against Nodal Axillary Clearance (ALMANAC) trial objectively measured shoulder movement and lymphoedema using a goniometer and tape measurement, respectively.[100] Nevertheless, measurements were deemed problematic due to a high level of inter-observer variation.[100]

On the other hand, WAMs have been validated to objectively monitor post-operative upper limb activity levels in a non-invasive manner, which could reduce measurement and operator variability.[78] Following the feasibility study discussed in chapter 5, a larger cohort of patients were recruited to further validate the use of WAMs in the acute postoperative setting comparing SLNB and ALND procedures. WAMs can be worn on both wrists to assess arm and shoulder activity post-surgery and provide discriminative data of the upper limbs. Objective longitudinal assessment of upper limb activity following ALND and SLNB permits the determination of standard recovery curves and further optimises patient outcomes by encouraging upper limb activity. Such interventions are valuable as evidence begins to strengthen the relationship between physical activity and survivorship after breast cancer surgery.[480] The objective of this chapter is to monitor the upper limb activity levels following SLNB and ALND in the first 2 weeks following surgery. The methodology used in this study was described in chapter 4. I conducted the patient recruitment with Dr Omar Ghandour, Dr Manolis Giannas, Dr Luqman Tenang, Dr Kieran Dhillon, Dr Zoha Imam and Dr Catharina Moenig.

6.3 Hypothesis

- ◊ *ALND patients would experience a greater reduction in upper limb activity compared with SLNB in the first 2 weeks-postoperatively.*

6.3.1 Outcomes

The primary endpoint was the upper limb activity level and intensity level (sedentary, light, moderate or vigorous) following SLNB or ALND (regardless of breast procedure). The secondary endpoint was a planned sub-group analysis of upper limb activity level, comparing simple mastectomy (Mx)-SLNB versus Mx-ALND and Deep Inferior Epigastric Perforator (DIEP)-SLNB versus DIEP-ALND, as well as investigating the relationship between DASH and pain scores with the upper limb activity level.

6.4 Results

6.4.1 Main findings

6.4.1.1 Study Participants

Between February 2020 and May 2022, a total of 157 patients (Figure 6-3) were identified as potentially eligible based on their electronic medical records at Imperial College Healthcare NHS Trust. The study was suspended from March to July 2020 due to the COVID-19 pandemic. Forty-one patients did not meet the inclusion and exclusion criteria, and 45 patients declined to participate for a variety of reasons, including stress related to cancer diagnosis, coinciding trials, and declined without reason. The surgeries of nine patients had to be rescheduled or cancelled. Two patients who were initially enrolled were subsequently excluded for technical reasons (e.g malfunctioning sensors). Four patients dropped out of the study due to noncompliance and local irritation. In total, 56 patients (35 SLNB and 21 ALND) provided data for analysis (Table 6-1). None of the patients had a history of restricted shoulder range of motion, movement disorders, or limb injuries that could restrict mobility. The list of patients' comorbidities is presented in Appendix 11.

6.4.1.2 Adherence of Patients to Wearable Activity Monitors (WAMs)

From all the patients in the study, 784 (56 patients x 14 days) data points in the postoperative period could have been captured. Out of 784 data points, 150 data points were not captured. Therefore, the overall adherence to the WAM application protocol was 80.9%.

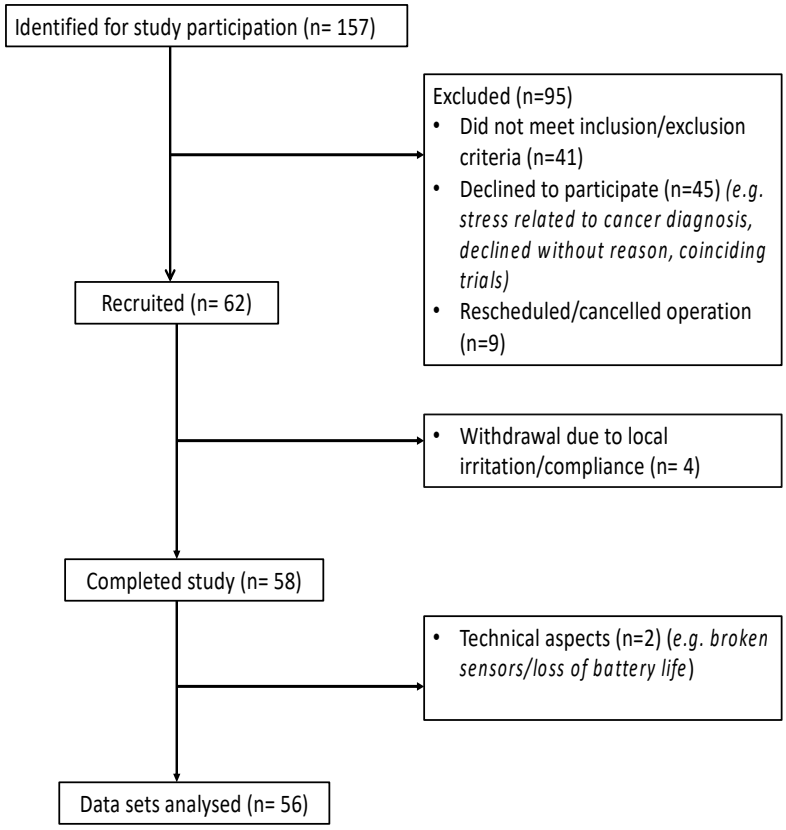


Figure 6-3 Participant flow diagram investigating the impact of sentinel lymph node biopsy and axillary lymph node dissection on upper limb activity

Table 6-1 Demographics of study population (n=56) (means presented with standard deviations and numbers presented with whole number percentage of total population in each group)

Characteristics	**SLNB (n=35)**	**ALND (n=21)**	**p value**
Mean Age, (yrs.) (SD)	59 (10.8)	56 (11)	0.463
Sex Ratio (M:F)	1:34	0:21	0.629
Comorbidities: n (%)	23 (65.7)	13 (61.9)	0.372
Mean BMI (SD)	27.1 (6.5)	30.8 (6.3)	0.073
Handedness Ratio (R:L)	34:1	21:0	-
Race/ethnicity: n (%)			
White British	11 (31.4)	2 (9.5)	0.338
White Irish	2 (5.7)	1 (4.8)	
White and any other White background	2 (5.7)	3 (14.3)	
Asian or Asian British – Indian/Pakistani	1 (2.9)	1 (4.8)	
Asian – any other Asian background	1 (2.9)	1 (4.8)	
Black or Black British African	3 (8.6)	2 (9.5)	
Black or Black British Caribbean	1 (2.9)	1 (4.8)	
Black or any other Black background	0 (0)	1 (4.8)	
Mixed – White and Black Caribbean	0 (0)	1 (4.8)	
Other – any other ethnic group	14 (40)	8 (38.1)	
Stage of Cancer: n (%)			
Stage 0	5 (14.3)	1 (4.8)	0.003
Stage 1	25 (71.4)	6 (28.6)	
Stage IIA and IIB	4 (11.4)	10 (47.6)	
Stage IIIA-IV	1 (2.9)	4 (19)	
Unknown	0 (0)	0 (0)	

Cancer Type: n (%)			
Ductal Carcinoma In-situ	6 (17.1)	0 (0)	0.028
Invasive Ductal Carcinoma	26 (74.3)	16 (76.2)	
Invasive Lobular Carcinoma	2 (5.7)	1 (4.8)	
Invasive Mucinous Carcinoma	0 (0)	1 (4.8)	
Other	1 (2.9)	3 (14.3)	
Previous Breast Surgery: n (%)	6 (17.1)	6 (28.6)	0.317
Patients with drain (n,%)	21 (60)	19 (90.5)	0.024
Drain in situ in axilla/breast: Mean days (SD)	3.71 (3.9)	9.8 (6.1)	<0.001
Length of Stay: Days (SD)	1.2 (1.6)	2.3 (2.1)	0.05
Advice about exercise: n (%)	35 (100)	21 (100)	-
Compliance to analgesia: n (%)	35 (100)	21 (100)	-
Type of Breast Surgery/Reconstruction: n (%)			
Wide Local Excision	11 (31.4)	1 (4.8)	0.211
Mastectomy	10 (28.6)	10 (47.6)	
DIEP	6 (17.1)	3 (14.3)	
TRAM	1 (2.9)	2 (9.5)	
TUG	1 (2.9)	0 (0)	
Implant	6 (17.1)	1 (4.8)	
No breast surgery	0 (0)	4 (19)	

Completion of ALND after positive nodes from SLNB	1 (1.8)	Nil	
Re-excision after positive margin from wide local excision (breast conserving surgery)	1 (1.8)	Nil	
Operation Laterality Ratio (R:L:BL)	17:16:2	11:9:1	0.772
Neoadjuvant Therapy (n,%):			
Radiotherapy	1 (2.9)	1 (4.8)	0.014
Chemotherapy	7 (20)	11 (52.4)	
Hormone therapy	2 (5.7)	2 (9.5)	
Immunotherapy	1 (2.9)	1 (4.8)	
Adjuvant Therapy Whilst Wearing WAMs (n,%):			
Radiotherapy	0 (0)	0 (0)	0.145
Chemotherapy	0 (0)	0 (0)	
Hormone therapy	1 (2.9)	3 (14.3)	
Complications (n,%):			
Seroma	2 (5.7)	2 (9.5)	0.995
Infected hematoma	1 (2.9)	0 (0)	
Abscess	0 (0)	1 (4.8)	
Cording	1 (2.9)	0 (0)	

Deep Inferior Epigastric Perforator: DIEP, Transverse Upper Gracilis: TUG, Transverse Rectus Abdominal Muscle: TRAM, SLNB; Sentinel Lymph Node Biopsy, ALND; Axillary Lymph Node Dissection

6.4.1.3 *Surgically Treated Side versus Control Arm*

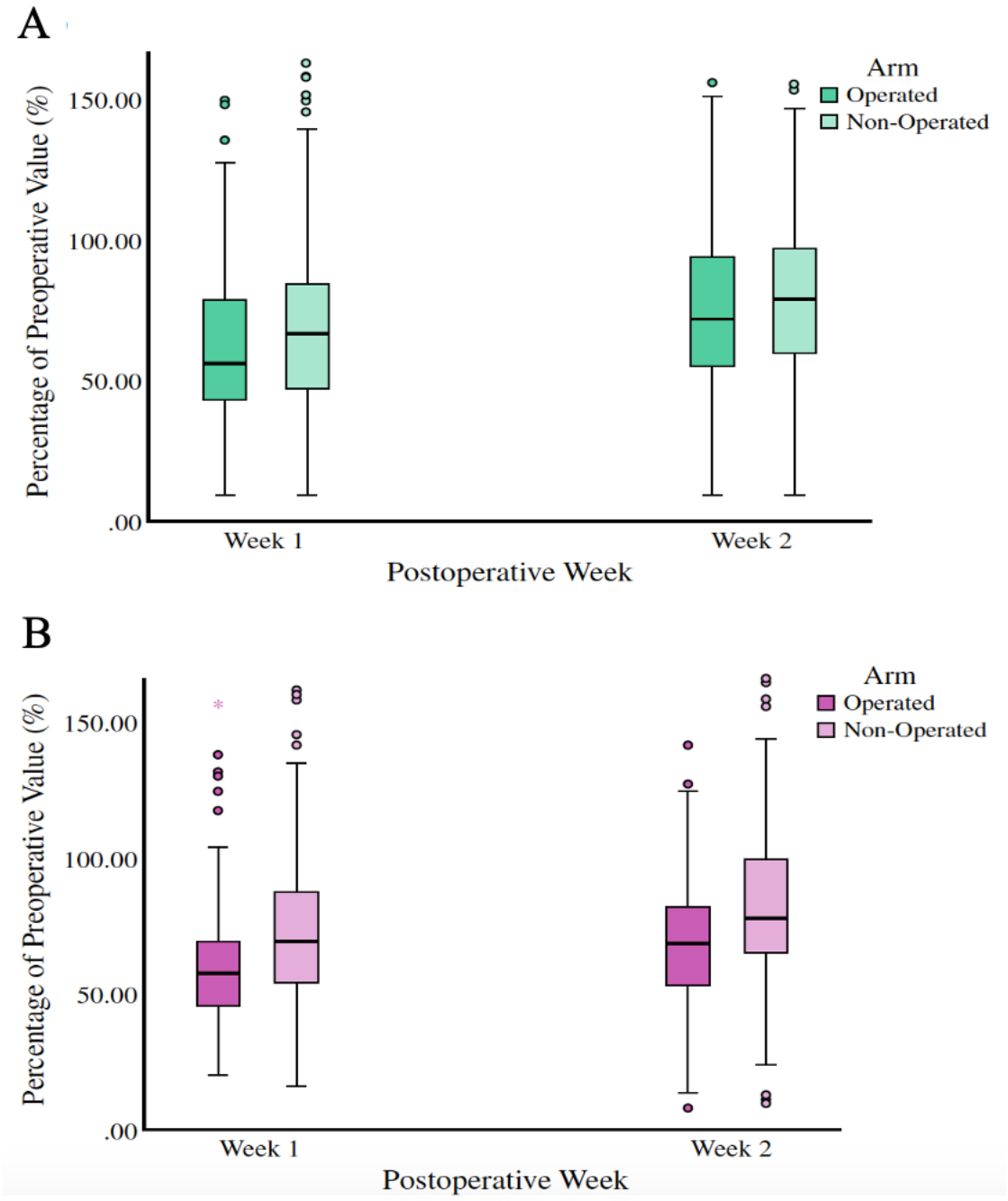


Figure 6-4 a) Surgically treated side versus control arm expressed as percentage (%) of preoperative level at week 1 and week 2 after SLNB. b) Surgically treated side versus control arm expressed as percentage (%) of preoperative level at week 1 and week 2 after ALND. SLNB, Sentinel Lymph Node Biopsy; ALND, Axillary Lymph Node Dissection.

As illustrated in Figure 6-4, greater upper limb activity level (as a percentage of preoperative level) was observed in the control arm compared with the surgically treated side in both SLNB and ALND groups

in week 1 (Median: SLNB= 66.9% vs 56.1.1%, p=0.006; Median: ALND= 69.4% vs 57.7%, p<0.001) and week 2 (Median: SLNB= 79% vs 71.8%, p=0.283; Median: ALND= 79.7% vs 68.9%, p<0.001), respectively.

6.4.1.4 Surgically Treated Side Only

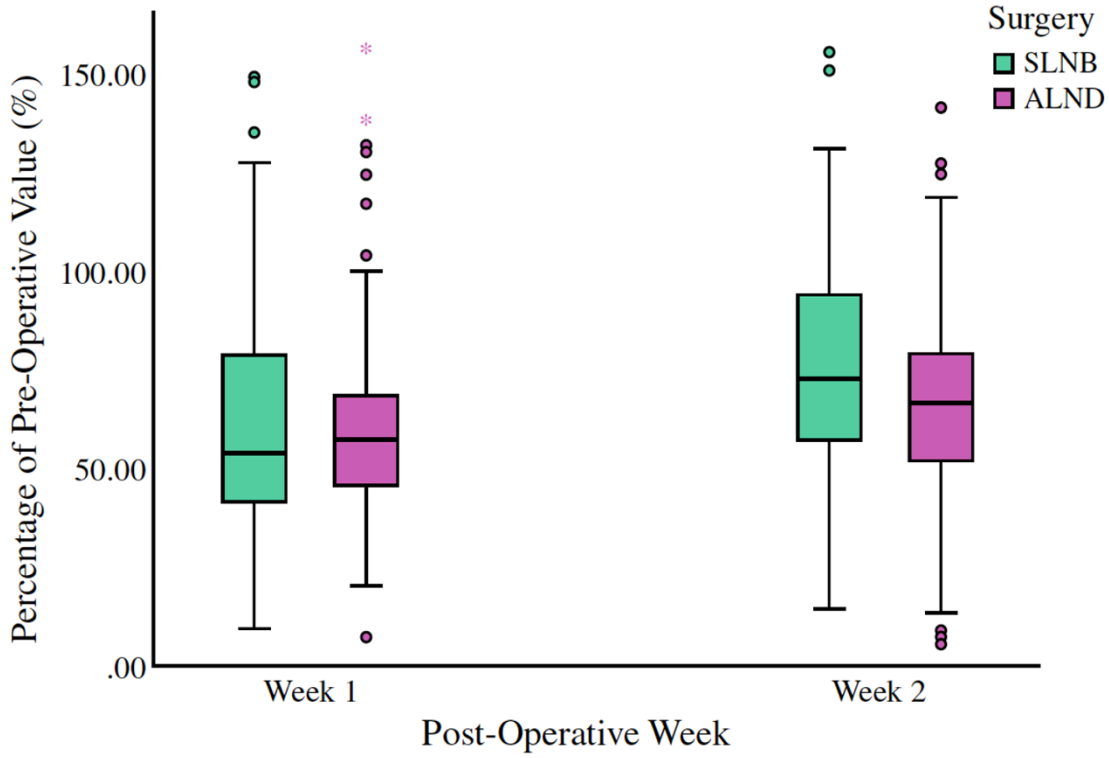


Figure 6-5 Surgically treated side only expressed as percentage (%) of preoperative level at week 1 and week 2 comparing SLNB with ALND. SLNB, Sentinel Lymph Node Biopsy; ALND, Axillary Lymph Node Dissection.

When comparing activities of the surgically treated side only, ALND group experienced a significantly greater reduction of upper limb activity level compared with SLNB group in postoperative week 2 (median: 66.4% vs. 72.2%, p=0.015) (Figure 6-5). There was no significant difference between ALND and SLNB in week 1 upper limb activity levels (median: 57.7% versus 56.1%, p=0.916).

6.4.1.5 Subgroup Analyses

Subgroup analysis was performed to compare surgically treated side of 'Mx-SLNB' versus 'Mx-ALND'. In week 2, upper limb activity levels were significantly lower in Mx-ALND than in Mx-SLNB (Median: 70.5% vs. 90.3%; p=0.015) but not in week 1 (Median: 57.4% vs. 68.8%; p=0.274).

Seven patients in SLNB group and eight patients in ALND group had drains inserted. Similar findings were observed when patients without drains were excluded in subgroup analysis (Appendix 12).

Interestingly, there was no significant difference in upper limb activity level between 'DIEP-SLNB' and 'DIEP-ALND' in either week 1 (median: 46% vs 52.6%, p=0.79) or week 2 (median: 50.7% vs 53.5%, p=0.86).

6.4.1.6 Intensity Analyses

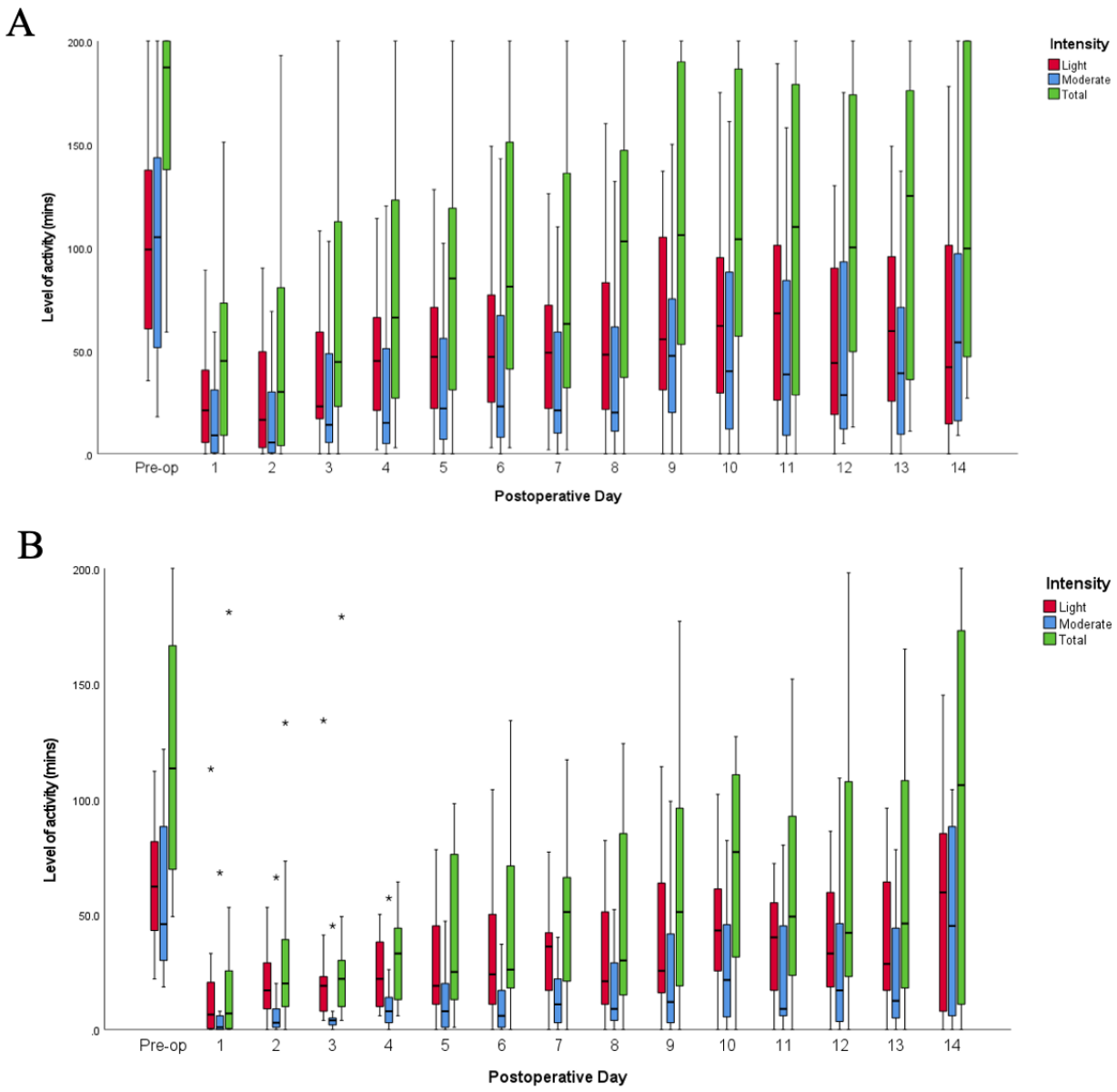


Figure 6-6 a) Level of activity spent in light and moderate intensity (min/day) for patients who underwent SLNB at week 1 and week 2; sedentary and vigorous intensity are not shown, total activity

(light + moderate + vigorous). b) Level of activity spent in light and moderate intensity (min/day) for patients who underwent ALND at week 1 and week 2; sedentary and vigorous intensity are not shown, total activity (light + moderate + vigorous). SLNB, Sentinel Lymph Node Biopsy; ALND, Axillary Lymph Node Dissection. Asterisks represent outliers.

On average, patients who underwent ALND and SLNB spent 95.8% and 92.8% of their time in sedentary state over 24 hours, respectively. A marked decline in activity was observed in both SLNB and ALND groups in the initial postoperative period, with a gradual increase of activity over the successive postoperative days. No sustained vigorous intensity activity was recorded in either SLNB or ALND groups. There was a statistically significance difference between light activity performed preoperatively and on postoperative day (POD) 1–14 ($p<0.001$) for SLNB and on POD 1–9 ($p<0.05$) for ALND. There was no statistically significance difference between the light activity performed preoperatively and on POD 10–14 for ALND. There was a statistically significant difference between moderate activity performed preoperatively and on POD 1–10 ($p<0.05$) for SLNB and POD 1–14 ($p<0.05$) for ALND. There was no statistically significance difference between moderate activity performed preoperatively and POD 11–14 for SLNB (Figure 6-6).

6.4.1.7 Correlation of Upper Limb Activity with DASH and EQ-5D-5L questionnaire

There was a moderately negative correlation between the upper limb activity level of the surgically treated side and the DASH score ($R=-0.4$, $p=0.01$) and a weak positive correlation between the upper limb activity level of the surgically treated side and the EQ-5D-5L score ($R=0.33$, $p=0.37$) in week 1.

6.4.1.8 *Analgesia Requirement and Correlation of Upper Limb Activity (surgically treated side) with pain score*

All patients in the study were prescribed regular analgesia and were compliant with their prescribed analgesia. Patients who underwent ALND were found to have a higher analgesia requirement (need as required analgesia at least once on top of the regular analgesia) compared with those who underwent SLNB (23.6% versus 6.6%). There was a weak negative correlation between upper limb activity level

and pain scores (R=−0.283, p=0.06) (Appendix 13) and a weak negative correlation between upper limb activity level and pain on movement score (R=−0.357, p=0.015) in week 1 (Appendix 14). Additionally, there was a very weak correlation between upper limb activity level and pain score (R=−0.208, p=0.341) (Appendix 13) and no correlation between upper limb activity level and pain on movement score (R=−0.031, p=0.89) in week 2 (Appendix 14).

6.4.1.9 Complications

Two patients in the SLNB group developed seroma, 1 patient had an infected hematoma, and another patient experienced cording, whereas 2 patients in the ALND group developed seroma and 1 patient had an abscess.

6.5 Discussion

This chapter provides novel insights into the objective upper limb assessment of the impact of ALND and SLNB, as well as the significance of reducing upper limb morbidity through axillary de-escalation. When examining the upper limb activity level on surgically treated side, particularly during the second week after surgery, it is evident that ALND is linked to a higher degree of upper limb morbidity compared to SLNB. In light of this, it is important to note that although the recovery process after SLNB is generally more favourable when compared to ALND, our observations indicate that SLNB does indeed have an impact on upper limb activity levels that can persist for up to two weeks following surgery.

The findings are consistent with those of the ALMANAC trial,[100] which found that after a one-year follow-up, ALND patients experienced greater arm/shoulder morbidity and reduced quality of life compared with SLNB patients. As previously discussed in chapter 2,[27] the meta-analysis demonstrated that there was a 13.7% difference in the prevalence of lymphoedema between SLNB and ALND. At greater than 24 months after ALND procedure, the prevalence of lymphoedema can reach as high as 30.9%. In addition, the incidence of pain, decreased range of motion, and weakness have been shown

to be greater following ALND than SLNB.[27] Axillary de-escalation is motivated by the desire to prevent upper limb injury and a growing awareness of the oncological safety of axillary conservation.[481] Five clinical trials namely IBCSG 23-01,[475] AATRM,[482] ACOSOG Z0011,[474] AMAROS,[40] and POSNOC,[483] investigated the potential for de-escalation of axillary surgery.[484] The NSABP-32 trial[472] provided evidence that there was no significant difference in overall survival between patients who were randomly allocated to have SLNB + ALND and those who underwent SLNB alone with ALND performed only if sentinel nodes were found to be positive. As a growing body of evidence has demonstrated that women who undergo less invasive surgical treatment achieve equivalent clinical outcomes, multiple techniques have been proposed to replace ALND including SLNB,[485] targeted axillary dissection,[486] and MARI (marking the axillary positive lymph node with an iodine seed).[487]

However, it is important to note that SLNB in isolation can present notable complications, as evidenced by the findings of the present study.[100] Specifically, the current study observed a decline in upper limb activity levels over a span of two weeks following the surgical procedure, with no subsequent return to the initial baseline level. While it is not surprising, I would have expected that patients who underwent minimally invasive surgery such as SLNB would return to their baseline level in the short-term postoperative period. According to the meta-analysis discussed in chapter 2, the occurrence of lymphoedema, pain, decreased ROM, and reduced strength can reach percentages of up to 8%, 22%, 20%, and 15%, respectively, following SLNB.[27] Similarly, in the NSABP B-32 trial, the prevalence of lymphoedema was 9% and the prevalence of sensory and other mobility impairments ranged from 5.7% to 14.5% following SLNB at 6 months follow-up.[135] Nevertheless, the reduction in upper limb activity following SLNB could also be influenced by fear of movement, which was not assessed in this study.

Since the current study was conducted and published,[488] the SOUND trial,[489] which was recently published, have demonstrated that patients who did not undergo axillary surgery had a noninferior 5-year distant disease-free survival compared with those who underwent SLNB. The trial examines the effects of SLNB vs no SLNB in a cohort of 1463 patients with small (≤2cm) node-negative breast cancer. The preliminary result of the SOUND trial demonstrated that the SLNB group had worse

postoperative physical function as assessed by the DASH questionnaire, in comparison with those who did not undergo an axillary operation.[457] The findings of this study support the omitting of axillary surgery on a subset of patients which represents approximately 25% of the breast cancer population. In addition to using routine ultrasound as an alternative to axillary surgery in subset of patients, other alternatives such as intradermally injected microbubbles and contrast-enhanced ultrasound[490] or an adjunct procedure such as axillary reverse mapping (ARM)[491] should be further explored to decrease the occurrence of upper limb complications. The INSEMA trial[477] aims to determine if omitting axillary surgical staging is as effective as doing SLNB or ALND in patients with clinically node negative breast cancer (tumour size ≤5 cm) who have upfront breast-conserving surgery. From HRQoL point of view, during an 18-month period following surgery, the de-escalated treatment arms had a tendency towards improved breast and arm symptoms, as assessed by the EORTC QLQ-C30 and its breast cancer module (BR23).[477] The highly anticipated oncological results from INSEMA trial[477] may further confirm the futility of SLNB in low-risk breast cancer patients, thereby potentially obviating the need for unnecessary surgical procedures. PROMs were used in all of the aforementioned studies to evaluate upper limb function. In order to provide a more comprehensive and objective evaluation of patients having axillary and breast operations, objective assessment of upper limb activity using WAMs may be able to supplement the use of PROMs in future trials.

The current study suggests that patients spent the majority of their 24-hour period in a sedentary state. This finding aligns with a prior study which revealed that breast cancer survivors spent approximately 66.4% of their waking time in sedentary state, 31.1% in light activity, and a mere 2.6% in moderate to vigorous intensity activity (MVPA).[492] The present study also observed a significant decrease in light and moderate-intensity activities between the pre-operative and post-operative periods for both SLNB and ALND. Engaging in increased levels of physical activity has been observed to be linked with a reduction in adverse effects from treatment, better QoL and overall survival.[199 5,6] For example, a meta-analysis of 134 studies demonstrated that exercise is an effective intervention to improve HRQoL, cardiorespiratory fitness, physical function and fatigue.[493] Additionally, physical activity has an important role on the primary prevention of breast cancer risk.[200-203] Patients in the current study were

advised to mobilise on day 1 and do postoperative exercise as discussed in chapter 4. It is concerning to note that many breast cancer survivors fail to meet the recommended 150 minutes per week of MVPA.[494-497]

WAMs have the potential to be integrated with exercise regimens in order to allow healthcare professionals to closely track upper limb activity levels and offer real-time feedback and support. A prior study showed that WAMs could increase patient's MVPA time and this behaviour is sustainable, at least in the short term.[498] A systematic review and meta-analysis investigated the impact of wearable sensors on physical activity among cancer survivors.[341] The findings of this review revealed that WAMs had significant effects on various aspects of physical activity, including moderate-intensity physical activity, MVPA time, total physical activity, daily step count, quality of life, aerobic fitness, physical function, and fatigue reduction when compared with standard care practises.[341]

While there was solid evidence of the significance of increasing overall physical activity levels, prior systematic reviews emphasised the lack of data on the effectiveness of postoperative upper limb structured exercise programme on upper limb function.[240,241,245] Nevertheless, many published studies did not include high risk individuals, who would most benefit from personalised programme to avoid upper limb impairment following surgery. The optimal timing, quantity, and regimen of physical exercise was also unknown, despite its acknowledged favourable impact. There was also a concern regarding the potential for early exercise to exacerbate wound-related problems, such as seroma formation and surgical site infection.[240] Therefore, Bruce *et al.,*[4] conducted an RCT of breast cancer patients who were scheduled for surgery and considered to be at high risk of upper limb disability after surgery. Prior studies showed that patients who had planned axillary lymph node dissection, planned radiotherapy to the axilla or supraclavicular fossa, high body mass index (≥30), and existing shoulder problems are at high risk of developing upper limb complications.[27,39,149] One group received usual care only and the other group received usual care plus structured exercise programme. They demonstrated that structured exercise programme was clinically effective at reducing upper limb morbidity in individuals at risk of developing complications one year following breast cancer treatment. The

structured exercise programme examined in the PROSPER trial included shoulder strength and mobility exercises in addition to increasing overall activity levels.[4] The improvement in upper limb function, as determined by the DASH questionnaire, occurred without a change in overall physical activity levels. Similar to the protocol of Fusari *et al.*,[499] WAMs can be developed to send behavioural cues or motivational messages to encourage breast cancer patients to do the recommended exercises, which provides a self-management programme for stroke patients via a wearable-linked application. Although the use of technology in this way may reduce in-person healthcare interactions, the collected data may be shared confidentially among patient groups or through social media platforms. Studies have demonstrated that virtual patient support groups have been successful in improving patient engagement and increasing satisfaction.[500] Particularly for those who have recently been diagnosed, the sharing of the physical process of upper limb recovery from breast cancer is anticipated to be an invaluable resource. The PROSPER trial[4] provides patients who have undergone breast surgery with a compelling reason to promote early physical exercise. Technology innovation implemented correctly in this setting has the potential to improve patient satisfaction, cost effectiveness, and functional outcomes.

Despite observing a significant difference in upper limb activity levels between SLNB and ALND during the second week, it is possible that the true effect of ALND may have been underestimated due to the heterogeneous characteristics of the patients in the study. The percentage of reconstruction procedures was found to be higher in the cohort that underwent SLNB compared with the cohort that underwent ALND (40% vs. 28.6%), which could be linked to increased post-operative morbidity and lower levels of upper limb activity. A significant difference in upper limb activity level was observed during week 2 after eliminating heterogeneity through subgroup analysis of Mx-SLNB versus Mx-ALND, which showed the true impact of ALND. When patients without drains were excluded from this subgroup, similar findings were observed. No significant difference in upper limb activity levels was observed between patients who had DIEP-SLNB and those who underwent DIEP-ALND. The observed pattern may be attributed to the considerable morbidity resulting from the abdominal component of the DIEP operation, which may dominate any comparatively mild impact stemming from the axillary procedure. In addition to axillary treatments, the DIEP surgery may have a significant impact on arm

activity, as evidenced by a reported 14.1% incidence of shoulder morbidity among patients who underwent this procedure.[16] It is important to note that the finding from the subgroup analyses should be interpreted with caution due to the small sample size, which could lead to type II errors.

Furthermore, the findings of the present study indicate that patients who underwent ALND had more analgesic requirements compared with those who underwent SLNB. The observed outcome was anticipated, as patients who had ALND would typically experience higher levels of postoperative pain in comparison with those who underwent SLNB.[27] Systematic review by Li *et al.,*[171] provides evidence indicating that ALND is associated with a greater incidence of chronic postoperative surgical pain. This finding is likely attributed to the sacrifice of the intercostal brachial nerve.[171] Hence, effective pain management holds a significant importance in these individuals. There was a weak correlation observed between the postoperative activity of the surgically treated side and the pain score experienced during movement in the first week, although there was no correlation in the second week. This particular observation indicates that during the first postoperative week, the presence of pain has an influence on the level of upper limb activity. However, it is important to note that pain does not appear to have a significant impact on upper limb activity levels during the second week. This observation suggests that the greater reduction in upper limb activity levels following ALND compared with SLNB may have been influenced by iatrogenic morbidity. It is crucial to note that the nature of the mastectomy or reconstruction procedure may also have an impact on the experience of pain. In this particular study, it was observed that patients who underwent DIEP procedures necessitated a greater amount of analgesia compared with those who underwent Mx procedures (44% versus 20%) (Appendix 15). This observation implies that individuals who underwent DIEP surgery may potentially experience increased pain, consequently impacting their levels of upper limb activity. Prior studies have demonstrated that uncontrolled postoperative pain is associated with increased opioid consumption, extended hospital stay, and chronic pain syndromes.[501,502] By conducting subgroup analyses, I attempted to account for the influence of Mx and DIEP on the level of upper limb activity. The impact of mastectomy, DIEP and implant-based reconstruction surgery on upper limb activity will be further elaborated in the next chapter.

It is important to collect long-term data to determine the longitudinal trajectory of patient recovery from different types of breast and axillary surgeries, which is discussed in chapter 7 and 8. Developing a methodology that optimises adherence while obtaining an adequate amount of data should be prioritised. In this particular study, the patients may have limited motivation to wear the devices as they do not receive immediate feedback, which is crucial in order to prevent any potential biases due to the Hawthorne effect.[503] Periodic evaluation of patient feedback has resulted in slight modifications aimed at improving the overall comfort and usability. Our compliance rate stands at approximately 81%. This figure surpasses the average compliance rate typically observed in studies of this nature.[504,505]

The present study has a few limitations, which must be acknowledged. One of the limitations is the presence of selection bias, stemming from the exclusion of patients who face language barriers. Additionally, it is plausible that younger patients may be more likely to participate in the study due to their greater familiarity with technology. In order to mitigate this issue, efforts were made to communicate via an interpreter and to provide examples illustrating the ease of wearing WAMs with the aim of encouraging patients. Furthermore, the COVID-19 pandemic had a significant impact on the recruitment of patients due to a suspension of the study for a duration of 5 months. The generalisability of the findings may have been affected as a result of recruiting patients exclusively from a single institution. Nevertheless, it is worth noting that the characteristics of this cohort closely resemble those reported in national audits.[506,507] The patients were monitored for only two weeks following their surgery. Long-term follow up at >6 months will be further elaborated in chapter 7 and 8.

While it was not feasible to carry out blinding in this particular study, patients were identified in a systematic and consecutive manner, aiming to mitigate any potential bias in the data collection process. Although subgroup analyses were performed in order to minimise the influence of confounding factors from concurrent operations, it is important to note that the limited sample size within each subgroup could potentially lead to a false negative result. There is a possibility that attrition bias might have arisen as a result of a greater number of patients experiencing issues with their arm choosing to withdraw or

being lost to follow-up, potentially leading to an underestimation of the overall morbidity. This was effectively mitigated by sensitively encouraging patients to continue participation and personalised communication with patients through telephone calls. Factors such as handedness, neoadjuvant/adjuvant therapy, the presence of drains, and the experience of pain may all exert an influence on levels of upper limb activity. Neoadjuvant/adjuvant therapy such as radiotherapy is not accounted for in this study, as the primary objective of the study is to investigate the impact of SLNB and ALND on upper limb activity. In this study, only 2.9% and 4.8% (Table 6-1) of the patients who underwent SLNB and ALND, respectively, had neoadjuvant radiotherapy. Future research should intentionally recruit patients to compare those receiving neoadjuvant/adjuvant therapies with those who do not. By collecting pre-operative data and comparing the post-operative upper limb activity levels to the baseline, the potential impact of handedness and neoadjuvant/adjuvant therapy may be minimised. Additionally, a subgroup analysis was conducted to ensure that patients without drains were excluded, and the trends observed were consistent with the findings of the primary analysis.

6.6 Clinical Implications

In comparison with SLNB, ALND has been shown to result in greater upper limb morbidity. This is characterised by a reduction in upper limb activity, as assessed by WAMs. The findings of the study also demonstrate the longitudinal impact of SLNB, which have an impact on upper limb activity levels, persisting for up to 2 weeks following surgery. This finding is of great significance as it indicates the possibility of prolonged morbidity even in de-escalated surgical procedures. This information is important for patient counselling and for informing the development of new clinical trials potentially using WAMs. It is imperative that we thoroughly explore non-invasive alternatives and adjunct procedures in order to effectively reduce the occurrence of upper limb complications. Additionally, we should consider the possibility of safely omitting nodal mapping altogether, while ensuring the safety and well-being of patients. Furthermore, objective monitoring of recovery following axillary surgeries has the potential to improve patient outcomes. This may be achieved by identifying individuals who are more susceptible to developing upper limb complications and would benefit from early exercise

intervention via a personalised rehabilitation programme. Patients who are more susceptible to upper limb complications include those who receive adjuvant/neoadjuvant therapy such as radiotherapy. The long-term impact of radiotherapy on upper limb activity should be measured and accounted for using WAMs in future studies for risk stratification and determining appropriate intervention based on their activity levels.

This chapter provides evidence that WAMs can be applied as an objective tool to measure upper limb activity during the short-term postoperative period. In the subsequent chapter, WAMs will be applied in a complex surgical setting with a long-term follow up (>6 months) to provide novel insights into the upper limb activity levels following breast reconstruction surgery in comparison to simple mastectomy.

7 THE USE OF WEARABLE ACTIVITY MONITORS (WAMS) IN COMPLEX SURGERY – COMPARISON STUDY BETWEEN SIMPLE MASTECTOMY, DEEP INFERIOR EPIGASTRIC PERFORATOR RECONSTRUCTION AND IMPLANT-BASED RECONSTRUCTION USING VALIDATED WAMS

7.1 Abstract

Background: The demand for breast reconstruction has increased due to the established benefits for patients, allowing them to overcome the psychological burden associated with simple mastectomy. Given the long-term survivorship, objective data is vital to aid patients in making treatment decisions. This study aimed to objectively quantify the impact of simple mastectomy (Mx), implant-based reconstruction (IBR), and Deep Inferior Epigastric Perforator (DIEP) on upper limb activity using wearable activity monitors (WAMs) in the short-term (perioperative period) and long-term (>6 months).

Methods: A prospective, single-centre, observational study was conducted from February 2020 to May 2022. Consecutive patients undergoing breast and reconstructive surgery were identified from operating schedules. Recruited participants were invited to wear WAMs on both wrists for an average of 3 days preoperatively, for 2 weeks post-operatively and at greater than 6 months post-operatively. In total, 48 patients with breast cancer were recruited of whom 17 underwent DIEP, 22 underwent Mx and 9 underwent IBR.

Results: A significantly greater reduction of gross upper limb activity as a percentage of pre-operative activity was observed in DIEP compared with Mx and IBR patients across week 1 (Median: 40.1% versus 62.1% versus 61.8%; $p<0.001$) and week 2 (Median: 60.1% versus 77% versus 83.9%; $p<0.001$). In the long-term follow-up, the average upper limb activity had reached or exceeded their baseline levels for all operative procedures, Mx=113.9%, IBR=98%, and DIEP =102.9%. Multivariate analysis demonstrated that DIEP surgery was an independent predictor that influence upper limb activity in week 1 ($F=4.796$, $p=0.043$) and 2 ($F=7.306$, $p=0.015$) while adjuvant immunotherapy ($F=11.153$, $p=0.004$)

was found to be an independent predictor for upper limb activity at greater than 6 months postoperatively.

Conclusion: Despite DIEP patients having the lowest upper limb activity level in the acute post-operative period when compared with Mx and IBR, average upper limb activity levels returned to baseline in the long-term for all procedures. This information may help physicians and patients have informed discussions about expectations for recovery. Objective monitoring of recovery using WAMs can support the development of a personalised rehabilitation programme for those at risk of developing upper limb complications.

Sections of this chapter have been published in Journal of Plastic, Reconstructive and Aesthetic Surgery: Che Bakri NA, Kwasnicki RM, Giannas E, Dutta T, Hunter JE, Henry FP, Wood S, Ashrafian H, Darzi A, Leff DR. Delineating upper limb longitudinal recovery after simple mastectomy, implant or autologous breast reconstruction using wearable activity monitors. J Plast Reconstr Aesthet Surg. 2025 May;104:113-122. doi: 10.1016/j.bjps.2025.02.012. Epub 2025 Feb 13. PMID: 40120218.

7.2 Introduction

Mastectomy continues to be regarded as one of the primary and most effective treatment choices for individuals diagnosed with breast cancer.[508] A significant number of patients who undergo mastectomy express a preference for and are presented with the option of undergoing either prosthetic-based reconstruction or autologous tissue reconstruction, such as the deep inferior epigastric perforator (DIEP) flap technique.[506,509,510] The need for reconstruction has increased, primarily due to advancements in cancer treatment. Additionally, the documented benefits in terms of functionality, psychology, and social aspects have contributed to this growing demand.[508] These advantages enable patients to effectively address the psychological challenges associated with mastectomy.[511] Given that a significant proportion of women are expected to survive cancer in the long term,[69] it is imperative to consider the risks and upper limb morbidity that are linked to mastectomy and breast reconstruction. This consideration is vital in order to facilitate informed treatment decisions for both patients and surgeons.

Despite the wealth of evidence on the effects of breast reconstruction surgery on abdominal morbidity (donor-site) and the subjective measurement of complications post-breast reconstruction through questionnaires, the objective impact of reconstruction on upper limb morbidity remains under-reported.[79] DIEP and pre-pectoral implant-based reconstruction (IBR) were chosen as they are two of the most frequently performed breast reconstructions internationally[512-514] as comparison groups to simple mastectomy (Mx) in this study (Figure 7-1). DIEP reconstruction does not require sacrificing any muscle around the shoulder joint, although it is a major surgery involving abdominal donor site. The flap is reconstructed into the pre-pectoral region that has already been created by mastectomy. Nevertheless, previous research has shown that DIEP reconstruction is linked to shoulder dysfunction, suggesting a potential iatrogenic impact on upper limb function resulting from the procedure.[16] It is reasonable to anticipate that the major abdominal surgery performed during DIEP surgery would also impact patients' overall upper limb activities and functional capacity. The abdominal muscles are essential for core stability and overall body mechanics.[22,515,516] Post-abdominal surgery, the abdominal muscles may weaken or patients may refrain from using their core muscles, potentially resulting in altered posture (e.g. hunched forward), which may affect upper limb activity.[22,23] Pain from the

abdominal incision and surrounding areas may adversely affect patient's overall activity as well as upper limb activity which may impede activities of daily living such as reaching and lifting.[517-519] Pre-pectoral IBR does not involve manipulation of the pectoralis major muscle. Therefore, it is hypothesised that DIEP patients exhibit the lowest levels of upper limb activity in comparison with IBR and Mx. This chapter focuses on investigating the impact of breast reconstructions versus simple mastectomy on upper limb activity using WAMs.

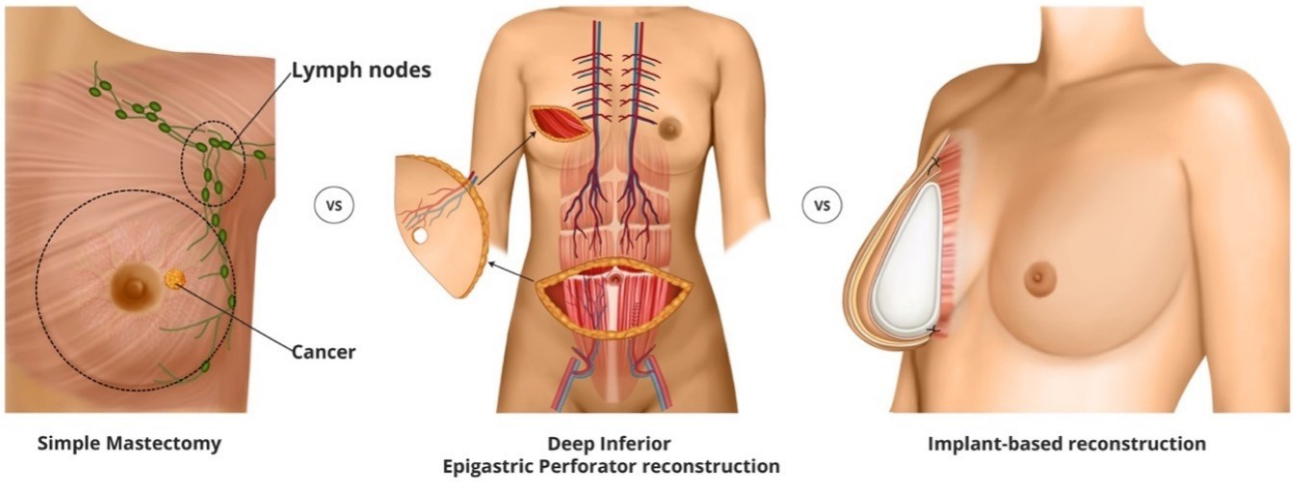


Figure 7-1 Simple mastectomy versus deep inferior epigastric perforator reconstruction versus implant-based reconstruction (The figure was created by Mohesh Mohan, used with permission)

7.2.1 Mastectomy

Mastectomy was initially performed by Halsted in 1882 in a form of radical mastectomy which was deemed to be the "gold standard" until the 20th century.[520-522] In this radical mastectomy, breast and skin, pectoralis major muscle, axillary nodes, and sometimes the supraclavicular region are also removed.[521] Later on, less invasive surgical procedures together with radiotherapy were invented to spare the breast from radical surgeries.[520] Robert McWhirter, a pivotal figure in less radical mastectomy made an intriguing discovery where 757 patients were treated with simple mastectomy followed by radiotherapy. They were compared with 411 patients treated with radical mastectomy and radiotherapy, and the former had a better survival rate compared with the latter.[522,523] This less invasive procedure

with radiotherapy was initially thought to be scandalous when it was introduced by Geoffrey Keynes in 1930s.[523] In 1948, a modified radical mastectomy was introduced by Patey and Dyson from Middlesex Hospital.[524] McWhirter's method and Patey's method were studied intensively and had similar outcomes, which led to the invention of breast conserving surgery.[525] A total or simple mastectomy is the removal of breast tissue and related skin, either with or without axillary surgery.[526] This is carried out on patients who cannot be treated with breast conserving operations, such as those who have larger tumours (compared to the size of the breast) or who have already received chest wall radiation therapy.[526] Skin-sparing is performed by preserving the skin envelope, whereas nipple-sparing is performed by preserving the skin envelope and the nipple areola complex.[526] This will be offered to individuals with small tumours that are not close to the nipple, or as prophylactic mastectomy for those who have genetic abnormalities or a high-risk family history.[526]

7.2.2 Complication of Mastectomy

Systematic review in chapter 2 described the impact of mastectomy on upper limb function such as lymphoedema and impaired range of motion. Several well-documented complications of different types of mastectomies can be found in Table 7-1.

Table 7-1 Complications of mastectomy.

Type of Mastectomy	**Risks and Complications**
Halsted's radical mastectomy	Lymphoedema, extensive scars, reduced shoulder function, chronic pain[527]
Patey's mastectomy	Lymphoedema, seroma, infection, haematoma[528]
Total or simple mastectomy	Flap necrosis, seroma, haematoma[508]
Skin-sparing mastectomy (normally followed by reconstruction)	Nipple necrosis, recurrence, nipple malposition, recurrence, complications related to construction[529] (see Table 7-3)

7.2.3 Breast Reconstruction

As breast reconstruction was found to have psychosocial benefits and causing improvement in HRQoL, it is becoming more popular in the late 1990s.[530] In the UK, approximately 30% of women undergo breast reconstruction after mastectomy.[506] There are many advantages of breast reconstruction including; better aesthetics, improved self-esteem and confidence, increased satisfaction, decreased anxiety and depression, and improved HRQoL.[531] Despite having psychosocial benefits, there are numerous factors preventing patients from having breast reconstruction, including a lower educational level, increased age, major comorbidities, and chemotherapy.[532] More recently, based on the survey conducted by Breast Cancer Now and the latest data from Hospital Episode Statistics, many women could not access the breast reconstruction service due to the COVID-19 pandemic.[533] There are two major groups of breast reconstruction techniques: autologous techniques, which utilise the patient's own tissue to form a new breast, and alloplastic techniques, which use synthetic implants.[534] Each technique has fundamental advantages and disadvantages and therefore the optimum technique should be chosen after considering the patient's specific circumstances, including the timing of adjuvant therapy, the duration of the recovery period, and any comorbid conditions.[534] The most common autologous reconstruction is DIEP technique (Table 7-2).[512] The alloplastic technique using synthetic implants can be done immediately after a mastectomy (during the same operation) or at a later stage after radiotherapy (delayed).[535]

Table 7-2 Type of breast reconstruction

Type of Breast Reconstruction
Deep Inferior Epigastric Perforator (DIEP) flap
Latissimus Dorsi (LD) flap
Transverse Rectus Abdominal Muscle (TRAM) flap
Superior Gluteal Artery Perforator or Inferior Gluteal Artery Perforator (SGAP or IGAP)
Transverse Myocutaneous Gracilis flap or Transverse Upper Gracilis flap (TMG or TUG)

7.2.4 Deep Inferior Epigastric Perforator (DIEP) flap

DIEP flap is a procedure where the skin, fat, and blood vessels in the abdomen are used to rebuild the breast shape while leaving the underlying rectus abdominus muscle intact and remains the "gold standard" for autologous reconstruction.[536] DIEP became popular in the 1990s as a means of breast reconstruction as it has advantages over the TRAM procedure, sparing the rectus abdominus and reducing the possibility of muscle weakness or ventral hernia.[536,537] The DIEP flap procedure is suitable for individuals with sufficient tissue available for transfer, as well as for women seeking an alternative to breast implants. This type of reconstruction is not appropriate for individuals who have a slender physique, have previous abdominal surgeries, have small or unsuitable deep inferior epigastric perforator or those who have a pressing need to resume their regular daily routines quickly.[538,539] In a study conducted by Thorarinsson *et al.,*[540] it was demonstrated that individuals who underwent DIEP breast reconstruction expressed higher levels of satisfaction with their reconstruction and overall outcome in comparison with alternative reconstruction methods, such as latissimus dorsi (LD) flap with implant, lateral thoracodorsal flap with implant, and an expander with secondary implant.

7.2.5 Implant-Based Reconstruction

There has been a trend toward greater use of implants for breast reconstruction.[541] IBR is a popular choice for post-mastectomy reconstruction since recovery is relatively faster without a donor site, the procedure is safe, and it improves patient's quality of life.[542] IBR was reported in 1971 by Snyderman and Guthrie and the implant is placed under the remaining chest wall following mastectomy.[543] Implants can be inserted sub muscularly (under the pectoralis muscle) or sub glandularly (pre-pectoral) (above the pectoralis muscle).[534,544] IBR can be performed in two stages. In the first stage, a tissue expander is put beneath the skin and gradually filled with saline at regular intervals, followed by the second stage where the implant is inserted 2-6 months later.[534,544] It can also be performed concurrently with a mastectomy when no tissue expander is required.[534,544] The usage of acellular dermal matrix as a sling to support tissue expanders or implants is increasing.[542]

7.2.6 Complication of Breast Reconstruction

Bennet *et al.,*[545] conducted a study with a cohort of 2343 patients who were followed up for a duration of two years. The findings of their research indicate that those who underwent any autologous reconstruction type had considerably higher likelihoods of experiencing complications in comparison with those who underwent expander-implant reconstruction.[545] Furthermore, an analysis of complications over a one-year period revealed that women who underwent pedicled transverse rectus abdominis musculocutaneous (pTRAM) and DIEP flap procedures had significantly greater likelihood of experiencing major complications in comparison with women who underwent implant-based techniques.[546] The occurrence of abdominal bulge/hernia is lower in DIEP and muscle-sparing free TRAM (fTRAM) flaps as compared to pTRAM and non-muscle-sparing fTRAM flaps.[547-549] However, DIEP flaps, which involve the preservation of the abdominal rectus muscle, has been linked to an increased incidence of flap loss and fat necrosis. This is likely due to a comparatively less efficient blood flow and the procedural challenges associated with dissecting the perforator.[549,550] A systematic review and meta-analysis demonstrated that bilateral DIEP flap reconstruction is linked to a notably higher likelihood of experiencing complete flap failure as compared to unilateral reconstruction.[551] He *et al.,*[547] suggested that whenever feasible, it is advisable to consider doing DIEP or muscle-sparing fTRAM flaps in the case of obese individuals, as this approach has the potential to mitigate the likelihood of abdominal bulge or hernia development. Despite the increased risk of flap loss, pTRAM flaps remain a viable alternative in situations when microsurgery is not accessible.[547] It is important to note that the evidence regarding upper limb morbidities post-breast reconstruction surgery is still lacking as discussed in chapter 2, particularly by objective means. Complications of different types of breast reconstructions can be found in Table 7-3.

Table 7-3 Complications of Breast Reconstruction

Type of Breast Reconstruction	**Risks and Complications**
Deep Inferior Epigastric Perforator (DIEP)	Flap loss, fat necrosis, hernia, infection, seroma, venous congestion, arterial thrombosis[552-555]

Implant-based reconstruction (IBR)	Capsular contracture, flap necrosis, failure of reconstruction/implant loss, infection, seroma[556-558]
Transverse Rectus Abdominal Muscle (TRAM) flap	Flap loss, fat necrosis, abdominal bulge/hernia, muscle weakness, wound infection[559-561]
Latissimus Dorsi (LD) flap	Flap loss, skin necrosis, shoulder dysfunction, infection, haematoma, infection, donor-site seroma[562-564]
Superior Gluteal Artery Perforator or Inferior Gluteal Artery Perforator (SGAP or IGAP)	Flap loss, fat necrosis, nerve injury, functional deficits in the lower extremity, pain in the donor site, haematoma[565-567]
Transverse Myocutaneous Gracilis flap or Transverse Upper Gracilis flap (TMG or TUG)	Flap loss, fat necrosis, numbness, infection, haematoma, seroma, lymphoedema, pain[568,569]

7.2.7 Shared-decision making (SDM)

Several international guidelines advocate shared decision making (SDM), which enables patients and physicians to agree on the surgical reconstructive care based on the patient's values and choices.[570] SDM is a patient-centred approach and may assist patients in comprehending the data around breast reconstruction and informing their expectations of surgical outcomes, thereby improving their satisfaction with the procedure.[571] Up to 47% of women who had breast reconstruction had decisional regret.[572,573] It is vital to highlight that, according to a research study, less than half of women have the knowledge necessary to make an informed decision on breast reconstruction.[574] In spite of the significance of SDM, there is an unmet need for support in the context of breast reconstruction decision-making following mastectomy.[575,576] Therefore, it is important to develop a tool to provide objective evidence of the patient's recovery after their choice of surgeries. This could help surgeons and patients make informed treatment decisions for breast cancer.

7.2.8 Outline of the Clinical Problem

The aesthetic and psychosocial benefits of breast reconstruction have been discussed previously. However, research also suggests that breast reconstruction does not always confer improved satisfaction.[577] In comparison with a simple mastectomy, reconstruction is associated with a longer hospital stay and higher rates of wound complications.[578,579] DIEP is more complex and time-consuming than IBR, but it is also more economical and less likely to need long-term revisional surgery.[580,581] While donor-site morbidity has been investigated and the subjective morbidity of reconstruction is documented (e.g., through questionnaires), the objective effect of reconstruction on upper limb dysfunction is comparatively unknown. This is further illustrated in a systematic review presented in chapter 2, where, despite growing evidence on the impact of breast reconstruction on upper limb function, the evidence, especially objective data, remains insufficient.

Unidentified consequences of breast reconstruction can lead to long-term complications. While significant postoperative issues are likely to be disclosed by the patients, those having trouble with daily activities because of manageable causes might not be identified until their next follow up. Some of these patients may lack understanding or motivation, and thus may have to endure a slower convalescence if not identified early.[224]

There are many ways to evaluate the success of breast reconstruction, including the BREAST-Q questionnaire, which includes scales for HRQoL, psychosocial, physical, and sexual well-being. This questionnaire primarily targets patients who have undergone reconstructive procedures for breast cancer.[274] As previously discussed in chapter 3, there are also DASH questionnaires or goniometry that assess the shoulder function and range of motion respectively (see Table 3-2). For example, Humar *et al.*,[582] used DASH questionnaire to assess upper limb morbidities in breast reconstruction patients. Woo *et al.*,[282] investigated the impact of breast reconstruction on the upper limb using objective measurements such as goniometry. However, this measurement can have inter-operator variability and is challenging to perform in clinical setting.[282] There is no consensus method in assessing upper limb

outcomes of breast reconstruction surgery. Assessment of outcome is important due to many reasons. An objective, longitudinal assessment of upper limb activity across the post-operative period using WAMs would help patients and surgeons understand the activity levels associated with their surgery and facilitate shared decision-making, including the patient's preferences and the feasibility of undergoing a more complex surgery based on their individual circumstances. The team responsible for the patient must have access to information regarding the patient's progress in order to modify the care approach. Without regular patient evaluations, the plan for following up with a patient is generic and slow to change as the patient gets better. There is an ongoing work in order to deliver appropriate treatment into the community, where patients and non-specialist centres play a more active role in the management of sub-acute conditions in order to achieve the best patient outcomes, but it requires investment across primary care, social care, public health and community health.[583] From an economic and hospital resource perspective, the objective data measured by WAMs allow the hospital and the community to estimate short-term and long-term care demands, which is essential so that appropriate support can be given.

The objective of this chapter is to monitor the upper limb activity levels following DIEP, Mx and IBR in the short-term and long-term as well as determine the independent predictors of upper limb activity levels in this patient cohort. The methodology used in this study was described in chapter 4. I conducted the patient recruitment with Dr Omar Ghandour, Dr Manolis Giannas, Dr Luqman Tenang, Dr Salem Elias, Dr Zoha Imam and Dr Catharina Moenig.

7.3 Hypothesis

- ◊ *Patients who have deep inferior epigastric perforator reconstruction demonstrate the lowest upper limb activity level compared with patients who undergo implant-based reconstruction and simple mastectomy during the 2-week post-operative period. All groups of patients return to their preoperative baseline levels at the long-term follow-up*

7.3.1 Outcomes

The primary endpoint of the study was to assess the levels of upper limb activity after undergoing DIEP, Mx and IBR (independent of the specific axillary operation performed) in the short-term (2 weeks after surgery) and long-term (greater than 6 months after surgery). The secondary endpoint of the study involved a planned subgroup analysis to compare the levels of upper limb activity between patients who underwent DIEP+SLNB, IBR+SLNB, and Mx+SLNB, as well as between patients who underwent DIEP+ALND and Mx+ALND, perform a multivariate analysis to determine independent predictors of upper limb activity levels and examine the association between pain scores and upper limb activity levels.

7.4 Results

7.4.1 Study Participants

Between February 2020 and May 2022, a total of 125 patients at Imperial College Healthcare NHS Trust were identified as potentially eligible from the electronic records (Figure 7-2). The study was halted from March to July 2020 due to the COVID-19 pandemic. Eleven patients did not meet the inclusion criteria, 49 patients declined to participate due to the stress of the cancer diagnosis, coinciding trials or else no reason was given. In 11 cases, surgeries were rescheduled/cancelled. Four patients withdrew from the study (e.g., irritation from sensors, non-compliant), 2 patients were excluded due to technical reason (e.g., broken sensors) leaving a total of 48 patients for analysis (17 DIEP, 22 Mx, 9 IBR) (Table 7-4). Twenty-five patients agreed to participate in the long-term data collection (9 DIEP, 10 Mx, 6 IBR). The median follow-up for long-term data is 19 months (11–47 months). All IBR patients had direct-implant pre-pectoral reconstruction. All DIEP reconstructions were performed in one stage. The list of patients' co-morbidities is presented in Appendix 16.

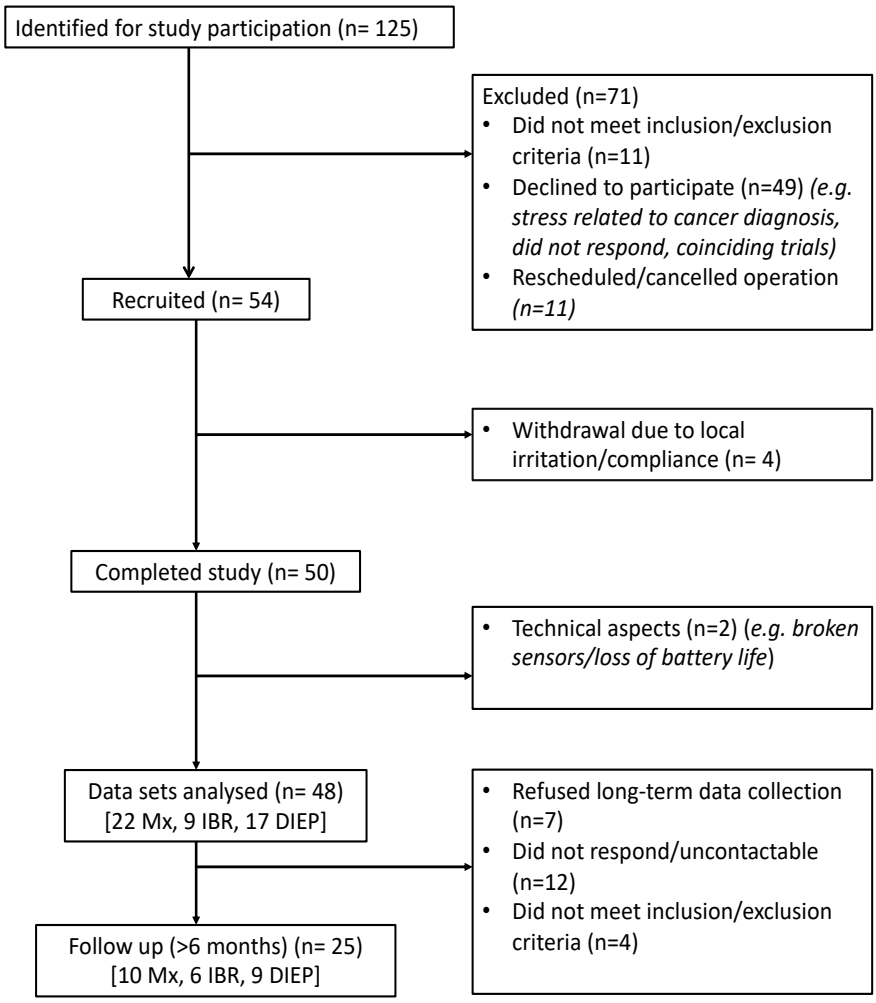


Figure 7-2 Participant flow diagram investigating the impact of DIEP, IBR and Mx on upper limb activities. DIEP, Deep Inferior Epigastric Perforator; IBR, Implant-Based Reconstruction; Mx, Simple Mastectomy.

Table 7-4 Demographics of study population (n=48) (means presented with standard deviations (SD) and numbers presented with whole number percentage (%) of total population in each group)

Characteristics	**Mastectomy (n=22)**	**DIEP (n=17)**	**Implant (n=9)**	**p value**
Mean Age, (yrs.) (SD)	59 (10.4)	51 (11.4)	46 (9.6)	0.311
Sex Ratio (M:F)	1:21	0:17	0:9	0.443
Comorbidities: n (%)	13 (59.1%)	10 (58.8%)	5 (50%)	0.878
Mean BMI (SD)	28.7 (7.1)	28.6 (6)	22.5 (3)	0.311
Handedness Ratio (R:L:BL)	22:0:0	15:2:0	8:1:0	0.153
Race/ethnicity: n (%)				
White British	3 (13.6%)	4 (23.5%)	1 (11.1%)	0.165
White Irish	2 (9.1%)	0 (0%)	0 (0%)	
White and any other White background	2 (9.1%)	1 (5.9%)	2 (22.2%)	
Asian or Asian British – Indian/Pakistani	0 (0%)	4 (23.5%)	0 (0%)	
Asian – any other Asian background	1 (4.5%)	2 (11.8%)	0 (0%)	
Black or Black British African	2 (9.1%)	1 (5.9%)	0 (0%)	
Black or Black British Caribbean	1 (4.5%)	0 (0%)	1 (11.1%)	
Black or any other Black background	0 (0%)	0 (0%)	0 (0%)	
Mixed – White and Black Caribbean	1 (4.5%)	0 (0%)	0 (0%)	
Other – any other ethnic group	10 (45.5%)	5 (29.4%)	5 (55.5%)	
Clinical and pathological characteristics				
Stage of Cancer: n (%)				
Stage 0	1 (4.5%)	4 (23.5%)	2 (22.2%)	0.195
Stage 1	12 (54.5%)	10 (58.8%)	4 (44.4%)	
Stage IIA and IIB	6 (27.3%)	2 (11.8%)	0 (0%)	
Stage IIIA-IV	2 (9.1%)	1 (5.9%)	1 (11.1%)	

Risk-reducing	1 (4.5%)	0 (0%)	2 (22.2%)	
Cancer Type: n (%)				
Ductal Carcinoma In-situ	1 (4.5%)	3 (17.6%)	2 (22.2%)	0.112
Invasive Ductal Carcinoma	16 (72.7%)	9 (52.9%)	5 (55.6%)	
Invasive Lobular Carcinoma	3 (13.6%)	1 (5.9%)	0 (0%)	
Invasive Mucinous Carcinoma	0 (0%)	2 (11.8%)	0 (0%)	
Other	1 (4.5%)	2 (11.8%)	0 (0%)	
BRCA carrier	1 (4.5%)	0 (0%)	2 (22.2%)	
Previous Breast Surgery: n (%)	3 (13.6%)	8 (47.1%)	3 (33.3%)	0.068
Patients with drain (n,%)	17 (77.3%)	17 (100%)	9 (100%)	0.05
Drain in situ in axilla/breast: Mean days (SD)	6.8 (5.9)	8 (5.5)	6.7 (3.8)	0.020
Length of Stay: Days (SD)	1.3 (1.8)	4 (1)	1.7 (0.9)	<0.001
Advice about exercise: n (%)	22 (100%)	17 (100%)	9 (100%)	-
Compliance to analgesia: n (%)	22 (100%)	17 (100%)	9 (100%)	-
Direct to implant pre-pectoral reconstruction	n/a	n/a	9 (100%)	
Treatment received				
***Type of Axillary Surgery: n (%)**				
Sentinel Lymph Node Biopsy	10 (45.5%)	6 (35.3%)	4 (44.4%)	0.006
Axillary Lymph Node Dissection	11 (50%)	3 (17.6%)	1 (11.1%)	
Completion of ALND after positive nodes from SLNB	Nil	Nil	Nil	N/A
Operation Laterality Ratio (R:L:BL)	11R:11L:0BL	6R:7L:4BL	6R:0L:3BL	0.083
Neoadjuvant Therapy (n,%):				
Radiotherapy	0 (0%)	1 (5.9%)	1 (11.1%)	0.089

Chemotherapy	8 (36.4%)	3 (17.6%)	3 (33.3%)	
Endocrine therapy	0 (0%)	2 (11.8%)	1 (11.1%)	
Immunotherapy	0 (0%)	1 (5.9%)	2 (22.2%)	
Adjuvant Therapy Whilst Wearing WAMs in perioperative period (n,%):				
Radiotherapy	0 (0%)	0 (0%)	0 (0%)	0.906
Chemotherapy	0 (0%)	0 (0%)	0 (0%)	
Endocrine therapy	2 (9.1%)	1 (5.9%)	1 (11.1%)	
Adjuvant Therapy (n,%):				
Radiotherapy	7 (31.8%)	1 (5.9%)	1 (11.1%)	0.238
Chemotherapy	6 (27.3%)	1 (5.9%)	1 (11.1%)	
Endocrine therapy	9 (52.9%)	4 (18.2%)	3 (33.3%)	
Immunotherapy	7 (31.8%)	1 (5.9%)	2 (22.2%)	

BMI, body mass index; SD, standard deviation; WAM, wearable activity monitors; BRCA, BReast CAncer gene; SLNB; Sentinel Lymph Node Biopsy, ALND; Axillary Lymph Node Dissection

7.4.2 *Gross Upper Limb Activity (Combined Activity Levels)*

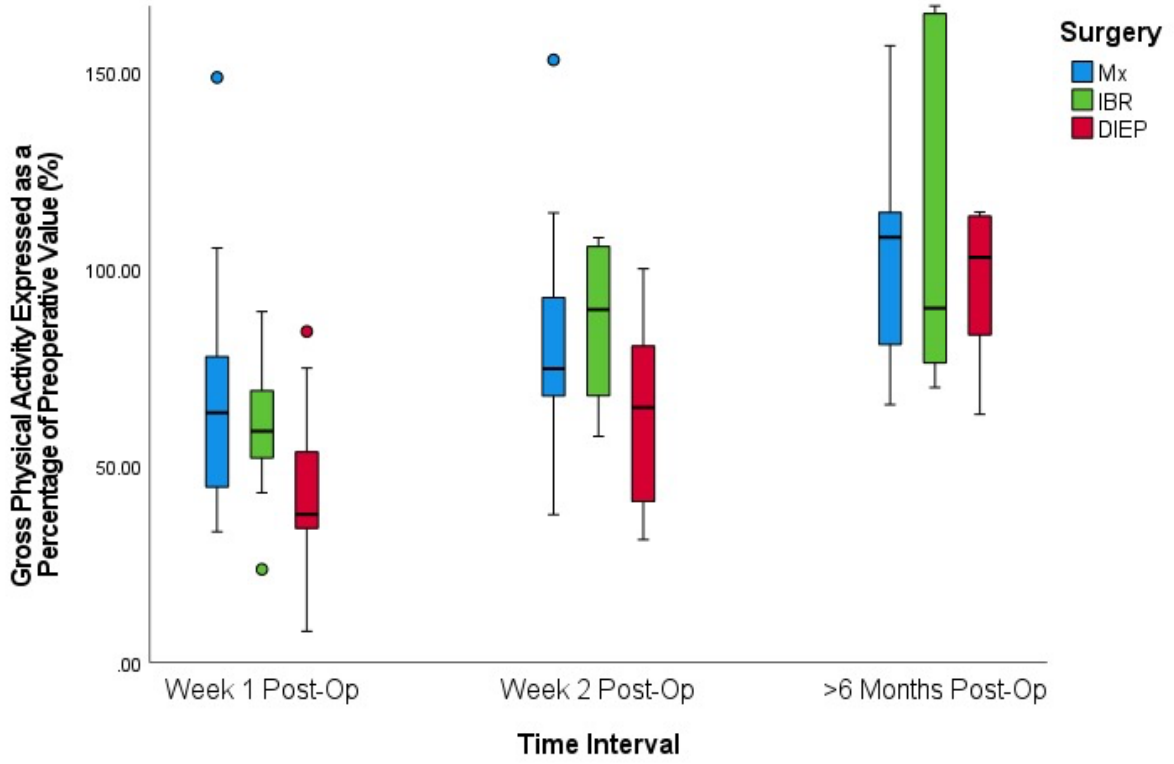


Figure 7-3 Gross upper limb activity (combined activity levels) expressed as percentage (%) of pre-operative level at week 1, week 2 and >6 months post-operatively comparing DIEP, Mx and IBR. DIEP, Deep Inferior Epigastric Perforator; Mx, Simple Mastectomy; IBR, Implant-Based Reconstruction.

Over two weeks post-operatively, DIEPs were the least physically active (as a percentage of pre-operative level) compared with Mx and the IBR group where DIEP patients had the lowest upper limb activity compared with Mx and IBR in both week 1 (Median: 40.1% [interquartile range (IQR) 25.5-58.2] versus 62.1% [IQR 47.1-81] versus 61.8% [IQR 47.5-74.3]; $p<0.001$) and week 2 (Median: 60.1% [IQR 42.2-80.8] versus 77% [IQR 60.8- 100.3] versus 83.9% [IQR 66.1-103.8]; $p<0.001$) respectively (Figure 7-3). Post-hoc analysis demonstrated that while there was significant difference in activity levels between DIEP versus IBR (Week 1: $p<0.001$; week 2: $p<0.001$) and DIEP versus Mx (Week 1: $p<0.001$; week 2: $p<0.001$), there was no significant difference in activity levels between Mx and IBR group in week 1 ($p=0.585$) and week 2 ($p=0.164$) respectively. It is also important to note that there was no significant difference between the pre-operative baseline levels between 3 different procedures

(p=0.697). When analysed according to the combined PODs, there was a significantly greater reduction in upper limb activity following DIEP surgery compared with Mx and IBR across PODs 1-3, 4-6, 7-9 and 10-12 (Figure 7-4) (Table 7-5).

While all patients in the DIEP and IBR groups received drains in the immediate post-operative period, no drain was inserted in 5 patients in the Mx group. The trend remained the same upon sub-group analysis, excluding the patients without drains (Appendix 17).

In the long-term follow up (median: 19 months [11-47 months]), on average, their upper limb activity had reached or surpassed their baseline levels for all operation types, with activity levels of Mx (Median: 113.9% [IQR 102.3-119.6]), IBR (Median: 98% [IQR 83.2-194.5]), and DIEP (Median: 102.9% [IQR 86.8-112.8]) for each respective group.

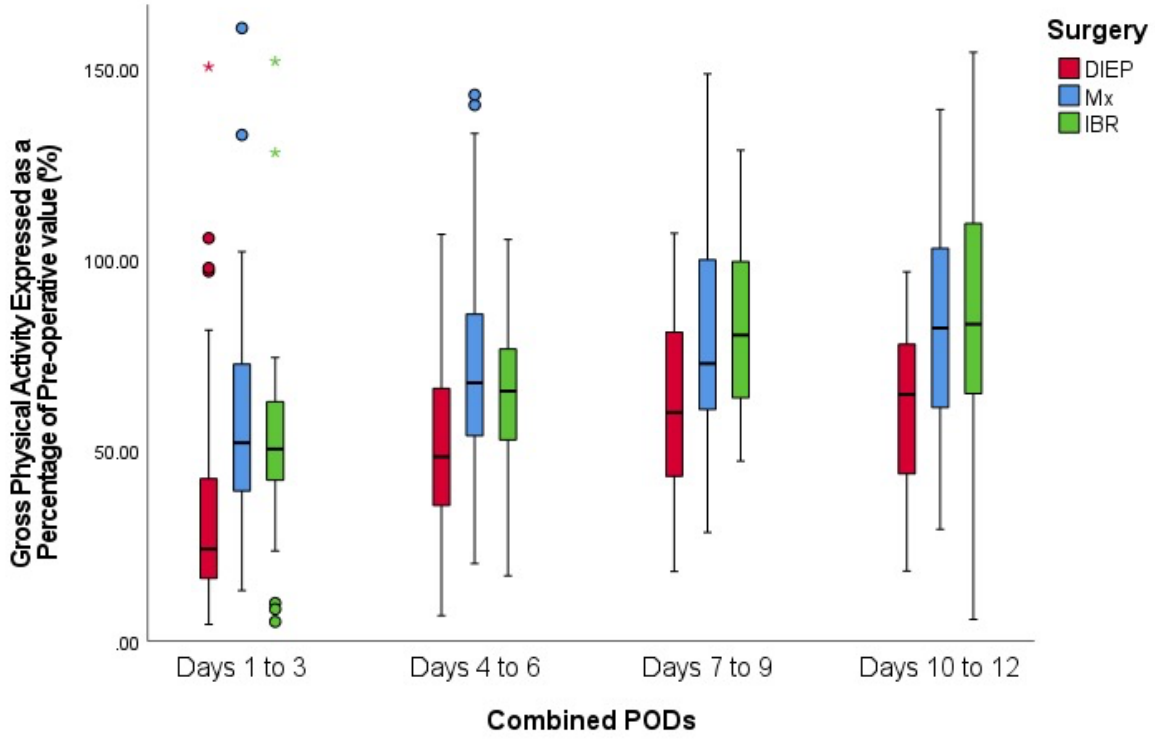


Figure 7-4 Gross upper limb activity (combined activity levels) at different combined post-operative days (PODs) for Deep Inferior Epigastric Perforator (DIEP), Mastectomy (Mx) and Implant-Based Reconstruction (IBR)

Table 7-5 Gross upper limb activity (combined activity levels) at different combined post-operative days (PODs) for Deep Inferior Epigastric Perforator (DIEP), Mastectomy (Mx) and Implant-Based Reconstruction (IBR)

Surgery	**Combined PODs**	**1-3**	**4-6**	**7-9**	**10-12**
DIEP	Median (%)	24.10	48.31	59.85	64.57
	IQR (%)	26.07	29.54	37.74	33.91
Mx	Median (%)	51.91	67.65	72.71	81.99
	IQR (%)	39.32	53.79	60.79	61.39
IBR	Median (%)	50.29	65.43	80.10	82.99
	IQR (%)	20.56	23.76	33.14	41.77
p values		<0.001	<0.001	0.003	0.008

7.4.3 Surgically Treated Side

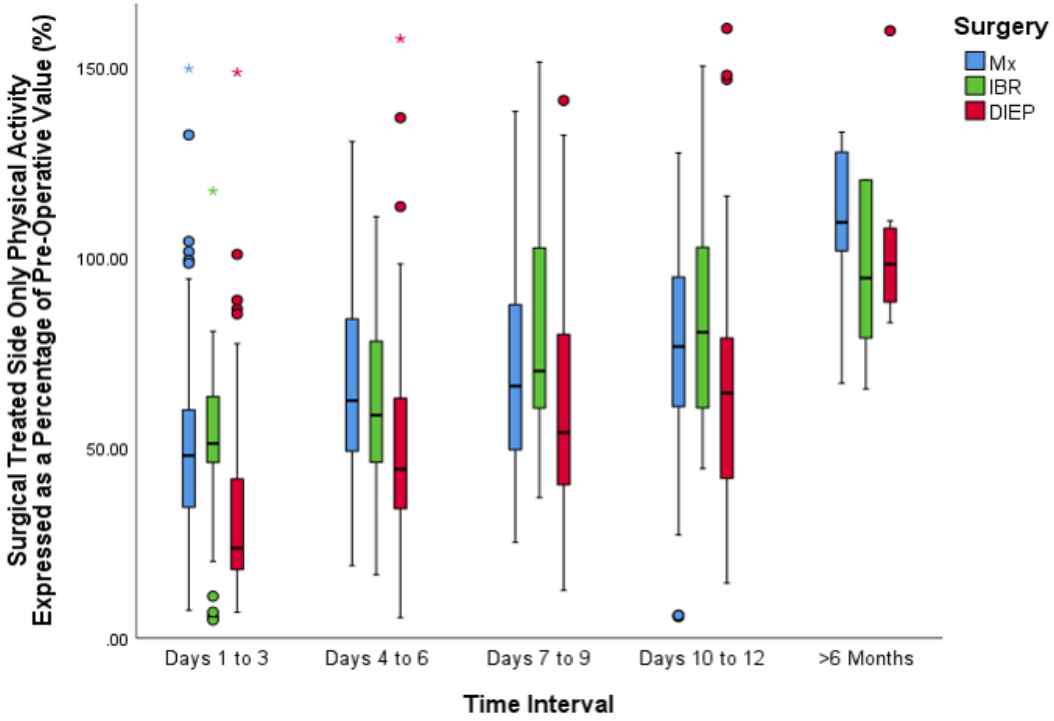


Figure 7-5 Surgically treated side only expressed as percentage (%) of pre-operative level at different combined post-operative days comparing Deep Inferior Epigastric Perforator (DIEP), Mastectomy (Mx) and Implant-Based Reconstruction (IBR)

When comparing activities of ipsilateral treated side only across different PODs, DIEPs had the most significant reduction in upper limb activity levels compared with Mx and IBR especially across PODs 1-3 (Median: 23.6% [IQR 18-41.8] versus 47.9% [IQR 34.9-59.7] versus 51.2% [IQR 43.9-67.5]; p<0.001) (Figure 7-5). Post-hoc analysis demonstrated that while there was significant difference in upper limb activity levels of ipsilateral treated side between DIEP versus IBR (p<0.001) and DIEP versus Mx (p<0.001), there was no significant difference in upper limb activity levels of ipsilateral treated side between Mx and IBR (p=0.260).

In the long-term follow up, there was no significant difference (p=0.219) in the upper limb activity levels of the ipsilateral treated side between Mx (Median:109.2% [IQR 101.7-127.6], IBR (Median:104.2% [IQR 80.6-105.5] and DIEP (Median:105.7% [IQR 94.5-124.9]. Comparison between ipsilateral versus contralateral side are summarised in Appendix 18.

7.4.4 Subgroup Analyses

Subgroup analysis was performed to compare 'DIEP+SLNB' versus 'Mx+SLNB' versus 'IBR+SLNB'. DIEP was observed to have a significantly greater reduction of upper limb activity in both week 1 (Median: 46.5% [IQR 25.1-67.5] versus 68% [IQR 49.9-86.5] versus 58.7% [IQR 49.8-67.4]; p<0.001) and week 2 (Median: 51.4% [IQR 35.9-74] versus 86.5% [IQR 62.9-42.1] versus 77.9% [IQR 60.3-28.7]; p<0.001) respectively. At median follow up of 19 months post-surgery, there was no significant difference (p=0.561) in the upper limb activity levels between Mx+SLNB (Median: 112.5% [IQR106-1119.3], IBR+SLNB (Median 105.2% [IQR 81-224.3]) and DIEP+SLNB (Median 105.4% [92.9-112.8]).

The subgroup analysis for patients who received ALND was not performed due to sample size limitation.

7.4.5 Multivariate Analysis

Table 7-6 Multivariate analysis of risk factors that influence upper limb activity levels in week 1, week 2 and at greater than 6 months postoperatively

Week 1	**F**	**P value**
DIEP	4.796	0.043*
Adjuvant radiotherapy	0.032	0.861
Adjuvant immunotherapy	3.276	0.088
Adjuvant endocrine therapy	3.697	0.071
Week 2		
DIEP	7.306	0.015*
Adjuvant radiotherapy	0.008	0.930
Adjuvant immunotherapy	2.779	0.114
Adjuvant endocrine therapy	2.205	0.156
>6 months		
DIEP	0.055	0.817
Adjuvant radiotherapy	0.204	0.657
Adjuvant immunotherapy	11.153	0.004**
Adjuvant endocrine therapy	1.949	0.181

Outcome of multivariate regression analysis on factors affecting upper limb activity levels at week 1, week 2 and greater than 6 months postoperatively. DIEP (Deep Inferior Epigastric Perforator), adjuvant radiotherapy, adjuvant immunotherapy and adjuvant endocrine therapy have been included in this multivariate analysis.
*** $p<0.001$, ** $p<0.01$, * $p<0.05$

Multivariate analysis showed that DIEP surgery was an independent predictor that influence upper limb activity in week 1 ($F=4.796$, $p=0.043$) and 2 ($F=7.306$, $p=0.015$) (Table 7-6). Adjuvant immunotherapy ($F=11.153$, $p=0.004$) was found to be an independent predictor for upper limb activity at greater than 6 months postoperatively (Table 7-6). Univariate analysis can be found in Appendix 19.

7.4.6 Analgesia Requirement and Correlation of Upper Limb Activity with Pain Score and Complications

All patients were prescribed and were compliant to regular oral/intravenous analgesia and as required analgesia post-operatively. Reconstruction (IBR and DIEP) led to increased analgesia requirement (needing as required analgesia at least once) for breakthrough pain, in addition to regular analgesia [Increased analgesia: 29.4% DIEP, 10% Mx and 20% IBR]. A moderate negative correlation was found

between postoperative pain scores for performance of specific activities and combined activity data (R = -0.425, p = 0.003) in week 1 (Appendix 20).

In the DIEP group, one patient had delayed healing on the breast and abdominal wound and 1 patient had seroma in their breast. Two patients had seroma in their breasts and 1 patient developed reduced shoulder range of motion in Mx group. All patients who developed complications experienced reduced gross upper limb activity level (combined activity levels) during the short-term follow-up. None of the patients in the IBR group developed complications during the 2-week post-operative period.

During the long-term follow up, 1 patient experienced lymphoedema and delayed breast and abdominal wound healing. This is reflected in their diminished gross upper limb activity level (63%) during the long-term follow-up period. One patient in the IBR group reported shoulder pain and limited mobility on the side that was operated on which is consistent with a reduction in gross upper limb activity level (69%) in the long-term.

7.5 Discussion

This chapter describes the novel objective assessment of upper limb activity using WAMs in complex surgical procedures, comparing breast reconstruction surgeries with simple mastectomy. There are limited objective data pertaining to the upper limb morbidity after breast reconstruction surgery. As far as I know, this is the first time that WAMs have been used to quantify the upper limb activity in this patient group. The use of WAMs have enabled detailed, objective comparisons with high time resolution. The main finding is that DIEP is associated with a significantly greater reduction of upper limb activity compared with Mx and IBR in the acute peri-operative setting. Nevertheless, in the long-term follow-up, the upper limb activity levels of every type of surgical procedure have reached their baseline levels.

The results of the current study are consistent with Bennett *et al.*[545] in which DIEP had a significantly higher risk of developing upper limb morbidity compared with IBR. The current study indicates patients who underwent DIEP had the slowest recovery in the first two weeks following surgery compared with Mx and IBR. Additionally, the median upper limb activity levels for DIEP, Mx and IBR had not returned to baseline by the fourteenth day after surgery. Furthermore, multivariate analysis demonstrated that DIEP surgery was an independent predictor that affect upper limb activity in week 1 and week 2. However, in the long-term, there was no significant difference in the activity levels of different types of surgeries compared in the study. This implies that the recovery plateau must be at some point after the initial 2-week period and before the median follow up of 19 months following surgery. Ideally, the recovery plateau of each surgery could be determined by capturing data on a more frequent or continuous basis following surgery.

Gross upper limb activity levels after DIEP may be affected by the abdominal surgery (donor site). They may experience abdominal hernia[584-587] and reduced abdominal muscle strength,[588] which could affect patient's functional outcomes.[587] The abdominal muscles are crucial for general body mechanics and core stability.[22,515,516] DIEP surgery may weaken core muscles, potentially leading to postural changes and affecting upper limb activity.[22,23] Pain resulting from the DIEP operation and adjacent regions may also affect general and upper limb activity.[517-519] When comparing the surgically treated with the control side, there was a significant difference in upper limb activity in week 1 (Appendix 18). This data suggests that the shoulder morbidity on the operated side may also contribute to reduced activity levels, in addition to abdominal morbidity. This finding is consistent with another study in which 14.1% of DIEP patients developed reduced shoulder movement.[16] Unfortunately, subgroup analysis for ALND was not performed due to the small sample size. However, subgroup analysis of patients who underwent DIEP, Mx, or IBR with SLNB revealed consistent findings, with DIEP showing the lowest upper limb activity levels compared with the other procedures. Similarly, when comparing surgically treated and control sides after Mx surgery, there was a significant difference in upper limb activity in week 1 and 2 suggesting that Mx may also affect ipsilateral upper limb function. Prior studies have demonstrated that Mx is associated with ipsilateral shoulder dysfunction, which is worse compared

with breast conserving surgery.[307,589] Interestingly, there was no significant difference between the surgically treated and control groups after IBR. We would expect differences in upper limb activity levels across both limbs, as prior studies suggested that prepectoral IBR can cause upper limb functional impairment, even though to a lesser extent compared to subpectoral IBR.[147,590] Nevertheless, the lack of significant differences between upper limb activity of both limbs may be explained by the prepectoral placement of the implant without pectoralis muscle manipulation, and therefore may not significantly impact upper limb activity, as further elaborated below.[147]

DIEP patients demonstrated the lowest upper limb activity level of the surgically treated side compared with the other 2 groups across the first 2 post-operative weeks. In contrast, a study by Woo *et al.,*[16] found that the expander-implant caused more shoulder morbidity on the surgically treated side than DIEP (23.8% versus 14.1%) at 52 months following surgery. This is thought to be the result of pectoralis tightness and pain, which can be aggravated during the post-operative expansion period of the tissue expander which can limit shoulder movement.[16] However, all patients in the current study had direct to implant pre-pectoral reconstruction, which is more likely to be associated with shorter physical recovery time as the surgery does not involve manipulation of pectoralis muscle. As evidenced by the long-term data, the upper limb activity levels of the surgically treated side in the current study returned to their baseline levels following IBR surgery. Additionally, there was no significant difference in the level of upper limb activity between Mx and IBR patients during the perioperative period. Another study by Lang *et al.,*[591] investigated the impact of breast reconstruction on shoulder kinematics and performance during upper-limb focused functional tasks.[591] Compared with the control and the mastectomy only group, the breast reconstruction group, which comprised of DIEP, IBR, and latissimus dorsi flap, demonstrated the lowest upper limb performance outcomes (reduced internal rotation and reduced scapular anterior tilt) and a reduction in arm extension and abduction.[591] As previously discussed, reduced internal rotation is believed to be caused by the subpectoral implant positioned beneath the stretched pectoralis major muscle, which hinders its movement as the primary internal rotator of the humerus.[16] Moreover, the decreased upper limb performance coincided with increased impairment

scores, as assessed by the DASH questionnaires, highlighting their inability to do daily activity tasks, which may impact their ability to return to work and their HRQoL.[591]

In the current study, DIEP patients had longer hospital stay compared with Mx and IBR patients. Prior studies demonstrated that mobilising out of bed during the first few days after surgery were significantly related to a decreased length of hospital stay.[592-594] This could partially account for the extended hospital stays of DIEP patients in comparison with those who underwent other procedures. Nevertheless, the duration of hospital stay could also be impacted by other external factors, such as patient's expectations, local postoperative protocol, or the absence of social or support networks. ERAS protocol is adopted in our unit and increasingly being used worldwide after autologous tissue breast reconstruction.[267] Initiating early mobilisation on the first day after surgery is a component of an ERAS regimen. Although ERAS protocols have been proven to significantly decrease the duration of hospitalisation compared with standard protocols, the majority of ERAS protocols still report an average length of stay of 3–4 days for autologous breast reconstruction,[267] which aligns with the results of the present study. According to a recent study, patients who are healthy and have limited comorbidities can be effectively discharged from the hospital by postoperative day 2 without compromising their recovery or outcomes, provided that they are appropriately selected.[271] To promote early mobilisation and monitor patients' activity levels while they are at home, the WAMs may be integrated into the ERAS protocol as part of a targeted rehabilitation programme.

The correlation between the upper limb activity and pain scores for performance of specific activities, especially in week 1, suggests that pain impacts activity levels. Previous studies showed that axillary and reconstruction surgery are associated with increased postoperative pain[221,595,596] and increased use of opioids.[597] This is evidenced in the current study, where more DIEP and IBR patients required more analgesics on top of their regular medications compared with the Mx group. It has been demonstrated that good pain control is associated with improved outcomes following vascular, orthopaedic, breast reconstruction and general surgery.[267,598-600] Effective post-operative pain management with multimodal

analgesia is crucial to improve patient comfort, accelerate recovery from surgery, result in significant cost advantages and further support the ERAS programme.[267,598-600]

Furthermore, patients who developed upper limb complications in the long-term had a reduction in their upper limb activity levels suggesting that WAMs are a sensitive outcome measure for detecting complications. Ghomrawi *et al.,*[601] demonstrated that there was a correlation between a decrease in mobility scores, as evaluated by accelerometers, and the occurrence of postoperative complications. The decreased activity level preceded the reported onset of symptoms.[601] WAMs can be used as an adjunct tool to monitor and facilitate earlier detection of complications, thus allowing for earlier intervention. The present study and previous chapters and publications[78,488] proved the application of WAMs in the postoperative period, as well as the methodology for assessing outcomes. Nevertheless, to implement this on a larger scale, it is logical to use patients' own devices (e.g smartwatches with an application specifically design to monitor upper limb activity). Sharing patients' personal data with the clinical team after surgery could stimulate conversations on the optimal utilisation of the data. If patients or the healthcare team deem the data valuable, incorporating an intervention such as personalised activity goals after establishing clear baseline recovery curves is a logical next step. Patients may also participate in a virtual rehabilitation group to motivate them to increase their upper limb activity levels. However, this would require safety considerations to avoid any potential complications. This may also empower patients to take control of their own care and motivate patients to improve their upper limb activity as part of a feedback-enabled personalised rehabilitation programme. Inviting all patients to participate in this study would produce datasets with more meaningful conclusions. From an economic and hospital viewpoint, the data provided by WAMs would enable us to allocate crucial resources and help the hospital and the community predict short-term care requirements, such as early physiotherapy.

While it is acknowledged that certain upper limb functional impairments may occur post-breast reconstruction surgery, there is evidence to suggest that these can be reduced by optimising postsurgical function through the implementation of exercise.[240,602] Nevertheless, there is a paucity of studies on the subject of physical activity after breast reconstruction surgery. Plastic surgeons also have concerns that

exercise may potentially result in postoperative complications or even failure of the reconstruction procedure.[603] In the UK, breast reconstruction patients are provided with early routine postoperative physiotherapy by a physiotherapist, starting within the first week after surgery. This practice is recommended by the British Association of Plastic Reconstructive and Aesthetic Surgeons Guidelines for Best Practice in Oncoplastic Breast Surgery.[604] In our unit, patients are seen by physiotherapist on day 1 after surgery. However, the approach in the US may differ from that in the UK. Albaster *et al.,*[603] conducted a study which revealed that only a small number of American plastic and reconstructive surgeons endorse the early initiation of exercise. Some plastic surgeons recommend that patients restrict arm movement above the shoulder during the first 2 weeks postoperatively, even though there is no compelling evidence supporting the difference in outcomes between early and delayed exercise.[603] A collaborative effort between plastic surgeons and physiotherapists are vital to promote a safe and gradual return of upper limb movement and performance of activities of daily living (ADLs) that considers functional, aesthetic, and technical outcomes in equal measure.[603]

Interestingly, the current study also showed that adjuvant immunotherapy is an independent predictor for upper limb activity. The extent of immunotherapy-related adverse events (irAEs) has long been underreported.[605] Although it is less frequent than joint pain brought on by aromatase inhibitors, arthralgia or myalgia has been observed in as many as 10–20%[606-608] of individuals who were treated with immune checkpoint inhibitors, which is a type of immunotherapy used to treat breast cancer.[609] Immunotherapy was reported to cause arthralgia where the shoulder joint is commonly affected, which may impact upper limb activity.[54,55] This was hypothesised as a result of the T-cell response and anti-tumour effect being amplified by immunotherapy, which can result in irAEs that frequently cause arthralgia.[55,610] Immune checkpoint inhibitors function to elicit an anti-tumour immune response by inhibiting immune checkpoints.[609] It enhances the immune system's capacity to recognise and eliminate cancer cells. In certain cases, this augmented immune response may incorrectly attack healthy tissues, such as joints, leading to inflammation that induces stiffness, pain, and swelling in various joints.[609,611] However, due to the small number of patients included in the current study analysis, the finding that

adjuvant immunotherapy is an independent risk factor for upper limb activity must be verified in a larger, appropriately powered study.

Despite causing greater short-term morbidities, DIEP patients reported greater psychosocial and sexual well-being 1 year after surgery compared with women who chose implants.[612] While the current study suggests that IBR may have a faster short-term recovery time than DIEP, some women may prefer to have more natural-looking breasts with like-for-like tissue replacement.[16,613] DIEP surgery could be an option for patients with high BMI. Implants can be offered to those who are too thin and may not have enough tissue for flap transfer. However, sub-pectoral/submuscular implants may cause pain and tightness in the long-term, which may limit shoulder movement.[16] Achieving acceptable symmetry may be difficult when using implants for large breasts. Some patients may not be keen to choose IBR due to its association with anaplastic large cell lymphoma.[614,615] Furthermore, there is maintenance surgery, higher complication risk with radiotherapy and higher loss rate associated with implants.[616,617] Some patients may choose to forego breast reconstruction altogether and only undergo a simple mastectomy to avoid breast reconstruction-related complications. The combination of real-time objective data, PROMs, and patient preferences should be utilised to support patient counselling and the shared decision-making process. For women to choose between treatment options wisely they must be aware of the physical recuperation that follows.

This study has several limitations. The results cannot be generalised to the entire study population due to the single-centre design. Possible confounding effects such as handedness, neoadjuvant/adjuvant therapy, pain, age, and the presence of drains may have affected the results. Upper limb activity for example may decline with age due to reduced muscle coordination or reduced grip strength.[618,619] It is also important to note that the findings of the subgroup analyses should be interpreted with caution, as the small sample size could potentially result in a type II error. Attrition bias may have occurred due to the withdrawal of patients with complications/discomfort while wearing the WAMs. It may be difficult to differentiate if the reduced upper limb activity level is due to the patient doing less (i.e., being generally unwell/tired) versus reducing upper limb activity on the operated side of an otherwise well

patient. However, this can be addressed by placing WAMs on each wrist. To mitigate other limitations, pre-operative upper limb activity levels were collected to allow individualised calibration of post-operative measurements and therefore minimise the effect of handedness and other factors such as neoadjuvant therapy. Several multivariable analyses were conducted, with different combinations of variables tested to account for confounding factors. The selected model was the most relevant because it identified the most consistent and clinically meaningful predictors, although there was variation in model outcomes. The model that best reflects both the data and known clinical effects was chosen. A small sample size could lead to overfitting, particularly in the multivariable models, which is why the variables that were both statistically significant and clinically relevant were carefully chosen. Additionally, although several important variables were accounted for, there may be residual confounding from unmeasured factors such as surgeon-specific techniques, which could influence the outcomes. Future analyses should also consider patient motivation, adherence to postoperative exercise, and psychological factors that could influence upper limb activity levels. All patients were compliant with prescribed analgesia where DIEP and IBR patients had an increased analgesia requirement. Pain scores correlated with upper limb activity in week 1. The data were similar when re-analysed only considering those with drains. Future work will include recruitment from multiple sites to improve the study's applicability to a broader patient population. Comprehensive analyses of the patterns of activity throughout the day and differences between dominant and non-dominant arms may uncover additional insights into recovery patterns of each surgery.

7.6 Clinical Implications

Despite DIEP patients having the lowest upper limb activity level in the acute post-operative setting compared with Mx and IBR, the activity levels of all surgeries returned to baseline in the long-term. DIEP was also found to be an independent predictor of upper limb activity in the first 2 weeks following surgery. This study gives meaningful insight into a novel objective measure of upper limb activity levels that have not been widely reported in the literature after breast reconstruction. The findings of this study also lend support to the use of WAMs as a supplement to the measurement of clinical outcomes and

PROMs. This information helps us have informed discussions about expectations for recovery. Monitoring recovery objectively using WAMs can support the development of a personalised rehabilitation programme for those at risk of developing complications after breast reconstruction surgery.

This chapter provides empirical evidence that WAMs are appropriate for use in complex surgical patients with an extended longitudinal follow-up. The following chapter will explore whether short-term upper limb activity level measured by WAMs can be used as a reliable predictor of long-term upper limb activity and further understand its clinical relevance in the management of upper limb dysfunction post-breast cancer treatment.

8 SHORT TERM UPPER LIMB ACTIVITY PREDICTS LONG-TERM UPPER LIMB FUNCTIONAL OUTCOMES FOLLOWING BREAST CANCER SURGERY

8.1 Abstract

Background: Characterisation of longitudinal recovery and identification of predictors of patient outcomes following breast cancer surgery are important to identify at risk populations, targeted interventions, and prevention of long-term morbidity. This study is aimed to characterise upper limb longitudinal recovery and identify predictors of recovery using wearable activity monitors (WAMs).

Materials and Methods: This prospective observational cohort study was conducted from April 2019 to May 2022. Breast cancer patients were identified from operating schedules. Recruited participants wore WAMs on both wrists for an average of 3 days preoperatively, 2 weeks postoperatively, and for 3 days at greater than 6 months postoperatively as well as complete the disability of arm, shoulder and hands (DASH) and quality-of-life (QoL) questionnaires.

Results: Upper limb activity (n=39) was significantly reduced at 1 and 2 weeks postoperatively (median: 60.3% and 71.7%, $p<0.001$). At median follow up of 21 months, on average upper limb activity returned to baseline (median: 105.6%, $p=0.491$). Out of 39 patients, 59% of patients reached their preoperative baseline (median: 116.4%) whereas 41% of patients did not reach their preoperative baseline (median: 75.7%). Multivariable regression analysis demonstrated that the magnitude of upper limb activity at 2 weeks ($\beta=0.552$, $p<0.001$) and preoperative activity level ($\beta=-0.368$, $p=0.004$) were independent predictors of long-term upper limb activity. Upper limb activity and DASH score correlated well with QoL score.

Conclusions: The magnitude of early postoperative upper limb activity and preoperative activity level are independent predictors of long-term upper limb activity. This highlights the importance of quantifying preoperative activity and early recovery and acting towards reducing long-term functional

morbidity with early physiotherapy. WAMs are well suited for this purpose as they can measure activity in a non-invasive manner and provide feedback to patients and clinicians.

Sections of this chapter have been submitted to The Breast journal: Che Bakri NA, Kwasnicki RM, Dutta T, Rizk C, Giannas E, Hunter J, Henry F, Wood S, Darzi A, Leff DR. Short-Term Upper Limb Recovery Predicts Long-Term Functional Outcomes Following Breast Cancer Surgery – A Prospective Longitudinal Observational Cohort Study (in review).

8.2 Introduction

De-escalation strategies, particularly in the context of axillary surgery, [100,620] have been shown effective in mitigating the long-term adverse effects associated with breast cancer treatment. However, it is important to note that reduction in upper limb activity may still develop even after undergoing less-invasive surgeries such as SLNB, [621] as outlined in chapter 6. Furthermore, as discussed in chapter 7, patients who underwent DIEP breast reconstruction had the lowest upper limb activity in the perioperative period compared with Mx and IBR, with patients who developed complications in the long term having reduced upper limb activity, indicating the need to continuously monitor these patients to identify patients who require additional support throughout their recovery.

Identification of reliable modifiable predictors, such as upper limb activity in the acute preoperative setting, would allow targeted interventions for those at risk of long-term upper limb morbidity. While numerous studies have been conducted to identify potential predictors, many focus on subjective measures or a specific component of upper limb morbidity without examining functionality as a whole and its impact on ADLs [15,622-624]. Early identification of patients with impaired upper limb activity may be achieved by the use of WAMs, potentially reducing their long-term risk of upper limb morbidities. This chapter focuses on investigating whether short-term upper limb activity can become a predictor of long-term upper limb activity as measured by WAMs. This is the first study to assess the link between short-term postoperative upper limb activity and long-term upper limb outcomes using WAMs.

8.2.1 Long-term Complications

Despite advancements in treatment strategies for breast cancer, such as the use of less invasive surgical techniques like SLNB and adjunct procedures such as axillary reverse mapping (ARM), the occurrence of upper-body morbidity remains prevalent.[27] Chapter 2 outlines that breast cancer treatment may lead to several upper limb morbidities, such as pain, lymphoedema, reduced range of motion, and decreased strength. These morbidities are often underestimated and undertreated which affect patient's daily activities and their quality of life. Failure to acknowledge the enduring consequences of breast cancer

treatment can result in delays in referring patients for treatment and could contribute to increased shoulder morbidity in the long term.[3] Prior studies have indicated that many patients who have survived breast cancer continue to face adverse effects in their upper limbs for a duration of two or more years following their treatment.[71,625-627] Hauerslev *et al.,*[628] discovered that a significant proportion of participants experienced one or many subjective symptoms related to shoulder and arm morbidity, persisting for over 11 years following breast cancer surgery.

According to a systematic review and meta-analysis by Rietman *et al.*,[56] the prevalence of pain, restricted range of motion, lymphoedema, and reduced strength one year or more after any breast cancer treatment ranged from 12-51%, 2-51%, 6-43%, and 17-33% respectively. There was a strong correlation observed between the number of arm morbidities, 18 months after breast cancer treatment and increased levels of psychological distress.[56] Another systematic review by Levangie *et al.,*[439] demonstrated that patients who had ALND and radiotherapy experienced late effects morbidity up to 20 years post breast cancer treatment. Less invasive surgery, such as SLNB, is also associated with late morbidity (>6 months). Even though to a lesser extent compared to ALND, it still remains a huge burden to the healthcare system and should not be neglected.[629]

8.2.2 Predictors of Outcomes

Upper limb morbidities can affect patient's HRQoL many years after breast cancer treatment. Hence, it is important to identify patients who are susceptible to experiencing postoperative complications, and to evaluate the impact of these morbidities on HRQoL and their daily function. Levy *et al.,*[622] demonstrated that the extent of node dissection (i.e. ALND), stage II breast cancer and having mastectomy were critical predictors of early range of motion impairment, whereas positive nodes, older age and BMI≥25 were significantly associated with shoulder range of motion impairment at more than 12 months after surgery. Based on the findings by Klein *et al.*,[15] having more than 3 dissected lymph nodes, radiotherapy, and the extent of tissue removed were all factors that can contribute to a reduction in range of movement. Furthermore, pain levels during hospitalisation, tumour size, and breast

reconstruction were all risk factors for functional disabilities.[15] Other factors such as comorbidity, low socioeconomic level and African-American ethnicity were associated with prolonged arm morbidity.[630]

Liu *et al.,*[629] performed a systematic review of late morbidity associated with a tumour-negative SLNB in primary breast cancer patients and separated the risk predictors based on the quality of the studies reviewed. There was strong evidence that young age and time after surgery were predictors of late morbidity after SLNB. For instance, studies have reported a higher risk of numbness, increased pain, and reduced shoulder strength in younger patients compared with older women.[629] There was moderate evidence that the type of breast surgery, axillary radiation, and tumour location were important predictors of late morbidity effects.[629] Compared with breast conserving surgery, women who underwent mastectomy were more likely to develop late morbidities, and those who underwent radiotherapy were more likely to develop lymphoedema and impaired range of motion in the long term.[629] Interestingly, tumour location in the upper outer quadrant was associated with an increased risk of lymphoedema. Finally, there was weak evidence that the 2-step axillary lymph node dissection, the use of radiopharmaceutical and BMI were predictors of late morbidity.[629]

In addition, there is compelling evidence that postoperative physical activity can reduce the prevalence of chronic pain, and consistent physical activity may mitigate long-term functional disabilities.[15] Nillson *et al.,*[631] reported that patients who were physically active prior to surgery were more likely to experience a greater degree of physical recovery three weeks after their surgery. Another study by Klein *et al.,*[632] demonstrated that patients who performed moderate to vigorous physical activity were more likely to experience lower disability scores as measured by DASH at 6 months post-surgery. The abduction and flexion range of motion were also superior to that of sedentary women. Furthermore, women who were more physically active were also more inclined to resume their previous employment status in comparison with women who were less physically active.[632]

The identification of reliable yet modifiable predictors, such as the activity levels of patients in the acute postoperative setting, would enable targeted interventions and engage people in exercise for those who are at risk of developing long-term functional deficits, which will be further discussed in chapter 9. Previous research studies have elucidated the correlation between engaging in physical exercise and the subsequent improvement of outcomes and upper body function among individuals who have undergone breast cancer surgery.[4,632] Based on the data, it is evident that the early identification of patients with suboptimal activity levels using WAMs and an early start of comprehensive physical therapy rehabilitation programme, has the potential to prevent the likelihood of long-term upper limb complications. The objective of this chapter is to determine if the short-term upper limb activity can predict the long-term upper limb activity following breast cancer surgery. The methodology used in this study was described in chapter 4. I conducted the patient recruitment with Dr Manolis Giannas, Dr Luqman Tenang and Dr Tanusree Dutta.

8.3 Hypothesis

- ◊ *Short term upper limb activity levels predict the long-term upper limb functional outcome.*

8.3.1 Outcomes

The primary outcomes were to measure upper limb activity both preoperatively and during the immediate postoperative period (2 weeks after surgery), as well as in the long term (more than 6 months after surgery) using WAMs, and to determine whether short-term upper limb activity can predict long-term upper limb activity.

The secondary outcomes were to identify factors that predict recovery after breast surgery as well as to assess the impact of upper limb activity and DASH score[185] on QoL score (EQ-5D-5L)[186] at greater than 6 months postoperatively. Age, BMI, comorbidity score, upper limb activity at 2 weeks postoperatively, DASH score[185] at 1 week postoperatively, preoperative activity, surgery type and adjuvant/neoadjuvant therapies were assessed in relation to long-term upper limb outcomes, including upper limb activity levels and DASH score at greater than 6 months postoperatively. Comorbidities were scored according

to Age-Adjusted Charlson Comorbidity Index (ACCI) and were sub-categorised into those with an ACCI≥5 and those with an ACCI<5, while BMI groups were sub-categorised into those with a BMI<25kg/m^2 and those with a BMI≥25kg/m.[430,431]

8.4 Results

8.4.1 Study Participants

Patients (n=68) who were recruited for postoperative monitoring in previous chapters and published studies were contacted again at greater than 6 months post-surgery for long-term data collection.[78,488] Nine additional patients who were recruited since the last 2 published studies were also contacted. Eight patients who had any additional operations since their initial surgery or a new diagnosis that significantly affected their recovery or mobility levels were excluded. A further 16 patients were unwilling to participate in additional data collection, fourteen patients did not respond or were uncontactable. Ultimately, 39 patients provided data for analysis (Figure 8-1) (Table 8-1). The median follow-up was 21 months (11–48 months). The list of patients' co-morbidities is presented in Appendix 21.

8.4.2 Adherence to WAMs protocol

Five hundred and forty-six data points (14 days x 39 patients =546) could have been captured in the immediate postoperative period (2 weeks after surgery) and 117 data points (3 days x 39 patients =117) in the longitudinal period (>6 months after surgery). Quality assessment of the data revealed that 43 data points were missing in the initial postoperative period and 2 data points were missing in the longitudinal period. Consequently, sensor compliance was 92% and 98% in the immediate postoperative and longitudinal period respectively.

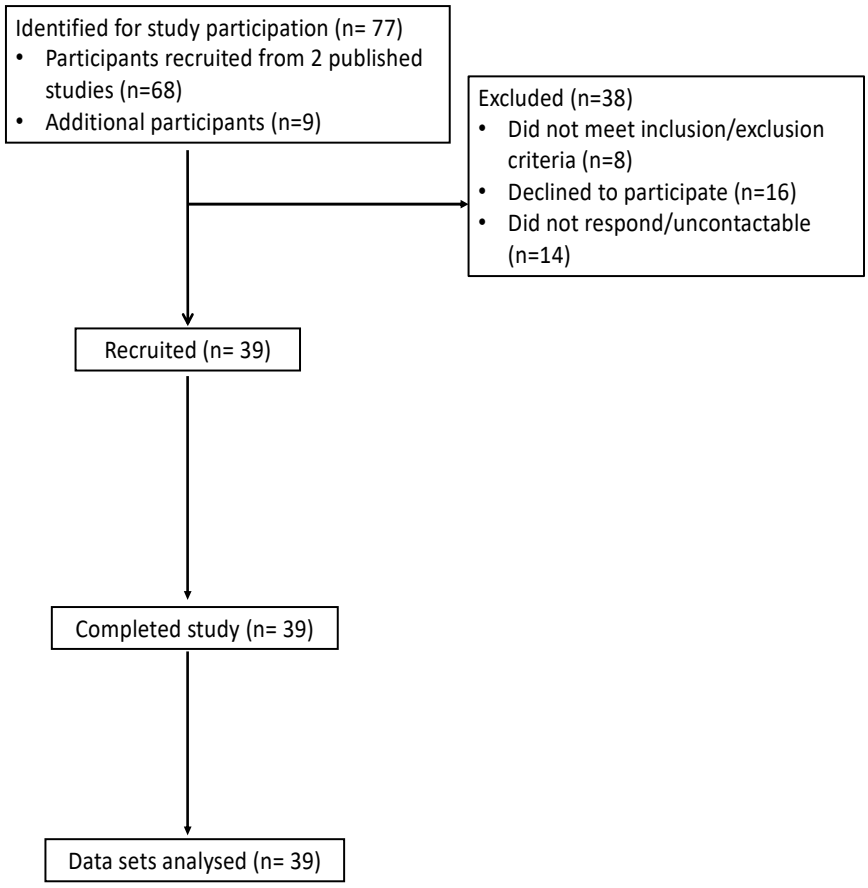


Figure 8-1 Participant flow diagram investigating whether short-term upper limb recovery predicts long-term upper limb functional outcome following breast and axillary surgery

Table 8-1 Demographics of Study Population (n=39)

Characteristics	**Total (n=39) n (%)**
Mean age, (yrs.) (SD)	57.4+/-10.8
Sex (Female)	39 (100)
Comorbidities: n (%)	25 (64.1)
Mean BMI (kg/m2) (SD)	27.4 +/-6.1
Handedness ratio (R:L)	39:0
Race/ethnicity: n (%)	
Asian – any other Asian background	4 (10.2)
Black or Black British African	2 (5.1)
Black or any other Black background	1 (2.6)
White British	10 (25.6)
White Irish	2 (5.1)
White and any other White background	5 (12.8)
Other – any other ethnic group	15 (38.5)
Clinical and pathological characteristics	
Stage of cancer: n (%)	
Stage 0	2 (5.1)
Stage 1	22 (56.4)
Stage IIA and IIB	7 (17.9)
Stage IIIA-IV	4 (10.3)
Risk-reducing	2 (5.1)
Benign	2 (5.1)
Cancer type: n (%)	
Ductal Carcinoma In-situ	2 (5.1)
Invasive Ductal Carcinoma	28 (71.8)
Invasive Lobular Carcinoma	3 (7.7)
Invasive Mucinous Carcinoma	1 (2.6)
Other	1 (2.6)
BRCA carrier	2 (5.1)
Benign	2 (5.1)
Previous breast surgery prior to initial operation: n (%)	11 (28.2)

Patients with drain during the 2 weeks post-operative period (n,%)	31 (79.5)
Advice about exercise: n (%)	39 (100)
Treatment received	
Surgical treatment	
Simple Mastectomy	15 (38.5)
Implant-based reconstruction	6 (15.4)
DIEP	7 (17.9)
TUG	1 (2.6)
TRAM	2 (5.1)
Wide local excision (breast conserving surgery)	8 (20.5)
Type of axillary surgery: n (%)	
Sentinel Lymph Node Biopsy	21 (53.8)
Axillary Lymph Node Dissection	10 (25.6)
Completion of ALND after positive nodes from SLNB	0 (0)
Re-excision after positive margin from wide local excision (breast conserving surgery)	0 (0)
Operation laterality ratio (R:L:BL)	21:14:4
Neoadjuvant therapy (n,%):	
Radiotherapy	1 (2.6)
Chemotherapy	8 (20.5)
Endocrine therapy	5 (12.8)
Immunotherapy	1 (2.6)
Adjuvant therapy (n,%):	
Radiotherapy	10 (25.6)
Chemotherapy	6 (15.4)
Endocrine therapy	21 (53.8)
Immunotherapy	3 (7.7%)
Complications	9 (24%)

BMI, Body Mass Index; R, right; L, left, BL, bilateral; BRCA, Breast Cancer Gene; DIEP, Deep Inferior Epigastric Perforators; TUG, Transverse Upper Gracilis; TRAM, Transverse Rectus Abdominus Muscle; SLNB; Sentinel Lymph Node Biopsy, ALND; Axillary Lymph Node Dissection. Means have been presented with standard deviations and numbers with percentage of the total study population.

8.4.3 Main Findings

8.4.3.1 Return to preoperative activity levels and functionality (combined activity levels)

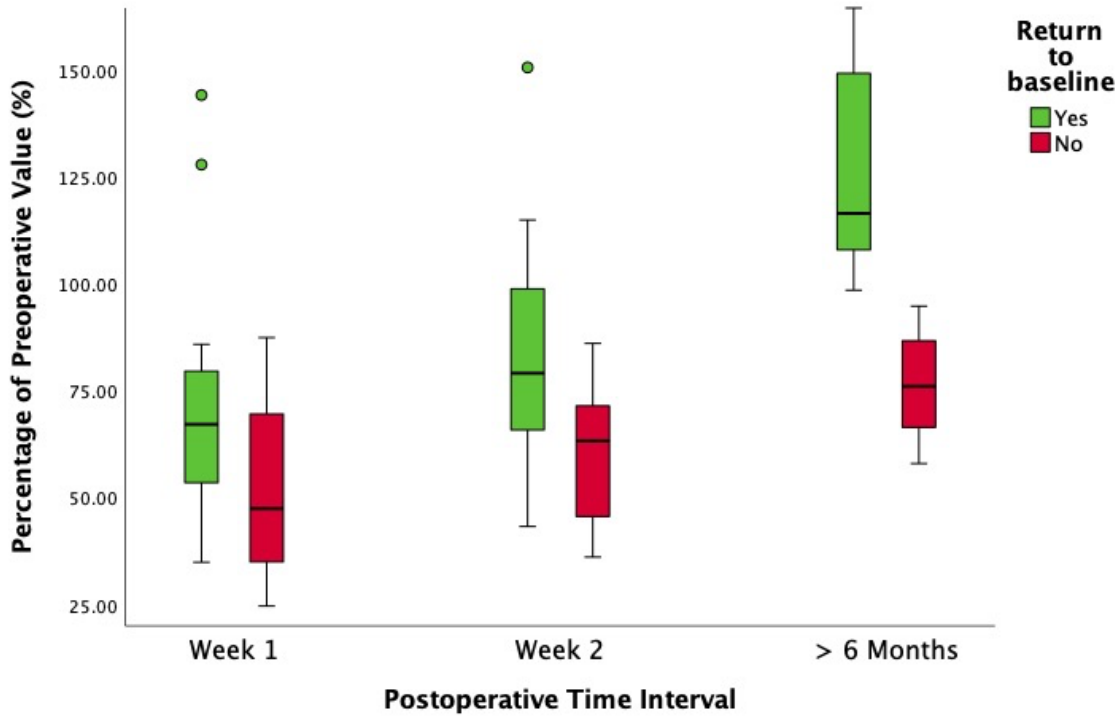


Figure 8-2 Return to preoperative activity levels and functionality (combined activity levels)

As a percentage of the preoperative baseline, postoperatively upper limb activity significantly reduced to 60.3% (IQR 43.2-73.4, p<0.001) and 71.7% (IQR 53.9-85.2, p<0.001) at week 1 and week 2 respectively. At median follow up of 21 months after surgery, on average upper limb activity returned to preoperative baseline (median: 105.6% (IQR: 79.8-119.7), p=0.491). Out of 39 patients, 59% of patients reached preoperative baseline where median upper limb activity was 116.4% (IQR: 107.9-149.1, p<0.001) whereas 41% of patients did not reach preoperative baseline (median: 75.7% (IQR: 66.4-86.7), p<0.001) (Figure 8-2).

8.4.3.2 Univariate analysis

In univariate analysis, greater upper limb activity at 2 weeks was found to be significantly correlated with greater long-term upper limb activity (r= 0.500, p<0.001). Upper limb activity was more likely to return to baseline if the 2-week activity was greater than 75% (OR:7.5, 95% CI: 1.63 to 34.59, p=0.010).

Preoperative activity level was also found to be significantly correlated with long-term upper limb activity level (r=-0.588, p<0.001). In contrast, other variables such as age (r=-0.075, p=0.330), DASH score at week 1 (r=-0.130, p=0.450), comorbidity score (p=0.870) and BMI (p=0.950) were not significantly correlated to upper limb activity in the long-term (Table 8-2).

In univariate analysis, variables such as age (r=0.254, p=0.129), 2-week upper limb activity (r=-0.20, p=0.234), preoperative activity level (r=-0.130, p=0.441), DASH score at week 1 (r=0.338, p=0.054) and comorbidity score (p=0.871) were not found to be significantly correlated to DASH score at a median follow up of 21 months postoperatively. However, individuals with a BMI≥25 had substantially higher DASH score in the long-term compared with those with a BMI<25 (p=0.029) (Table 8-3).

8.4.3.3 Multivariable regression analysis

Multivariable regression analysis showed that 2-week postoperative upper limb activity (β=0.552, 95% CI: 0.553 to 1.413; p<0.001) and preoperative activity (β=-0.368, 95% CI: -1.11 to -0.231; p=0.004) significantly predicted long-term upper limb activity (Table 8-4). Age (β=0.407, 95% CI: 0.25 to 1.97; p=0.012) and 1-week postoperative DASH score (β=0.361, 95% CI: 0.01 to 0.76; p=0.046) were found to be predictors of long-term DASH score (Table 8-5).

Table 8-2 Univariate analysis - upper limb activity levels

Independent variable	**Spearman's Rank Coefficient**	**P value**
Age	-0.075	p=0.330
Preoperative SVM activity level	-0.588	p<0.001***
2-week postoperative upper limb activity (as percentage of preoperative level)	0.500	p<0.001 ***
DASH score at week 1	-0.130	p=0.450
BMI	n/a	p=0.950
Comorbidity score	n/a	p=0.870

Type of axillary surgery	n/a	p=0.604
Type of breast surgery	n/a	p=0.742
Neoadjuvant radiotherapy	n/a	p=0.368
Neoadjuvant chemotherapy	n/a	p=0.686
Neoadjuvant endocrine therapy	n/a	p=0.366
Neoadjuvant immunotherapy	n/a	p=0.464
Adjuvant radiotherapy	n/a	p=0.613
Adjuvant chemotherapy	n/a	p=0.800
Adjuvant endocrine therapy	n/a	p=0.542
Adjuvant immunotherapy	n/a	p=0.332

Univariate analysis was carried out to identify an association between age, BMI, comorbidity score, upper limb activity at 2 weeks, DASH score at week 1, preoperative SVM activity level, type of axillary surgery, type of breast surgery, adjuvant/neoadjuvant treatments, and upper limb activity at greater than 6 months postoperatively (6 months+). Spearman's Rank Correlation Test was carried out to identify any significant correlations between age, upper limb activity at 2 weeks, preoperative activity level, DASH score at week 1 and 6 months+ upper limb activity levels. A Mann-Whitney U test was carried out to identify significant differences in 6 months+ upper limb activity levels between BMI and comorbidity subgroups as well as type of axillary surgery and adjuvant/neoadjuvant treatments. Two-week upper limb activity was expressed as a percentage of preoperative value. Preoperative activity level was expressed as signal vector magnitude (SVM). BMI groups have been split into those with a body mass index (BMI) <25 and those with a BMI ≥ 25. Age-adjusted Charlson Comorbidity Index (ACCI) <5 and those with an ACCI ≥ 5. Kruskal Wallis test was carried out to identify significant differences in 6 months+ upper limb activity levels between different types of breast surgeries. *** p<0.001, **p<0.01, *p<0.05

Table 8-3 Univariate analysis – DASH questionnaire

Independent variable	**Spearman's Rank Coefficient**	**P value**
Age	0.254	p=0.129
Preoperative SVM activity level	-0.130	p=0.441
2-week postoperative upper limb activity (as percentage of preoperative level)	-0.20	p=0.234
DASH score at week 1	0.338	p=0.054

BMI	n/a	p=0.029*
Comorbidity score	n/a	p=0.871
Type of axillary surgery	n/a	p=0.952
Type of breast surgery	n/a	p=0.971
Neoadjuvant radiotherapy	n/a	p=0.811
Neoadjuvant chemotherapy	n/a	p=0.955
Neoadjuvant endocrine therapy	n/a	p=0.724
Neoadjuvant immunotherapy	n/a	p=0.658
Adjuvant radiotherapy	n/a	p=0.674
Adjuvant chemotherapy	n/a	p=0.800
Adjuvant endocrine therapy	n/a	p=0.684
Adjuvant immunotherapy	n/a	p=0.711

Univariate analysis was carried out to identify an association between age, BMI, comorbidity score, upper limb activity at 2 weeks, DASH score at week 1, preoperative SVM activity level, type of axillary surgery, type of breast surgery, adjuvant/neoadjuvant treatments, and DASH score at greater than 6 months postoperatively (6 months+). Spearman's Rank Correlation Test was carried out to identify any significant correlations between age, upper limb activity at 2 weeks, preoperative activity, DASH score at week 1 and 6 months+ DASH score. A Mann-Whitney U test was carried out to identify significant differences in 6 months+ DASH score between BMI and comorbidity subgroups as well as type of axillary surgery and adjuvant/neoadjuvant treatments. Two-week upper limb activity was expressed as a percentage of pre-operative value. Preoperative activity level was expressed as signal vector magnitude (SVM). BMI groups have been split into those with a body mass index (BMI) <25 and those with a BMI ≥ 25. Age-adjusted Charlson Comorbidity Index (ACCI) <5 and those with an ACCI ≥ 5. Kruskal Wallis test was carried out to identify significant differences in 6 months+ DASH score between different types of breast surgeries. *** p<0.001, **p<0.01, *p<0.05

Table 8-4 Multivariable regression analysis- activity level at long-term follow up

	Standardised Coefficient	**P value**
Age	-1.879	p=0.069
Preoperative SVM activity level	-0.368	p=0.004**
2-week postoperative upper limb activity (as percentage of preoperative level)	0.552	p<0.001***

Table showing the outcome of multivariable regression analysis on factors affecting upper limb activity levels at greater than 6 months postoperatively. Age, preoperative SVM activity level and two-week post-operative upper limb activity levels have been included in this regression analysis. *** p<0.001, **p<0.01, *p<0.05

Table 8-5 Multivariable regression analysis - DASH scores at long-term follow up

	Standardised Coefficient	**P value**
Age	0.407	p=0.012*
1-week postoperative DASH score	0.361	p=0.046*
BMI	0.752	p=0.051

Table showing the outcome of multivariable regression analysis on factors affecting DASH scores at greater than 6 months post-operatively. Age, one-week post-operative DASH score and BMI have been included in this regression analysis. *** p<0.001, **p<0.01, *p<0.05

8.4.3.4 Assessment of Quality of Life (EQ-5D-5L questionnaire)

Spearman analysis showed a statistically significant but modest positive correlation between long-term (median follow up: 21 months) upper limb activity and the QoL score (R=0.364, p=0.012). Long-term (median follow up: 21 months) DASH score was observed to be highly correlated to QoL score (R=-0.874, p<0.001).

8.5 Discussion

There are two critically important findings of this study. Firstly, early postoperative upper limb activity and preoperative activity are independent predictors of long-term upper limb activity; and secondly that only 59% of patients returned to preoperative baseline at long-term follow up (median follow up: 21 months). This study provides additional objective insight into the longitudinal recovery trajectories of patients who have undergone breast surgery using WAMs.

The magnitude of upper limb activity at 2 weeks following surgery independently predicts for long-term upper limb outcome (upper limb activity). This means it is essential that clinicians pay attention to the magnitude of early postoperative activity and intervene where necessary. Similarly, Kootsra *et al.*,[130] found that shoulder-arm function measured by goniometer and dynamometer at 6 weeks

following breast cancer surgery is a good predictor of the shoulder-arm function at 7 years following surgery. This is significant because poor postoperative activity could be amenable to early intervention with intensive physiotherapy. Greater physical activity has previously been shown to correlate with better recovery.[480,633] As indicated by the NICE guideline, patients who are at risk of developing shoulder problems after surgery should be provided with supervised physiotherapy support. The exercise programme should be tailored to suit specific circumstances and requirements.[238] As previously discussed, Bruce *et al.,*[4] concluded that implementing a structured exercise programme reduced postoperative pain and arm symptoms and was more cost-effective than providing standard care, with exercise resulting in lower expenses per patient as well as improved health-related quality of life. A similar concept could be applied using WAMs to identify women most likely to benefit from targeted risk prevention strategies. Continuous activity monitoring during treatment with wireless wearable monitors could assist in predicting and monitoring treatment complications, allowing for timely and appropriate intervention with a personalised rehabilitation plan, as discussed in chapter 9. Furthermore, preoperative upper limb activity was identified as an independent predictor of long-term upper limb activity. Prior studies demonstrated that higher preoperative activity may improve postoperative outcomes[634] and optimise physical recovery,[631] which would support the implementation of prehabilitation programme (where patient's physical and mental health are optimised prior to their surgery) for patients awaiting for breast cancer surgery. Recent evidence suggests that self-directed care is superior for patients and promote self-empowerment.[635] Breast cancer survivors who are self-empowered have a substantial positive impact on their HRQoL.[636]

Patients had not regained full functionality 2 weeks after surgery, with median upper limb activity levels of 71.7% of baseline. At long-term follow up, 41% of the participants still experienced functional deficit as demonstrated by their reduced upper limb activity. Long-term upper limb activity restriction is significant as it directly impacts patients' daily activities and overall HRQoL. It is intriguing that only 59% of participants returned to preoperative upper limb activity, even though the average age of the group was relatively young at 57.4 years and only 15% and 26% of them underwent adjuvant chemotherapy and radiotherapy respectively. Prior research has demonstrated that younger patients

exhibit greater levels of physical activity in comparison to older patients.[637] In addition, chemotherapy may have a substantial negative impact on a patient's physical function and overall well-being, resulting in fatigue and a decrease in overall physical activity.[638] Furthermore, radiotherapy was reported to result in upper limb impairment in breast cancer survivors including lymphoedema, reduced range of motion, lymphoedema and pain.[27,39] Planned recruitment of breast cancer patients with and without radiation or chemotherapy in future studies may reveal significant impacts on upper limb activity. Nevertheless, most individuals in the group ultimately achieved baseline activity over an extended period. This implies that the recovery plateau must be at some point after the initial 2-week period and before the median follow up of 21 months following surgery. This finding is comparable to a study by Smoot *et al.,*[456] in which patients demonstrated a decreased in upper limb range of motion (measured by goniometry) at 1 month after surgery. Most patients demonstrated an improvement in function at 12 months after surgery. In an ideal scenario, the recovery plateau would be determined by the continuous or more frequent collection of data post-surgery. Other studies showed that upper limb complications persisted for up to seven years after surgery.[130,639] This is particularly evident in patients who have undergone axillary lymph node dissection and/or reconstructive procedures who likely experience a sustained functional impairment across long-term follow-up.[16,27,99,100,130]

The ratio of arm activity and hand dominance were thoroughly investigated in chapter 4.[78] Patients who were right-handed and underwent surgery in their non-dominant hand experienced an increase in dominant hand activity postoperatively. This ratio subsequently returned to its preoperative level 14 days postoperatively.[78] The normal variation of upper limb activity of 10 healthy subjects was also investigated and the difference in activity between both arms was approximately 8%.[78] The upper limb activity obtained from single arms may not be superior to those obtained from combined arms; they may not have adequately represented patients' recovery and introduced an additional confounding factor. By grouping the arms, the confounding effect of the dominant versus non-dominant surgical side may be eliminated. Previous research on the impact of upper limb dominance showed conflicting results.[640-647] Two studies demonstrated that having surgery on the dominant upper limb resulted in a greater improvement in disability[643,644] whereas other studies showed that the non-dominant upper limb

had better function than the dominant upper limb following surgery.[645,646] Conversely, 2 other studies demonstrated no difference between dominant and non-dominant surgical side.[640,647]

In the current study, age, BMI, comorbidity score, week-1 DASH score, surgery type, and adjuvant/neoadjuvant therapies were not predictors of long-term upper limb activity measured by WAMs. This finding is consistent with prior studies suggesting BMI did not predict upper limb complications following breast surgery and radiotherapy.[255,648] Although the finding is consistent with prior studies, it could also be attributed to the underpowered results resulting from the small number of participants and the numerous adjustments made. In another study, obesity was found to be an important predictor of breast cancer related-lymphoedema.[649] A systematic review and meta-analysis by Wu *et al.,*[650] demonstrated that obese patients were more likely to suffer from lymphoedema compared with overweight patients.[650] Lee *et al.,*[39] conducted a systematic review which presented conflicting results pertaining to the influence of age on upper limb morbidity. One study demonstrated a greater occurrence of "arm symptoms" in individuals under the age of 65 compared with those over the age of 65,[308] whereas Kiel *et al.,*[651] showed that older patients were more likely to develop lymphoedema. Additionally, Smoot *et al.,*[456] showed that number of comorbidities influenced the upper limb function as measured by DASH scores. Rietman *et al*[155] demonstrated that ALND and radiotherapy were independent predictors of shoulder range of motion.

Furthermore, here DASH score at week 1 was found to be predictive of long-term DASH score. Similarly, Hayes *et al.,*[652] discovered that having upper limb symptoms increased the likelihood of developing breast-cancer-related lymphoedema by 2 to 7 years after diagnosis.[652] Upper-body symptoms were associated with worse upper-body function, a higher prevalence of lymphoedema, lower levels of weekly physical activity, and a lower HRQoL.[652] In the present study, both DASH score and long-term upper limb activity correlated with EQ-5D-5L score, indicating that patient's upper limb activity and function impacted the patient's HRQoL many months after surgery. Additionally, age predicts long-term DASH score. This is consistent with previous studies that have employed subjective assessments, demonstrating that varying factors under the umbrella term of postoperative morbidity are

predictive of differing outcomes.[9,653,654] Overall, the results of the present study highlight the significance of employing objective metrics to precisely quantify functional recovery, alongside patient-reported outcomes that capture an individual's personal perception of the recovery process.[9,654] Given the subjective nature of the DASH score and specific outcome measures, such as pain, it is highly probable that they can be influenced by various psychosocial factors including anxiety, pre-surgical distress and personality characteristics.[653]

It is likely that using a combination of objective measurements and PROMs is essential to effectively assess the complete range of complications and implications of breast surgery. The patient's own evaluation is the most accurate measure of the extent to which upper limb symptoms are affecting them and their daily activities. This includes the assessment of their own physical, psychological, and social well-being as well as overall HRQoL.[9,655,656] Objective measurement on the other hand enables the collection of unbiased data and can provide more insight on patient's own upper limb activity and the severity of those complications.[9,40,78,80,488] Clear and accurate outcome measures are critical to assisting clinicians and patients in making informed treatment decisions.[9] In this breast surgery cohort, functional assessment using PROMs and WAMs pre- and postoperatively will provide additional insight into achieving better holistic health outcomes. Patients who are deemed to be at risk of developing complications can be promptly identified and offered interactive feedback support and continuous monitoring using WAMs and a structured exercise programme, which will be further discussed in chapter 9.[4,657,658] This can be further investigated through a randomised controlled trial that compares patients who are monitored and provided feedback by WAMs combined with an exercise programme, as opposed to standard care.

This study has several limitations. The small number of patients who agreed to participate in the long-term follow-up, losing approximately 50% of subjects recruited might introduce attrition bias. Attrition bias may have occurred because individuals with long-term complications were less likely to give consent for long-term data collection and may underestimate the extent of morbidity. Out of those who did not have long-term follow up, 16 patients were unwilling to participate in additional data collection,

while 14 patients did not respond or were uncontactable further limiting the reliability of the data. Neoadjuvant/adjuvant therapy such as radiotherapy and chemotherapy may have a negative impact on patient's upper limb activity and should be considered in future studies with planned recruitment comparing patients with and without neoadjuvant/adjuvant therapy. Moreover, despite the efforts to account for potential confounding variables, such as additional surgeries or new diagnoses, it is difficult to account for all eventualities. Age, BMI, comorbidities, week-1 DASH score, surgery type and adjuvant/neoadjuvant therapies were not found to be predictors of long-term upper limb activity measured by WAMs, probably due to limited statistical power given the small cohort size. The long-term data were acquired only over a 3-day period at a median follow-up of 21 months after the initial operation. Heterogeneity in types of breast surgery and reconstruction may influence the longitudinal recovery trajectory and therefore may underestimate or overestimate the extent of upper limb morbidity. Nonetheless, there are several important strengths of this study, including the use of WAMs, as an accurate and continuous objective measurement of upper limb activity levels. Gresham *et al.,*[207,435] noted some drawbacks of wearable device studies, such as the use of unvalidated sensors and the lack of data quality control. In contrast, the current investigation used a validated wearable technology.[78] To ensure the accuracy of the data, quality control steps were undertaken as previously described (see methodology in chapter 4). Finally, patients were interviewed and given instructions to record "start" and "stop" of device use in order to further ensure the reliability of the data.

8.6 Clinical Implications

This chapter demonstrates that 2-week postoperative upper limb activity and preoperative upper limb activity are significant predictors of long-term upper limb activity, allowing identification of patients in need of supportive rehabilitation and highlighting the importance of prehabilitation. Importantly, it also highlights that only 59% of patients reached their baseline upper limb activity level in the long-term. WAMs can supplement the existing PROMs as prediction tools that may be used to identify patients who require additional assistance in their recovery and facilitate self-directed rehabilitation (Figure 8-3).

Although WAMs were feasible for use in the breast cancer patient cohort, there were reservations regarding the design of the sensors, patient adherence, usability, and functionality. To address these issues, the following chapter will discuss the views of patients regarding the implementation of WAMs in this setting.

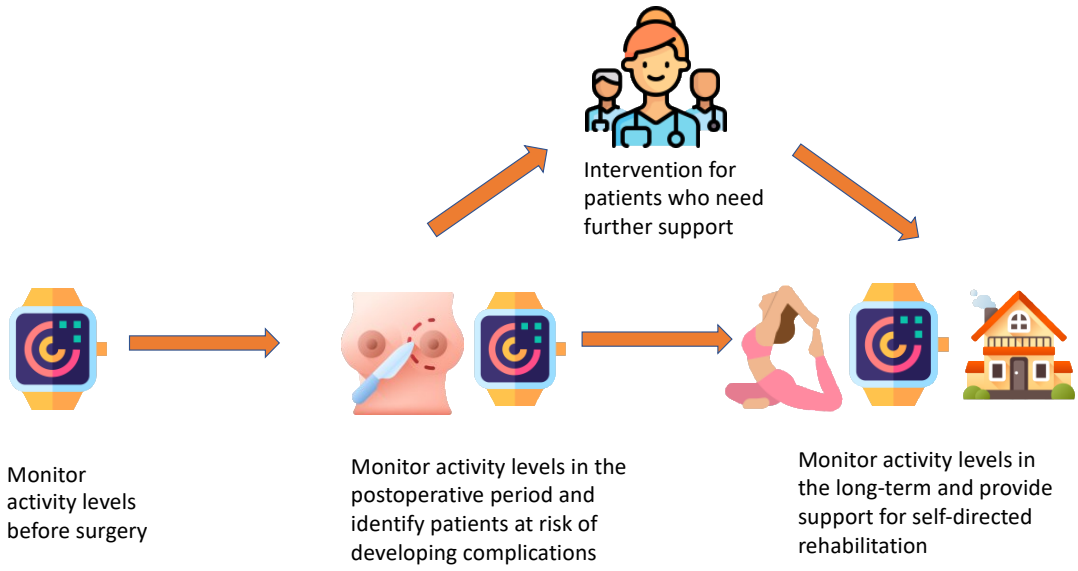


Figure 8-3 Wearable Activity Monitors Within the Healthcare Pathway

9 THE USE OF WEARABLE ACTIVITY MONITORS IN BREAST CANCER PATIENTS: PATIENT PERSPECTIVES

9.1 Introduction

The previous chapters highlighted the quantitative findings of the use of WAMs in the perioperative period and in the long-term. The selected methodology aims to effectively analyse the significance of the research data with respect to its practical implications. This chapter employs qualitative research methods using semi-structured interviews to provide an in-depth examination of patients' perceptions on the application of WAMs for postoperative monitoring.

9.1.1 Importance of patient perspectives

A systematic review by Bergmann *et al.*, [659] demonstrated that there was a lack of high-quality studies in the area of wearable technology due to the small number of participants, limited methodology and restricted reporting of the research processes. They also found that user preference is rarely considered when designing the WAMs.[659] In order to improve the effectiveness of wearable technology in clinical settings, it is imperative to incorporate user feedback during the implementation process. It is of utmost importance to understand the practical aspects, such as the design and aesthetics of WAMs, as well as their comfort, in order to create a device that is user-friendly and promotes adherence. Evidence shows that individuals with chronic conditions who assume greater responsibility for their own management experience an overall improvement in their health and general well-being.[660,661] Therefore, if WAMs are to be utilised in clinical behavioural interventions, then it is crucial to comprehend the practical and psychosocial factors that may influence patients' use of the technology.

There is a limited body of qualitative research conducted to date that explores the perceptions of breast cancer patients regarding wearable technology particularly for measuring upper limb activities. For example Nguyen *et al.*,[67] conducted a study to assess the efficacy of WAMs in post-menopausal breast cancer survivors. The findings revealed that a significant proportion of the participants expressed

positive perceptions towards WAMs, considering them as valuable and well-received interventions. This sentiment was particularly evident when WAMs were utilised in conjunction with additional strategies for behavioural modification, such as peer support.[67] The inclusion of patients in the initial phases of wearable technology development has the potential to improve adoption of the technology and proactively address any potential challenges or concerns that may arise. Nevertheless, a gap persists between the research conducted on this technology and its practical implementation in real-world scenarios. Previous studies have indicated that individuals participating in trials exhibited non-compliance with the prescribed study protocol, as evidenced by their failure to consistently wear WAMs during the designated study period or their decision to completely withdraw their involvement in the trial.[488,662,663]

One study by Hardcastle *et al.,*[664] explored the use of WAMs among cancer survivors living in regional and remote areas of Western Australia. Engaging in physical activity has the potential to decrease the likelihood of cancer recurrence as well as improve overall survival rates.[665-667] Smith *et al.,*[668] investigated the adherence to physical exercise guidelines among breast cancer survivors, demonstrating that only 54% of patients met the minimum requirements. Another study by Colleta *et al.,*[669] found that only 9% of cancer prevention patients and survivors adhered to both aerobic and resistance physical activity guidelines, 20% adhered to aerobic exercise guideline only and 12% adhered to resistance exercise guideline only. Hence, it is imperative to explore the feedback from patients in order to comprehend the underlying factors contributing to low physical activity of some breast cancer patients and to determine the potential effectiveness or the use WAMs in improving their levels of physical activity. Cancer survivors in this particular study indicated that the WAMs served as a source of motivation for them to engage in a greater number of activities.[669] This increased motivation stemmed from increased awareness of their own physical movement levels facilitated by WAMs.[669] Patient's own behaviour and motivations also play a factor in determining the effectiveness of WAMs at encouraging increased physical activity. Moreover, several participants expressed concerns regarding the limitations of the WAMs, such as failure to accurately capture certain activities like swimming.[669]

Additionally, there were instances where the WAMs displayed incorrect readings, resulting in a false sense of achievement for some.[669]

A systematic review by Moore *et al.*,[670] investigated older adults experiences with using wearable devices. This study holds significance due to the prevalence of older women among breast cancer patients, making their perspectives on the utilisation of WAMs crucial.[670] The adoption and utilisation of wearable devices among elderly people are influenced by various significant aspects, such as motivation for device usage, the convenience of use, the purpose of the device, and perceived added value in the user's life.[670] However, useful device features alone do not guarantee sustained usage. A support system is needed to encourage motivation and promote engagement with WAMs.[670]

It is essential to consider how WAMs could be utilised following breast cancer and reconstructive breast surgery, how patients would like to review activity data, how this information can be communicated to the clinical team, and what intervention is effective in motivating patients to increase their activity levels. The surgical team may benefit from knowing the patient's preoperative activity levels and baseline function in order to quantify the patient's pre-operative fitness level. Patients who are identified as unfit may not be able to have complex surgeries or may have to undergo a prehabilitation programme prior to their surgeries.

The objective of this chapter is to gain further insight of patients' experiences post-breast cancer treatment and improve the understanding of the user experience, their feedback and acceptance of utilising the WAM during pre- and postoperative period in both hospital and community settings. This study will provide significant insights into patients' perceptions of WAMs, and strategies for improving the design and implementation of wearable technology in future research and clinical settings.

9.2 Ontological and epistemological considerations

All study originates from a philosophical perspective concerning the essence of knowledge and the methods of its acquisition which shapes the execution of the research. The researcher's worldview, also known as a paradigm can lead to bias, distorting the study process and data interpretation.[671,672] As a result, understanding the researcher's paradigm allows others to evaluate the potential impact on their own research. There are numerous philosophical perspectives reported in the literature; however, there is no consensus on how these might be classified, and the nomenclature used is not consistent. I have chosen to present the most frequently referenced work of Lincoln, Lynham, and Denzin, who delineate five research paradigms: positivism, post-positivism, critical theory, constructivism, and participatory (Table 9-1).[673] The paradigm is based on ontology, epistemology, and methodology.

Ontology

Ontology encompasses the concepts that we regard as fundamental or basic, as well as the things that we believe can exist.[674] In other words, "what is the nature of reality?". For example, at one extreme of the spectrum, realism is the conviction that a single reality exists, which is unaffected by the individual and is guided by deductive reasoning and objectivity.[673,675] Relativism on the other hand, is the belief that there are multiple versions of reality depends on context and that knowledge is subjectively derived from interactions and lived experience.[675,676]

Epistemology

Epistemology describes ways of knowing, how we know what we know, and who can be a knower.[677] In other words, it refers to the process by which a researcher acquires knowledge and understanding. Similar to ontology, epistemology has a spectrum. At one extreme of the spectrum lies the dualist/objectivist epistemological perspective, wherein the researcher and the subject are regarded as independent entities, allowing for the study of the subject without any influence from the researcher or vice versa. Values and biases are mitigated to ensure outcomes are unbiased and findings are reproducible and accurate; this allows the researcher to objectively ascertain the genuine nature of phenomena.[675] Conversely, the transactional/subjectivist epistemological approach involves the

researcher and subject being interconnected, resulting in the creation of findings as the investigation progresses, which leads to a blurring of the boundaries between ontology and epistemology.[675] Participatory epistemology involves the theory of knowledge created by the interaction of the human mind with the world. It asserts that knowledge is most influential when produced collaboratively through action.[678]

Methodology

Research methodologies differ based on the researcher's ontology and epistemology. For example, in experimental manipulative methodology, questions or hypotheses are articulated in propositional form and empirically tested for verification, while potential confounding variables must be meticulously controlled to avoid incorrect impact on outcomes.[675] Conversely, the hermeneutical and dialectical methodologies generate interpretations or constructs through interactions between and among the researcher and the subjects.[675]

Table 9-1 Paradigm and their ontology, epistemology and methodology

	Positivism	**Post-positivism**	**Critical Theory**	**Constructivism**	**Participatory**
Ontology	Naïve realism	Critical realism	Historical realism	Relativism	Participative reality
Epistemiology	Dualist/ objectivist	Modified dualist/ objectivist	Transactional/ subjectivist	Transactional/ subjectivist	Critical subjectivity
Methodology	Experimental manipulative (verify a hypothesis)	Modified experimental manipulative	Dialogic / dialectical	Hermeneutical / dialectical	Political participation (shared experiential)

Table is based on Lincoln et al[673]

The positivist paradigms - positivism, and post-positivism are linked to quantitative research methodologies in which knowledge is assessed through the use of reliable instruments, to address a hypothesis with an objective 'one truth.' In contrast, interpretivist paradigms, such as critical theory, constructivism, and participatory approaches, are predominantly qualitative and increasingly

subjective, acknowledging various realities with the researcher actively engaged in the topic under investigation.[673,675] Consequently, researchers must acknowledge the paradigm they contribute to a study and elucidate how it influences the methodology of the study.

Defining my paradigm

I am a medical doctor with a background in surgery and radiology. I have received education and training primarily within a positivist paradigm. Medicine trains me on the significance of evidence-based practice and the application of quantitative methods and statistical data obtained from randomised controlled trials (RCTs). Therefore, I am influenced by realist ontology, of a single truth and an objectivist epistemiology where knowledge can be understood through objective measurement. Similarly, my main academic supervisors (Prof Lord Darzi, Mr Daniel Leff and Mr Richard Kwasnicki) are clinical academics and surgeons. In general, healthcare predominantly functions within a positivist paradigm, utilising evidence-based medicine and quantitative methods, along with a realist ontology.[679]

It is important to note that healthcare services and the NHS have progressively adopted a social sciences perspective. This approach has increasingly recognised the complexity and diverse viewpoints in health and healthcare, particularly concerning quality and service improvement. As the years passed in my clinical practice, I recognise that each patient is unique and responds variably to treatment. Diverse patients may perceive the same circumstance variably, indicating the existence of diverse views on a singular issue which may be due to different factors such as culture, religion, social status and education. For this reason, I can therefore relate with a relativist ontology and transactional subjectivist epistemology (interpretivist paradigm). As a result, my interpretivist paradigm has progressively developed throughout time. This has a significant impact on my research, as I am currently struggling with two conflicting paradigms in my clinical practice. From an ontological perspective, it is impossible to acknowledge the existence of both a single reality and multiple realities, and from an epistemological perspective, it is impossible to investigate these realities either objectively or subjectively.[680,681] Consequently, I am confronted with a philosophical quandary in my interactions with two completely

opposite paradigms. This contradiction between positivism and interpretivism is commonly encountered by healthcare researchers.

This distinction between ontological and epistemological stances have been challenged, emphasising the significance of the research question. As discussed by Broom *et al*, not all research questions in healthcare can be addressed by RCTs.[680] For instance, the number of individuals who die annually as a consequence of delaying the call for an ambulance due to severe chest pain is not a subject that could be investigated through a randomised trial due to ethical and practical limitations. The question of why cannot be answered by a randomised controlled trial design, as it is unable to investigate the factors in a person's life and relationships that may have influenced their decision to defer seeking assistance.[680] The interpretivist approach, conversely, presents several issues, including a lack of consensus among qualitative researchers regarding suitable methods for data collection and analysis, unwarranted generalisations based on the narratives of a limited number of individuals as well as reliance on convenience sampling techniques, leading to potentially 'biased' samples.[287,680] As a result, health researchers should adopt a pragmatic approach to research design and data collection which I can also relate to.[680] To address the conflict between two opposing paradigms, one should consider the nature of the specific research question, rather than being purely motivated by a philosophical standpoint.[287,680,681]

The research questions in this chapter necessitate an exploration of breast cancer patients' perspectives on their treatment and experiences with wearable technology for assessing upper limb activity following breast surgery, aligning with an interpretivist or constructivist paradigm. Taking into account both the study objectives and my personal philosophical assumptions and values, this chapter employs a qualitative approach to inquiry. The goal of qualitative research is to use participant experiences, and perspectives to construct ideas that help comprehend a phenomena in its natural environment.[682] Instead of eliciting the "outsider" view, qualitative research may offer an “insider” view by providing context and significance to human behaviour.[675] To provide additional support to this qualitative chapter, my supervisor (Mr Daniel Leff) suggested that I approach experienced relativist qualitative researchers (Dr Gemma Clunie, Prof Mary Wells and her research group).

9.3 Hypothesis

- ◊ *Patients have valuable opinions, personal preferences and insight on the utilisation of wearable activity monitors for the assessment of upper limb activity following breast and axillary surgery.*

9.4 Methods

I opted for one-to-one semi-structured interviews to investigate breast cancer patients' perspectives on their experiences following treatment and their views regarding the application of wearable technology in monitoring activity and postoperative rehabilitation. Semi-structured interviews facilitate the collection of open-ended data to investigate individuals' thoughts, feelings, and opinions regarding a certain topic, delving into the rationale behind their responses and, where appropriate, probing sensitive issues in depth.[683] In other words, participants are permitted to answer these open-ended questions at their discretion, and the researcher may further explore these responses (for example "In what way . . . ?" or "Tell me . . . ?" or "Such as . . . ?").[684] This method is semi-structured, as evidenced by the adaptability of the responses and the framework. It is unique among interview methods in that it maintains a high level of relevance to the subject matter while also being attentive to the participant.[684,685] I decided to conduct one-to-one semi-structured interviews over focus group discussions (which involve a collective dialogue on a specific topic) in order to offer a "safe" private space for disclosure given the potentially distressing experiences of the breast cancer survivors and attain a profound comprehension of individual perspectives and motivations. This method is potentially less susceptible to influence from others and easier to recruit and conduct.[686]

9.4.1 Outline

A qualitative study was performed using semi-structured interviews to assess patients' experiences following breast cancer surgery and their perceptions of wearable activity monitors used in healthcare settings.

9.4.2 Conducting a Qualitative Study

Ethical approval

Before starting data collection, ethical approval was granted by the National Research Ethics Committee London – City Road (Ref: 15/LO/1038) (Appendix 8).

Registration

The study methods were submitted to the ClinicalTrial.gov registry (NCT03635723). The study was registered under 'The Step Home Trial: Utilising Physical Activity Data in the Acute Post-Operative Setting'.

Setting

The study was set in Imperial College Healthcare NHS Trust, a large teaching hospital within Northwest London.

Participants

Potential participants were consecutively identified from a list of patients who were recruited from the previous chapters. The participants were aware that they would be contacted by telephone for semi-structured interviews after they completed the period of activity monitoring with WAMs. They were also aware of my background as a medical doctor outside their clinical care team and my research interest in the use of wearable technology to support patient recovery following breast surgery. The participants were recruited as a convenience sample, whereby they were recruited according to their availability. To obtain diverse perspectives from individuals who experienced various types of breast surgeries, patients who underwent wide local excision, mastectomy, or breast reconstruction +/- sentinel lymph node biopsy or axillary lymph node dissection, as well as patients who were diagnosed with lymphoedema post breast cancer surgery were invited to participate. The study provided no direct benefit to participants, aside from contributing to the improvement of postoperative management for breast cancer patients. Participants were informed that their participation or lack thereof would not influence the standard of care they received, and that participation was entirely voluntary. Before participating in the study, patients were given written information sheet and provided written informed consent.

Development of interview topic guide

A topic guide assists the interviewer in staying focused on the original research question, given the wealth of information that may arise during the interview. The interview topic guide was developed using published guidelines.[683,687,688] The semi-structured interview questions were shaped by research literature on wearable technology[689,690] and insights from the Patient and Public Involvement and Engagement (PPIE) representatives.

PPIE

The semi-structured interview topic guide was co-designed with members of a PPIE group (Appendix 22) hosted by Imperial College London. The PPIE group represents a panel of patients and members of the public. The demographics of the PPIE group are in Appendix 23. Recruitment was undertaken through advertisement in the Patient Experience Research Centre, Imperial College and the VOICE network. The PPIE session was facilitated by a Public Involvement Lead at the Institute of Global Health Innovation, Imperial College London. The PPIE session was conducted online through the Zoom (California, USA) platform, due to the restrictions of the COVID-19 pandemic. Participants were reimbursed for their time in accordance with National Institute of Health Research (NIHR) guidance. I presented the study background and the initial content of the semi-structured interview topic guide, which was revised based on the group input, incorporating linguistic issues and strategies to improve the interview experience for participants. Overall, the feedback highlighted the importance of open-ended questions to help participants feel comfortable, to use language they are familiar with and avoid jargon as well as sensitively explore their experiences and feeling. The co-design of a semi-structured interview topic guide was essential for achieving a more nuanced understanding of the research topic. This was achieved by incorporating the perspectives and lived experiences of the target population, ensuring that the questions were relevant, culturally sensitive, and could capture a broader spectrum of insights, particularly when addressing complex or sensitive topics.

Topics within semi-structured interview

The study met the research objectives by exploring views of breast cancer patients over the following:

- Patients' experiences following breast cancer treatment;
- Patients' experiences with wearable technology;
- Patients' opinions about their own recorded data;
- Patients' opinions about the best way to recognise patients with arm impairment and
- Patients' opinion about sensor-based scoring system.

Interviews

Due to the COVID-19 pandemic, I conducted the interviews via the telephone in a private setting. At the beginning of each interview, participants were provided with an overview of the study and the interview. They were reminded that the interview's content is confidential and anonymous, and they were provided with the opportunity to ask questions. They were notified that the sessions would be recorded using a digital voice recorder and that they had the right to terminate the interview at any point. The interview started with small conversation to develop rapport, while attentively listening to the participants and demonstrating genuine interest through insightful follow-up questions. The interviews were transcribed verbatim by a transcription service (McGowan Transcriptions - who had a confidentiality agreement in place with my department) and the transcripts were reviewed for accuracy. A series of open-ended questions were asked to participants (Appendix 22) to better understand their experience after breast cancer treatment and their perspectives on the use of wearable technology in daily life and in healthcare settings. Each patient had their individual activity data presented to them. Further questions were asked to gain an understanding of how they viewed the data and their feedback on how this data could be used in a personalised rehabilitation programme. At the conclusion of each session, participants were asked to whether there was anything they wanted to add or if there was anything that should have been addressed but had not. Field notes were taken after the interviews to reflect verbal responses and reflections.

9.4.3 Data Analysis

Study design and analysis

This was a qualitative study based on semi-structured interviews with patients on their perspectives about wearable technology used in the healthcare setting within the peri-operative period.

Qualitative research is defined as "*the study of the nature of phenomena",* including *"their quality, different manifestations, the context in which they appear or the perspectives from which they can be perceived"*, but excluding *"their range, frequency and place in an objectively determined chain of cause and effect".* In other words, it explores and provides deeper insights into real-world problems.[691]

There are 4 main types of qualitative research as described by Brannan *et al.,*:[692]

- ◊ **Ethnography** - This methodology entails the researcher actively engaging and immersing themselves within the environment of the participant. During this immersive experience, the ethnographer can employ a diverse range of data collection methodologies in order to generate a thorough narrative of the social phenomena seen over the duration of the research. [693]
- ◊ **Grounded Theory** – Development of a theoretical model is facilitated by the process of watching a study population and conducting a comparative analysis of their speech and behaviour.[694]
- ◊ **Phenomenology** - Focuses on exploring the "lived experiences" of the participants and seeks to analyse the motivations and rationales behind their behaviours, as perceived by the individuals themselves.[693]
- ◊ **Narrative Research** - Detailed description that involves the integration of a series of events, typically centred around one or two individuals, with the aim of constructing a coherent narrative.[693]

Qualitative data then can be analysed in several ways including:[695-697]

- ◊ **Thematic analysis** –"a method for identifying, analysing, and reporting patterns (themes) within data"[695]
- ◊ **Grounded theory analysis** – Continuous analysis of the data employing an inductive approach to identify themes that organically arise from the data itself[696]
- ◊ **Narrative analysis** - the examination of personal narratives or stories in order to better understand the significance and context of an individual's experiences
- ◊ **Discourse analysis** - examination of how individuals express themselves in various social settings
- ◊ **Content analysis** – the process involves methodically examining patterns that arise from written material, by categorising the content into individual words, concepts, and themes

In qualitative research, the most appropriate method of data collection and analysis depends on the research question. To achieve the study objectives, the interview transcripts were subjected to thematic analysis to provide an in-depth understanding of patients' perceptions on the use of wearable technology post-breast cancer surgery and how can they improve the rehabilitation process post-surgery. An inductive approach involves allowing the raw data to determine your themes, while a deductive approach involves examining the data with preconceived themes based on theory or existing knowledge.[698] In this study, an inductive thematic analysis was performed utilising the commonly cited Braun and Clarke thematic analysis.[695] The decision to adopt this approach was made in order to facilitate the formulation of the theory directly from the data, without relying on any pre-existing theories on the utilisation of WAMs in the peri-operative period. This was important because there was a limited amount of prior research conducted in the use of WAMs to measure upper limb activity following breast and axillary surgery. Reflexive thematic analysis, as described by Braun and Clarke,[699] was particularly suitable for collecting and analysing qualitative data in a way that honoured and conveyed the subjectivity of participants' perspectives, while simultaneously recognising and incorporating the reflexive impact of my interpretations as the researcher.

The study followed the six stages of thematic analysis as outlined by Braun and Clarke:[695] I meticulously reviewed the transcripts for data familiarisation, documented potential codes by line-by-line manual coding, noted data patterns, and extracted codes to formulate subthemes and overarching themes that encapsulate the data. I reviewed and refined the sub-themes and themes. The use of multiple coders in reflexive thematic analysis to achieve "accurate" coding contradicts the principles of purist reflexive thematic analysis.[699] Nevertheless, the use of multiple coders may prove advantageous in a reflective capacity, such as validating concepts or examining various assumptions or interpretations of the data.[699] I randomly assigned 20% of the interviews (n=2) using a random number generator to be second-coded by another researcher (AMB – a mixed method researcher, PhD with a background in oncology and mental health). The findings were discussed in a virtual meeting aiming to achieve richer interpretations of meaning. The remaining transcripts were coded by the primary researcher.

The themes and subthemes were subsequently presented to a group of qualitative research experts (MW and her research groups). I created a coding tree and an initial thematic map representing relationships between sub-themes and themes and constructed a report using quotations from participants as examples to demonstrate subthemes and themes. These were explored by the qualitative research experts to enhance the analysis, explore divergent views, resolve any differences in interpretation, and establish consensus if required. Based on the feedback received from the group meeting, the thematic map and coding tree were revised, and this was discussed with GC (qualitative research expert) to provide further rigour in analysis.

Sample size

The determination of suitable sample sizes in qualitative research remains controversial, and there are no established guidelines for obtaining them.[700] The methodology used should ultimately determine the sample size. The concept of data "saturation" from grounded theory is frequently discussed in the literature, as the primary objective of thematic analysis is to extract themes from the data. Although you could argue that some new findings will always be made, data saturation occurs when no new themes are identified in analysis of the interview transcripts.[701,702] This procedure complicates the estimation

of the required number of participants at the study's inception, particularly in the absence of comparable qualitative studies for reference. According to Braun and Clarke, data saturation is "not a particularly useful concept".[703] However, they noted that it is frequently important to compute the sample size ahead of time for research projects, grant applications, journal standards, or as required by thesis examiners. The concept of data saturation can help researchers choose an optimal sample size and determine when to cease collecting data. This can be accomplished by defining the concept of saturation, the focus of the research topic, and the definitions of codes and themes. For the purposes of this thesis, I have chosen to employ the concept of data saturation as described above, where no new themes were identified from reviewing existing transcripts. Based on the findings of Guest *et al* who conducted an experiment with sixty in-depth interviews and determined that data saturation was achieved after six to twelve interviews,[704] I chose to recruit 12 participants into this interview study, with only 10 interviews required before saturation occurred.[701]

Data Analysis

NVIVO software (Version 14, Lumivero, Colorado, USA) was used to analyse the interview data and generate initial themes. Data was systematically analysed using Microsoft Excel® for Mac (Version 16.28, Microsoft Corporation, Redmond, WA, USA) by indexing and charting to identify and summarise the main points, until a comprehensive understanding of the data was achieved. Post-it notes were also used to summarise the codes, subthemes and themes. The study was reported according to the COnsolidated criteria for REporting Qualitative research (COREQ) checklist.

9.5 Results

8.3.1 Study participants

Between July 2021 to October 2022, 12 patients who underwent breast surgery +/- reconstruction +/- axillary surgeries and patients who were diagnosed with lymphoedema post-breast surgery were recruited. Out of a total cohort of 12 patients who were recruited, saturation of themes was met after the tenth patient. Therefore, 10 participants were included in the data analysis. Patients' ages ranged from 28 to 78 years old. The participant demographics are presented in Table 9-2. The interviews lasted 30-45 minutes and occurred in a private setting via the telephone, however, if a patient requested a family member to sit in, this was permitted.

Table 9-2 Patient demographics (n=10)

Participant	Age range	Gender	Ethnicity	Surgery	Site of surgery	Handedness
1	65-75	F	White- British	WLE + SLNB	Right	Right
2	45-55	F	White- British	WLE + SLNB	Right	Right
3	55-65	F	Asian or Asian British - Indian	DIEP + SLNB	Right	Right
4	75-85	F	White-Irish	MX + SLNB	Right	Right
5	55-65	F	Other	DIEP + SLNB	Left	Right
6	45-55	F	White- British	DIEP + SLNB	Right	Left
7	55-65	F	Asian- any other Asian background	Mx + ALND	Right	Right
8	65-75	F	White-Irish	Mx + ALND	Right	Right
9	75-85	F	White- British	WLE + SLNB	Right	Right
10	25-35	F	Other	DIEP + ALND	Right	Right

WLE, wide local excision; Mx, simple mastectomy; DIEP, deep inferior epigastric perforator reconstruction; ALND, axillary lymph node dissection; SLNB, sentinel lymph node biopsy

8.3.2 Main Results

Four overarching themes were identified from the semi-structured interviews: 1) Breast cancer survivorship, 2) Features and impact of WAMs, 3) User experience of WAM application, and 4) The implications of WAMs on behavioural change. The thematic map displays the relationship between the themes (Figure 9-1). The themes are outlined in greater depth in the narrative report. The coding hierarchy and thematic analysis table are in Appendix 24.

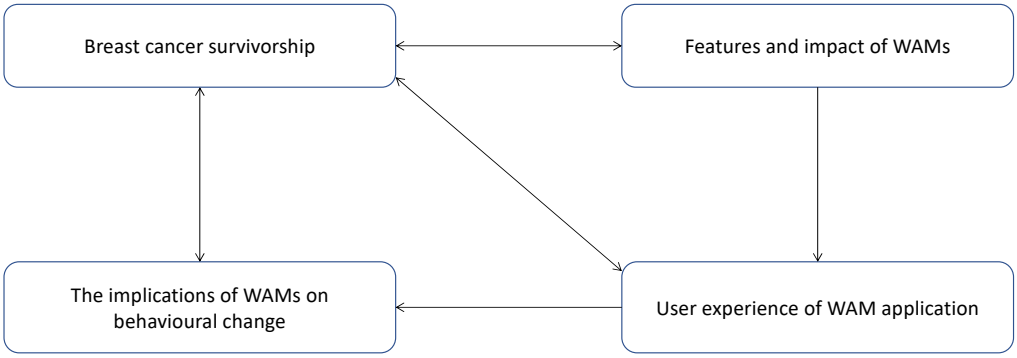


Figure 9-1 Thematic map of patients' experiences post-breast cancer treatment and their opinions on wearable activity monitors (WAMs)

General knowledge of wearable activity monitors

Most patients were aware of the use of wearable technology in the fitness industry. Four patients reported using Fitbit as a means of monitoring their physical activities. Four patients were familiar with wearable devices such as Fitbit and Apple watches, but none of them had used these devices. Two patients were completely unaware of the existence of these devices.

Theme 1: Breast cancer survivorship

Data analysis revealed 6 subthemes which will be further elaborated below (Figure 9-2).

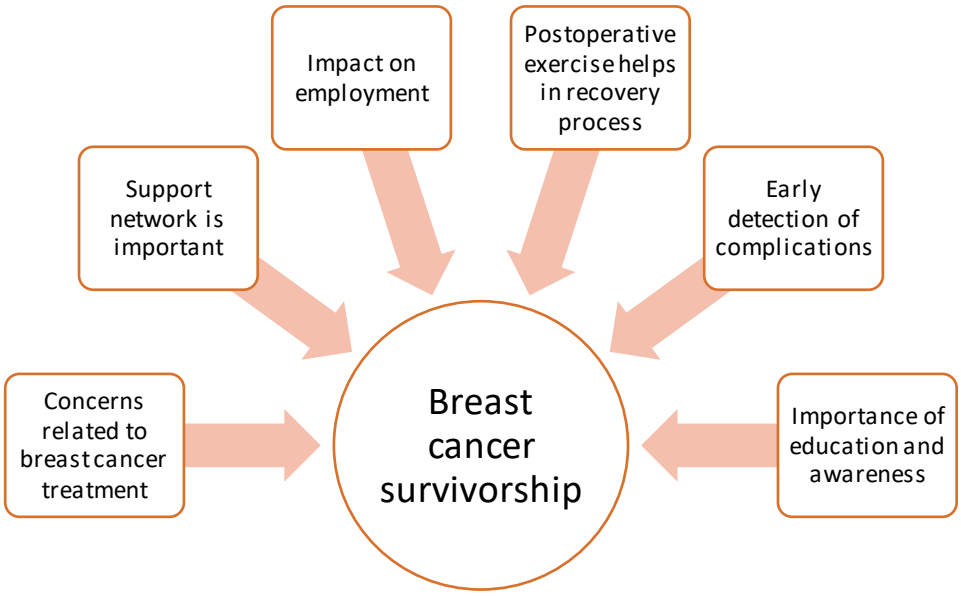


Figure 9-2 Breast cancer survivorship

Subtheme: Concerns related to breast cancer treatment

The majority of the patients mentioned that the surgery had an impact on their arm (e.g., pain, swelling, and stiffness), general mobility, and their day-to-day activities (e.g., eating and drinking, house chores, and getting dressed):

> *"...I literally could not shift it; and obviously, if I tried to, it was painful..." (P6)*

Subtheme: Support network is important

Throughout the interviews, participants described the emotional challenges of breast cancer treatment and how isolating the process could feel. For many, the existence of a support network, whether friends, family, or others, was key to being able to navigate both the emotional and physical challenges, even the most mundane day-to-day activities:

> *"...for quite a number of weeks, my husband had to wash my hair, and things like that, or comb my hair, because I couldn't do things like that"(P3)*

Subtheme: Impact on employment

Participants reported that their working lives were impacted by their breast cancer treatment, and that this often changed throughout the course of their care due to the different challenges of chemotherapy, radiotherapy and surgery. Employers were described as being supportive but unable to always offer solutions to the challenges of working life alongside or following cancer treatment. Some patients had to quit their jobs:

> *"It was brilliant until I got ill, and once I got the breast cancer, I was very ill and had all the treatment so in the end I did try go and go back. My manager furloughed me for a short time to see if I could go back, but it came to the point I was never going to go back. I wasn't able to carry out the duties that I did. So it wouldn't haven't been safe, so I packed up" (P8)*

Subtheme: Postoperative exercise helps in recovery process

All patients received advice on exercise post-breast surgery in the form of an exercise leaflet +/- verbal advice or a one-to-one session with a physiotherapist. The majority of patients perceived the exercise as beneficial for improving their process of recovery:

> *"Oh, very good, yes, it helped me because I was so stiff. My back was - I had so much pain on my neck and on my back, on my lower back and she... I still do some exercise still. She video me on my phone and she told me to do - she gave me leaflet with some of them, and then she video. I did some in St Mary's and when I was doing it she video me, and then when I came home I had to do every day for ten minutes, those exercise. Watch it on my phone and do the exercise, and they were very good, very useful exercise"(P7)*

Subtheme: Early detection of complications

The majority of patients emphasised the significance of early detection of complications. One method to achieve this is for clinicians to ask specific questions about arm morbidity and to conduct regular follow-ups. However, several patients discussed the impact of the COVID-19 pandemic, which caused restrictions and cancelled appointments, making communications between clinicians and patients difficult and potentially leading to late diagnosis of complications. Several patients also mentioned that

WAMs have a role in identifying upper limb complications and improve communication between patients and clinicians by monitoring their upper limb activity levels. WAMs could be integrated with clinical examinations (e.g., tape measurement to assess arm swelling) to provide clinicians with the necessary information to develop intervention strategies:

> *"... if you're able to get some sort of feedback from a clinician or regularly maybe earlier, or from the actual device itself telling you. Maybe you could plug it into your computer or something, and check your graph on pathway. They definitely do have a place in there" (P1)*

Subtheme: Importance of education and awareness

Most patients emphasised the significance of patient awareness and education regarding potential issues that may arise after breast cancer treatment. For example, certain patients were not aware that lymphoedema could occur many years after breast cancer treatment. Additionally, several patients expressed the necessity of patient education regarding the interpretation of WAM data in order to make well-informed decisions regarding their activity levels.:

> *"...if the patient has the information and the education, I suppose, to interpret it, the patient would be the first person to recognise that..." (P9)*

Theme 2: Features and impact of WAMs

The subthemes addressed were wearability and comfort, self-image, features of WAMs and design improvement and WAMs cause interference with wrist-worn accessories and lifestyle (Figure 9-3).

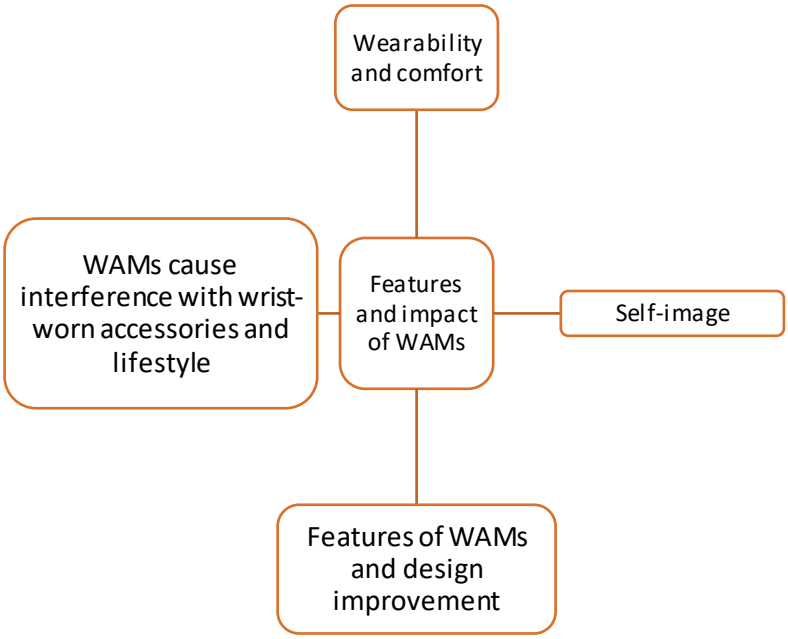


Figure 9-3 Features and impact of WAMs

Subtheme: Wearability and comfort

The majority of the patients found their WAMs to be comfortable, and they were either happy to wear them or felt indifferent. Most of the patients would wear the WAMs again in the future. At least one participant reported that the WAMs caused skin irritation and soreness:

> *"I think it had made my - I think it was right or it could have been my left, wrist, a little bit sore" (P2)*

Subtheme: Features of WAMs and design improvement

Participants had varying opinions on the features of the WAMs that they trialled. For some they were ambivalent to specific features, but others had stronger opinions around the colour, size (bulky) and style of the WAM. Recommendations for improving the design include a sleek and minimalist design with appropriate sizing, the incorporation of transparent straps, the addition of a clock face, and the seamless integration of sensors into the design:

"I think, relatively sleek, so nothing too bulky. I've seen people with quite thin ones, which look quite nice. I'd say that I wouldn't want them to be noticeable, especially if you're going out, for example. Especially if you're going out somewhere nice for dinner and you want to wear a wearable, you don't want to have a big watch or whatever that kind of ruins the outfit, so I think they should be quite sleek and unnoticeable"(P10)

Subtheme: Self-image

Some participants reported that the presence of WAMs on both wrists had an impact on their self-image, as they attracted people's attention and affected their privacy. Wearing WAMs also reminded them of their breast cancer:

"I guess it also made me conscious of the fact that I was undergoing treatment and post treatment and all of that" (P6)

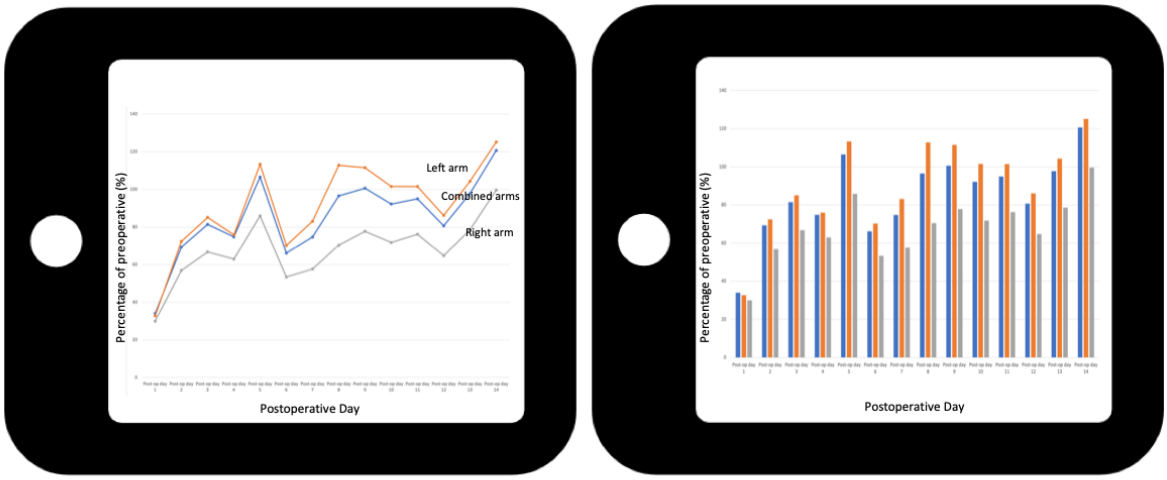
Subtheme: WAMs cause interference with wrist-worn accessories and lifestyle

Several participants also stated that WAMs caused interference with their wrist-worn accessories. Some patients reported being unable to wear their watches. Although some patients said that they just carried on as normal and could wear their accessories, like bracelets. Some other patients commented that WAMs interfered with their daily activities, including washing:

"I just thought it was a bit of an annoyance, occasionally - particularly getting in the way with things like washing and all that kind of stuff"(P5)

Theme 3: User experience of WAM application

Individualised data for each patient was presented as graphs and numbers (Figure 9-4). The subthemes discussed are presented in Figure 9-5.



Post-op Day	Combined arms (%)	Left arm (%)	Right arm (%)
Post-op day 1	33.96612634	32.66877974	29.92278705
Post-op day 2	69.34057466	72.41711539	56.89341386
Post-op day 3	81.42199391	85.13323138	66.73386957
Post-op day 4	74.80463692	75.92497389	62.98684999
Post-op day 5	106.5463083	113.318014	85.92317817
Post-op day 6	66.15402643	70.24618543	53.43152293
Post-op day 7	74.75100946	83.05954071	57.67669065
Post-op day 8	96.53572899	112.8120446	70.42339993
Post-op day 9	100.5821895	111.5321026	77.77587232
Post-op day 10	92.18795975	101.50625	71.8106582
Post-op day 11	94.96127554	101.4890727	76.21993194
Post-op day 12	80.65527669	86.15992199	64.76643249
Post-op day 13	97.74499746	104.3082989	78.56840715
Post-op day 14	120.6394253	125.1248082	99.6188513

Figure 9-4 Examples of how data were presented to patients. orange, left arm; blue, combined arms; grey, right arm

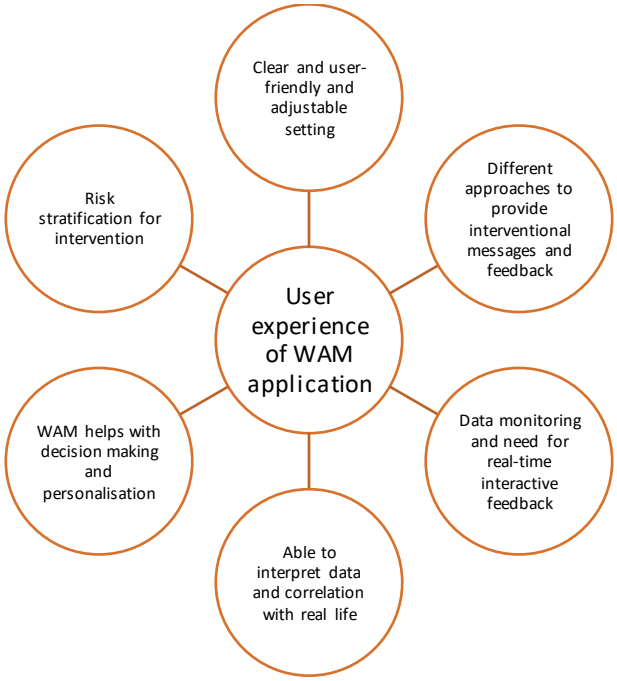


Figure 9-5 User experience of WAM application

Subtheme: Able to interpret data and correlation with real life

All the patients were able to understand the data produced from the WAMs when it was presented to them. Some patients attempted to analyse the upper limb activity of their surgically treated arm in comparison to the unaffected arm. They also tried to correlate the data presented with their real-life activities (Figure 9-4):

> "*"On the day ten and also the right hand, I remember one day I did cleaning in my house..."(P7)*

Subtheme: Clear and user friendly and adjustable setting

They also emphasised the importance of clear and user-friendly data presentation that can be adjusted based on a patient's preferences. Certain patients expressed a preference for viewing the data in the form of a graph or infographic, while others preferred to have numerical presentations:

> *"I suppose it would be nice to have more of an infographic. I think the way the Fitbit does their interface is quite useful because they've got little graphs and... I'll just have a look, actually, and see if I can - yes, having little graphs and quite simple charts to show progress. I think the*

Google Fit on my phone does it as well, but it's got a little circle and, basically, when you hit 10,000 steps, it fills the circle in. Then you've got, for example, other little circles, like how much distance you've walked or ran, and calories burned, and then the circle goes round, and it fills up the more you do, until you meet your daily target" (P10)

Subtheme: Data monitoring and need for real-time interactive feedback

Most patients preferred receiving real-time data with interactive feedback via WAMs, enabling them to monitor their progress and promptly access information that would help their understanding of their current levels of upper limb activity and reminding them to do exercise or seek appropriate help. Although certain patients are concerned about overburdening the clinicians with real-time monitoring. Interestingly, some patients reported that the WAM devices made them more aware that their exercise adherence was being tracked, which in turn encouraged them to complete the exercises prescribed:

"Yes, it felt you were being watched, and that if I didn't do the exercises, then you would be able to tell from tracking it… It's reassuring, because as you say, it does manage to track that you're doing exercises and everything and using it. It did remind me to do them, in a way. I thought this is being tracked, people are following me up" (P1)

Subtheme: Different approaches to provide interventional messages and feedback

The participants described different approaches to providing interventional messages and feedback via WAMs, including the direct approach (e.g., motivational messages or reminders/prompts to encourage patients to do their exercise) or the subtle approach (e.g., traffic light feedback, where "red" means that you need to do more exercise, "orange" means that you almost reach your goals, and "green" means that you achieve your goals for the day). They also emphasised that the interventional feedback should be achievable for the patient population. However, some patients preferred to interpret the data themselves without constant interventional feedback from WAMs:

"I'd regard it as too bossy, but I wouldn't mind reading it at the end of the day. In other words, intervention throughout the day, I personally would… [Laughs] My attitude would be, mind your own business, I'm doing something. I do think that sort of feedback, if I could read it off

at the end of each day, I would find that helpful, yes, but the constant interference is not the way I live" (P9)

Subtheme: WAM helps with decision making and personalisation

Furthermore, the participants described that WAMs could assist clinicians in making decisions about patients' management plans, which could be tailored to their specific goals:

"if patients who are wearing them are monitored, and especially if they're very high risk to lymphoedema, and then somebody who's medically trained can say…Look, we don't think you're moving enough. Maybe try this. If you can't do this, then try this….Give them good education on - or a physio and say…This is exactly what you need to do"(P3)

Subtheme: Risk stratification for intervention

WAMs could be used as a tool for risk stratification (i.e., scoring system), which could determine who needs intervention to prevent worsening of upper limb complications. The participants suggested that the scoring system should include the following: swelling/heaviness, stiffness, redness/hotness, pain/tenderness, activities of daily living, and upper limb activity as measured by WAMs. However, there were concerns that the scoring system should not replace in-person assessments and that it may not reflect real-time problems:

"I'm always a bit wary of scoring systems. You can have people who are classified as low risk for cancer, for example, based on a scoring system. That doesn't tell the whole story. I think technology is great, I think it's a good guideline as well, but then what about if someone - someone could fall through the crack. So I think it's a good idea, but I still think that shouldn't replace patients being able to see a doctor in person as well" (P9)

Theme 4: The implications of WAMs on behavioural change

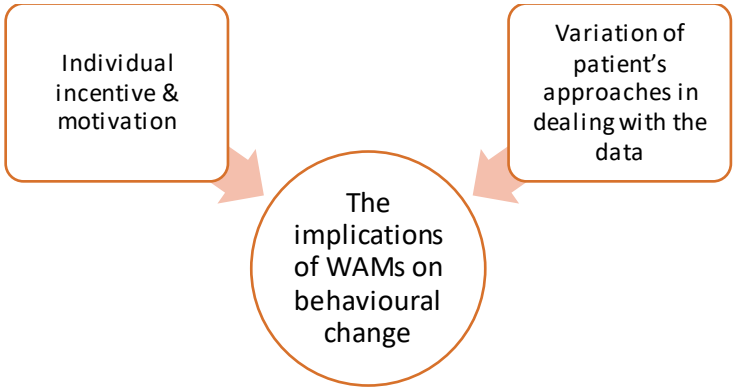


Figure 9-6 The implications of WAMs on behavioural change

Subtheme: Individual incentive and motivation

The majority of patients considered WAM as an important tool for motivating and promoting patients' engagement in physical activity, as well as for reinforcing positive behaviour. Certain patients, however, did not feel that they were personally motivated by wearing the WAMs; this could have been due to their inherent motivation to be as active as possible regardless or because they would prefer to listen to their own bodies:

> *"Not to me, because I obviously can tell, whether I can lift my arm or not… I was aware of when it started improving and getting better. As I say, I was doing the exercise I was given, and I could tell when I could do things" (P6)*

Subtheme: Variation of patient's approaches in dealing with the data

The participants described other potential impacts that WAMs could have on a patient's behaviour. The WAMs could improve their self-awareness regarding their activity levels and empower patients to assume responsibility for their care. Ultimately, it is the autonomy of individual patients to determine if they will increase their physical activity level in response to the WAM's data:

> *"It's up to people then, isn't it? You know, at the end of the day, if you're saying to somebody, 'You haven't had a lot of exercise, go for a walk,' and they decide to ignore you, well, that's fine" (P2)*

9.6 Discussion

This study explored patients' experiences when undergoing breast cancer treatments and their attitudes, experiences, and preferences about the usage of WAMs in healthcare settings. The key overarching themes explored in this study were breast cancer survivorship, features and impact of WAMs, user experience of WAM application and the implications of WAMs on behavioural change. The findings from this study are as follows: Firstly, the majority of patients described reduced upper limb and general mobility and some impairment in their physical and emotional well-being and day-to-day activities. They also highlighted the importance of early identification of complications, regular monitoring as well as patient education and awareness. Secondly, most patients generally found that WAMs were comfortable to wear but further improvement needs to be done to improve their usability. Thirdly, WAMs could provide real-time feedback and the intervention could be tailored to individual needs. Finally, WAMs could assist in behavioural change and provide an incentive to increase physical activity levels. The key messages are further elaborated below.

9.6.1 Breast cancer survivorship

The first theme discussed showed diverse experiences and coping mechanisms. Majority of the patients had treatment adverse effects such as arm swelling, reduced upper limb mobility, pain and stiffness which impact their daily activities as well as their employment. This was thoroughly explored in the systematic review and meta-analysis presented in chapter 2. The arm impairment experienced by breast cancer patients has a significant impact on their ability to do daily tasks such as zipping up a back zip, fastening a bra, reaching overhead, and lifting heavy objects. Approximately 34% of breast cancer patients experienced reduced upper body function following breast cancer treatment.[27] Factors that can influence patient's functional status are age, lower educational status, multiple comorbidities, lower income, pre-existing mobility restriction due to medical conditions including rheumatoid arthritis or shoulder pain and advanced stage of breast cancer.[705,706] Furthermore, the decline in functional status was more prominent in older cancer patients compared with younger cancer patients (43.6% versus 24.6%).[707]

Certain patients described the long-lasting emotional impact after going through extensive treatment for breast cancer. Thakur *et al*.,[708] demonstrated depression, anxiety, and stress in 27.8%, 31.5%, and 24.8% of cases respectively after a modified radical mastectomy.[708] Nevertheless, the psychological impact might differ depending on the specific type of breast surgery. Breast reconstruction surgery resulted in superior psychological outcomes compared with simple mastectomy alone, as it significantly reduced the incidence of depression and anxiety.[709-711] This is likely because individuals are able to regain a positive self-image through restoring chest symmetry and improving aesthetics, which enables them to better manage the progression of their disease.[711] Surviving breast cancer can lead to feelings of isolation and loneliness, particularly when the treatment took place during lockdown. They were unable to communicate their experiences with fellow patients, families and friends in-person or engage in their usual recreational activities as a result of the lockdown. Zhao *et al*., [712] showed that the feelings of isolation increased significantly during the pandemic. In a qualitative study conducted by Pini *et al.*,[713] enforced social restriction severely affected their connection to their loved ones and things that they enjoy doing. Their inability to participate in usual daily activities and leisure pursuits left them feeling extremely anxious, angry, bored, frustrated, depress and that they were going "stir crazy." These emotions could result in disagreements for those living together with friends or family members. Conversely, patients who resided alone had a lack of daily routine, resulting in emotions of seclusion.[713]

Some amount of psychosocial support is essential for the patients' well-being. Majority of the patients in the current study received great support from their partners, children, friends, and neighbours. Engaging in social interactions with friends and family following a diagnosis may lead to positive coping mechanisms as well as supplement emotional and practical support.[714] Nevertheless, certain breast cancer survivors reported that they did not wish to be a burden on their families, preferring to be the primary provider of care rather than the recipient.[715,716]

Early identification of complications is essential for managing long-term health in breast cancer survivorship.[717] The majority of patients emphasised the significance of consistent follow-ups and

monitoring to facilitate the early detection of complications and improve communication between patients and clinicians. WAMs may be used as a monitoring device for recognising possible complications early and could also motivate and empower patients to increase their physical activity levels. As previously discussed in chapter 3, physical activity after breast cancer diagnosis is associated with improved outcomes particularly in reduced breast cancer-specific and all-cause mortality,[718-720] highlighting the importance of a device that could potentially encourage patients to increase their levels of activity and prevent sedentary behaviour. The long-term survivorship and rehabilitation strategies could be improved further by a combination of clinician assessments and WAM which is tailored to individual needs.

In the current study, the patients also stressed the importance of education and awareness about what to expect and the potential complications that could arise from their breast cancer treatment. Some patients in the present study indicated their unawareness that lymphoedema could manifest many years post-treatment. Similarly, Khajoei *et al.*,[721] described that most of the breast cancer patients in their study were not provided with any information regarding the potential adverse effects of treatment, how to manage them, or where to seek assistance, which worsened their complications. Moreover, educating the patients on how to interpret the WAM data will guide their self-management. This information can be used to establish attainable goals, monitor progress, and modify exercise levels as necessary. It is also necessary to consider that wearable activity tracker devices may function inaccurately. Self-management is attainable with the requisite support from healthcare professionals when needed taking into account potential error from device measurements. Szeto *et al,*. recently developed the Wearable Activity Tracker Checklist for Healthcare (WATCH) guideline[722] for the implementation of WAMs in healthcare settings necessitating a comprehensive strategy including suitable technical support providing relevant data metrics and ensuring a positive user experience, alongside clinical support featuring appropriate intervention protocols to facilitate and motivate patients in their activity monitoring, as well as relevant patient educational materials. This will be elaborated upon in the subsequent sections.

9.6.2 Features and impact of WAMs

Most patients had a favourable attitude towards including wearable activity monitors into their rehabilitation process. Specific design criteria were recognised as essential for the effective implementation of a WAM. One of the major design issues that was flagged up was the straps. Despite the lightweight nature (16g) and silicone composition of the strap, a patient reported experiencing skin irritation and soreness when wearing it. A few patients proposed use of transparent straps as a suitable solution to complement the minimalistic design considering they are required to wear straps of different colours on each hand. A study conducted by Graeber *et al.*,[723] revealed that the AX6 wearable sensor, which was comparable to the one used in this study, was generally deemed comfortable. However, for some patients, it did not fit well, either being excessively tight or excessively loose. In addition, some patients experienced skin irritation due to sweating induced by the strap.[723] A further study assessing the acceptability of AX3 WAMs in individuals with Parkinson's disease emphasised that because the strap was too big, it was difficult for the sensor to stay in the upright position and needed occasional readjustment.[724] The strap can also cause irritation after prolonged wear.[724]

Another concern related to wearability was how "chunky" and noticeable the sensors were. This finding aligns with another study that reported the AX6 device to be bulky in size.[723] The majority of patients suggested that the design should be minimalistic, lightweight, compact, and inconspicuous, while also fitting the wearer comfortably and not causing any obstructions. Additionally, a patient in the current study proposed that the device would be benefited by the incorporation of a clockface. A participant in a study conducted by Fisher *et al.,*[724] reported that they often checked the wearable device to find out the time, mistakenly perceiving it as a wristwatch.

Understandably, certain patients mentioned that wearing the WAMs made them feel uneasy while they were out in public since they attracted attention, and they would rather keep their medical conditions private. The WAM also became a reminder of their breast cancer diagnosis. Similarly, a patient from another study stated that they are "happy to wear (in public) but would not like members of public

questioning what it is for as illness is private".[724] Moreover, some patients reported that they couldn't wear their watch or had to wear their watch differently due to the WAMs on both wrists. A comparable result was reported in another study, in which patients avoided wearing their personal watches while wearing their WAMs.[723]

9.6.3 User experience of WAM application

In order to achieve full integration into clinical settings, it is imperative that the data obtained by wearable devices is easily accessible, user-friendly, and comprehensible.[725,726] There were different ideas on the most effective way to represent the data, whether it should be in the form of graphs or numerical values. One patient described infographic like a circle that gradually fills in as you increase your physical activity. Nevertheless, it is important to display the data in various formats since individuals have diverse interpretations of data and figures, thus enabling patients to make their own choices. The presentation of the data should optimise the clinician's ability to make clinical decisions and enable the patient to take a more active role in self-care. Therefore, the way in which raw data is analysed and displayed is crucial for the effectiveness of these devices in this particular setting. From a clinician's perspective, the visualisation of physical data is not meaningful unless one understands the context, including the patient's levels of pain and stiffness, as well as how the patient's progress compares to the general population. Nonetheless, clinicians could see the potential value in the information provided by wearable devices in selected group of patients particularly those who require intervention that will improve their physical activity.[727] Importantly, the WAMs could be used within the enhanced recovery framework to facilitate early hospital discharge, enable home monitoring after discharge and predict patients who need more care, thereby improving patient outcomes.

Most patients in this study deemed it crucial to have the ability to access real-time data, enabling them to make well-informed decisions regarding their recovery process and identify opportunities for improvement. Currently, the WAM utilised in this thesis lack interfacing capability and so patients cannot interact with the system. Clearly, certain patients may not experience any apparent advantage

from wearing WAMs and hence may not consistently wear them. Nonetheless, some patients described the Hawthorne effect, where they were motivated to do exercises as prescribed by healthcare professionals because they knew they were being tracked. Similarly, systematic reviews by Larsen *et al.,*[728] and Bravata *et al.,*[729] have described the same Hawthorne effect in both participant and control groups, where individuals may improve their level of physical activity as a result of participating in the study.

Some patients in the current study suggested using WAM as an educational tool by sending messages to encourage activities during the peri-operative period or providing information through push notifications in the form of a traffic light system. A similar protocol can be adopted for future studies, where a feasibility study conducted by Fusari *et al*.,[68] used an apple watch to monitor the level of upper limb activity after stroke diagnosis. Motivating messages were sent to the patients, along with face-to-face sessions for self-management training. This study provided evidence that the wearable device is both functional and well-received for arm rehabilitation following stroke.[68] Moreover, a systematic review and meta-analysis by Brickwood *et al.,*[730] demonstrated that there is a positive overall effect when using wearable trackers alone as an interventional tool or when WAM is combined with other behavioural change techniques (BCTs) such as telephone consultation or group-based education. Behavioural-change theories should be implemented in future studies to improve the effectiveness of WAMs in the perioperative setting and explain why the observed effects occur. Goal setting, prompts and cues, rewards, and social support such as Strava app are the most prevalent strategies found in commercially available wearables to modify behaviour.[731,732] These strategies align with Oinas-Kokkunen's concept of behaviour change, which aims to shape, modify, or strengthen behaviours, or compliance without resorting to coercion or deception.[733] Patients for example can use daily goal setting to form behavioural change by doing upper limb exercise for 1 hour a day if they think it is going to be helpful for their recovery. Advancements in artificial intelligence enable the use of acquired data to further tailor activities and associated health goals based on parameters such as age, sex, and heart rate.[734] Nonetheless, potential negative impacts linked to data management raise concerns over privacy, data security, and ownership.[734,735] As a result, it is imperative to further investigate the ethical, legal,

and social implications of data ownership and access to ensure that personal data remains confidential and is not sold to third-party entities without specific consent.[734,735]

Furthermore, WAM could assist clinicians in formulating rehabilitation strategies tailored to individual needs. They also believed that the WAMs could be used as an early indicator (e.g., using a scoring system) to determine if certain patients needed more support. However, there was a concern about exclusive reliance on technology and that wearable technology should not replace in-person evaluation. It is important to note that wearable technology should complement rather than replacing healthcare providers. Prior study suggested that objective monitoring devices may lead to other forms of distrust if the patient's account isn't backed up by the corresponding "objective" data.[736] Doctors may dispute the validity of the patient's account of their symptoms which may negatively impact patient's management plan.[580] Additionally, it is imperative that the use of wearable technology promotes equitable access to care rather than exacerbates existing inequalities. Therefore, measures must be taken to prevent the gap from growing between those who have access to digital tools and those who do not.

To address digital exclusion in my PhD study, I used wearable sensors that are user-friendly. The wearable sensors were calibrated and ready to be worn by the patients upon recruitment, eliminating any need for patient setup involvement. Patients of any age from different ethnic backgrounds undergoing breast +/- axillary surgery were recruited to ensure diversity in the breast cancer population. As discussed in this chapter, one-to-one semi-structured interviews were conducted on patients with an age range of 28 to 78 years old in order to design wearable devices for future studies based on their needs, challenges, and preferences, in particular, how data are presented to the patients and how personalised feedback is given so they can act upon this function and embrace the use of WAMs as part of their rehabilitation programme. While the technology adopted in WAMs is similar to that seen in popular fitness devices like Fitbit and AppleWatch, the objective of this study is more intricate and not limited to merely counting steps, but to identify complications, monitor and improve recovery postoperatively. Hence, it is imperative to track and monitor preoperative activity in order to establish initial baseline, delineate behavioural trends, and detect any changes in behaviour after the operation.

This will allow for the introduction of appropriate lifestyle interventions, if needed. It is also critical to ensure that the patient's data is accurate in order to help them make self-directed decisions based on their level of activity. The cost of the wearable sensors used in this study was £129 per sensor. Before implementing this device in clinical practice, it is crucial to do a cost-utility analysis in order to determine the economic value of this intervention.

9.6.4 The implications of WAMs on behavioural change

In the current study, WAMs were considered to be an effective tool for encouraging breast cancer patients and facilitating behaviour change by improving their level of upper limb activity. A systematic review and meta-analysis conducted by Singh *et al.* revealed that wearable activity trackers significantly improved moderate-intensity physical activity, moderate-to-vigorous-intensity physical activity, total physical activity, daily step count, quality of life, aerobic fitness, physical function, and decreased fatigue in comparison to standard care.[341] This is crucial because physical activity has the potential to improve patient outcomes. In the context of upper limb activity, Bruce *et al.* have demonstrated that an early structured exercise programme of the upper limb can reduce the risk of developing upper limb complications in at-risk patients compared to usual care.[4] One of the themes described by Nguyen *et al.,*[67] when conducting a qualitative evaluation of wearable trackers among post-menopausal breast cancer survivors was that the trackers made them more aware of their level of physical activity and therefore prompt them to increase activity.[67] Certain patients in the current study identified that having goal settings inspires them to work towards achieving those goals. Similarly, Nguyen *et al.,*[67] commented that "participants reported feeling inspired and satisfied knowing that they achieved the targeted number of steps for a day. They also felt accountable and motivated to put in additional effort when they were close to achieving their target'.[67] In comparison to conventional (non-individualised) goals, interventions that incorporate individualised physical activity objectives have been demonstrated to be more effective in promoting physical activity.[737]

Wearables can empower and emancipate patients to take greater responsibility of their own care. By promoting patient empowerment in managing their own health, positive attitudes can be cultivated towards their health and overall well-being, which can subsequently improve their quality of life. As previously mentioned, interventions that involve extensive implementation of behaviour change techniques (e.g., supervised exercise programme, peer support) are more effective at increasing physical activity than those that involve minimal use of behaviour change techniques.[738] Interestingly, certain patients in the current study did not believe that real-time feedback and monitoring will affect their behaviour. The effectiveness of technology in promoting behavioural change is not only determined by the technology itself. Instead, it relies on the individual's existing behaviour (i.e. active or inactive), capacity and motivation to employ effective techniques that facilitate behaviour change. In spite of this, WAMs can continue to be employed as a means of delivering BCT that is customised to the unique requirements of each patient. It is ultimately the patient's decision to comply with the behavioural advice and recommendations.[730] It is also important to note that the science of behavioural changes is not exclusively related to changes in the way patients act or choose to complete the exercise, it also encompasses input and feedback from the clinicians. This study has not taken this aspect of the implementation of WAMs into account.[739]

Strengths and limitations

Strengths

The primary strength of this study is that it directly seeks the perspectives of breast cancer patients who have lived through breast cancer treatment and have used WAMs to monitor their upper limb activities. To my knowledge, this is the first study to evaluate the in-depth perspectives on wearable technology in this setting. The interview guide was co-designed with members of the PPIE group to examine the topic with sensitivity. The semi-structured interview method facilitates a more profound study by exploring the rationale behind opinions, in contrast to quantitative survey data. The study sample was heterogeneous, consisting of individuals who underwent various types of breast surgeries, with ages spanning from 28 to 78 years. Participants were given the opportunity to confidentially articulate their

perspectives to a researcher independent of their regular care team to promote disclosure. The data analysis was improved through discussion with a second coder and qualitative research experts.

Limitations

Firstly, this was a single-centre study, therefore the study population may not be an accurate representation of the breast cancer survivor population. There may also be selection bias for engaged patients, as patients who agreed to participate in the interviews were more likely to engage more with their illness and related topics, as well as more likely to be digitally and health literate than average patients. The interviews were performed solely with patients without soliciting opinions from healthcare professionals such as surgeons, ward nurses, breast specialist nurses, and physiotherapists. The input from healthcare professionals is crucial, as they play a role in the patient's journey and form the team responsible for developing and carrying out post-operative management plans for patients. The data presented to the patients were not in real-time, resulting in their perspectives being based on retrospective analysis of the data post-recovery. The interviews were stopped when data saturation was reached. Nevertheless, it could be argued that some new findings will always be made.

Table 9-3 Recommendations for future ideal WAMs

Recommendations	
Design	
Lightweight	Unobtrusive
Non-irritable/allergic material	Display interface
Colour options	Minimalist
Function	
Real-time feedback	Interactive function
Scoring system	Options of multiple data types
Personalised goals	Additional observations e.g. heart rate

9.7 Clinical Implications

This study provides encouraging data advocating the further development of WAMs to be used in peri-operative setting among breast cancer survivors. WAMs are perceived as a valuable tool to promote physical activity and facilitate self-directed rehabilitation, potentially leading to better patient outcome. WAMs could be integrated with BCTs such as incorporating virtual rehabilitation classes and support group to further improve the rehabilitation strategies. For future work, a multi-centre study should be conducted with feedback from healthcare professionals, where the data are presented in real time. Furthermore, it is crucial to investigate the specific aspects of design and interface that are more acceptable by the end users, particularly the materials used and the manner in which data is presented. Collaborating with the engineers and industry partners will be beneficial in designing WAMs that are specifically tailored for this patient cohort. The feedback scoring system and the interactive feature should be evaluated in future research to determine the most effective approach. Further work also needs to be done to refine the implementation process and the integration of WAMs into available electronic health records and routine NHS workflow to facilitate seamless communication and collaboration between healthcare providers and patients. Finally, it is crucial to examine the economic ramifications of WAMs. This is significant because there are costs associated with the technology, as well as possible opportunities for cost reduction and improved efficiency through its implementation. Potential developments to the existing WAMs and future directions for research implementing tri-axial accelerometer based wearable platforms are discussed in the final chapter.

9.8 Reflection

In this final section of this chapter, I would like to provide some personal reflections on conducting semi-structured interviews and the influence of this qualitative research on my clinical practice. I am a female Southeast Asian medical doctor with 12 years of experience working in the NHS. Throughout my PhD, I continued to work clinically and have since returned to full time clinical practice. This chapter marked a new beginning in the development of personal reflexivity in qualitative research, as it was my first time conducting semi-structured interviews. As a medical doctor, I am very familiar with

quantitative research. I found it refreshing to explore the realm of qualitative research, which was relatively new to me. I encountered a significant learning curve while trying to fully understand the theory and procedures that underlie qualitative research, and I welcomed this new learning experience.

Initially, I struggled to detach my viewpoint as a healthcare professional, since my role as doctor may have influenced my interview technique, whereby I do a focused medical history to devise an intervention and medical plan. I believed that my medical background may have positioned me as an "outsider" to the patients, possibly causing them to be hesitant to share their thoughts and feelings. It was crucial for me to consciously refrain from allowing my medical experiences and thoughts to influence the conversation during the interviews or my interpretation of the transcripts. Additionally, I needed to maintain curiosity towards all ideas and suggestions proposed by the patients and focus on open-ended questions with unbiased prompts. I attempted to minimise my medical background and emphasised my position as a PhD student conducting research to assist breast cancer patients throughout their surgical recovery. I assured them that our discussion will not influence the care they receive from their medical team. Furthermore, I have diligently worked to avoid imposing my clinical conceptualisation on the coding and subsequent theme development; this has necessitated revisiting original transcripts and codes to ensure the language used accurately reflects that of the patients. It was also refreshing to have meaningful discussions with a second coder who has a different specialty background compared to mine. The feedback from qualitative research experts helped to improve my data analysis as a novice in qualitative research.

While I was excited about what this research might uncover, I was also concerned about how the patients would view me as an interviewer and that they might not engage in the conversation. However, I soon discovered that patients were eager and willing to share their thoughts and experiences, with some of them feeling motivated to help other breast cancer patients in the future and hoping that their contributions to this study would improve the postoperative experience for the others.

As a result of the COVID-19 pandemic, the interviews were performed by the telephone. The principal difficulty in executing a semi-structured interview by telephone is the absence of visual cues, preventing the assessment of patients' emotions, the establishment of rapport, and the comprehensive understanding of their context, potentially resulting in misinterpretations of responses. Technical issues, such as poor network coverage, may arise and could disrupt the interview process. Due to the lack of non-verbal indicators and challenges in interpreting visual emotional expressions, I made a deliberate effort to offer verbal feedback or utilise vocalisations and clarifications to demonstrate my attentiveness. I recommended that the patient sit in a quiet space to minimise disturbances. A few potential advantages of a telephone interview are that it may reduce bias and stereotyping towards me, the interviewer while also minimising distractions for the interviewees. Several patients have indicated that telephone interviews are very convenient and less intrusive, as they prevent the need for travel and hence offer better scheduling flexibility.

It was an honour to engage in conversation with breast cancer survivors and gain a deeper understanding of their perspectives and life experiences than I have at other times when I interact with patients in clinical settings. I am now more cognisant of patients' experiences, particularly about the influence of my attitudes, behaviours, actions, and communication on patients' feelings. Understanding perceptions of breast cancer patients was also beneficial for myself as individual, since learning about breast cancer and the impact on their lives as well as how wearable technology can support their recovery is linked to lessons about cancer survivorship. Following the presentation of the findings of my thesis at national and international conferences, I received positive feedback and there was considerable interest for the translation and implementation of the wearable technology into clinical practice. I have recognised the potential of this doctoral study for improving breast cancer management, and I am eager to observe the practical implications it may have for postoperative rehabilitation following breast surgery.

10 CONCLUSIONS AND FUTURE WORK

The novelty of this body of work was fivefold. For the first time, WAMs were utilised to objectively assess upper limb activity in patients undergoing breast and axillary surgery, continuously and unobtrusively during acute postoperative period and beyond six months post-surgery. Secondly, patients having DIEP demonstrated the lowest upper limb activity levels in the short-term postoperative period compared with IBR and Mx; nevertheless, the long-term upper limb activity levels returned to baseline levels for all the procedures assessed. Thirdly, DIEP was found to be an independent predictor of upper limb activity in the first 2 weeks postoperatively. Fourthly, preoperative activity level and the short-term upper limb activity are significant predictors of long-term upper limb activity. Finally, semi-structured interviews revealed that breast cancer survivors largely supported the use of WAMs to assess upper limb activity, which could facilitate the development of a personalised rehabilitation programme. The series of investigations presented throughout the thesis provided the evidence in a systematic fashion. Due to the small sample size recruited for the studies, the analyses could potentially lead to a false negative result (type II error). Moreover, inadequate sample sizes increase the susceptibility of results to random error and potential bias, making conclusions less reliable. The single centre recruitment may also restrict the external validity of the findings, as they may not accurately represent the larger population. Therefore, the results should be interpreted with caution. In future studies, the compared surgical groups should be recruited based on appropriately powered sample size. Planned recruitment of patients undergoing adjuvant and neoadjuvant treatments particularly radiotherapy should be conducted given the established impact of radiotherapy on upper limb morbidities. Future analyses should also consider other factors such as patient motivation, adherence to postoperative exercise, and psychological factors (e.g fear of movement, behavioural change) that could influence upper limb activity levels.

10.1 Impact of Breast Cancer Treatment on Upper Limb Morbidity

First, a systematic review and meta-analysis was undertaken to determine the impact of breast cancer treatment on upper limb dysfunction. It is the first systematic review and meta-analysis of the six most common validated or objective outcome measures where possible in order to quantify lymphoedema, range of motion, strength, upper limb function, pain and HRQoL according to different time points (<12 months, 12-24 months, >24 months). A total of 85 studies were included. The findings of the review demonstrated that the prevalence of lymphoedema following ALND was higher than previously estimated by Di Sipio et al.,[28] (>24 months, 23,6% versus 18.6%). Compared with SLNB, patients who underwent ALND had higher rates of lymphoedema (difference in prevalence of 13.7%, $p<0.005$), pain (difference in prevalence of 24.2%, $p<0.005$), decreased strength (prevalence of SLNB: 15.2% versus prevalence of ALND: 30.9%), and range of motion (prevalence of SLNB: 17.1% versus prevalence of ALND: 29.8%). Additionally, there was insufficient objective evidence with regards to the impact of breast reconstruction on upper limb function. This review also highlighted the lack of standardisation in the assessment of upper limb morbidities, which complicates the comparison of various treatments and studies. Consequently, it is essential to establish a standardised, feasible, quantitative approach to assess upper limb morbidity that is clinically applicable to breast cancer survivors.

10.2 Measurement of Upper Limb Morbidity Post-Breast Cancer Treatment

Chapter 3 summarised the pathophysiology of upper limb dysfunction, the current assessment tools for measuring upper limb morbidities post-breast cancer surgery and the available wearable technology solutions that could be used as assessment tools for monitoring upper limb function. To follow up on this, chapter 5 investigated the feasibility of using WAMs to monitor upper limb activity following breast and axillary surgery.

10.3 The Feasibility of Using Wearable Activity Monitors for Objective Assessment of Upper Limb Activity Following Breast and Axillary Surgery

WAMs were initially trialled in a cohort of 39 breast cancer patients who were recovering from their breast and axillary surgery and 10 healthy participants in their home environment. To the best of my knowledge, this is the first feasibility study to monitor upper limb activities of patients undergoing breast surgery, continuously and unobtrusively, with WAMs during the whole peri-operative period, including their time at home after being discharged. The results indicated a decrease in upper limb activity from 100% to 45.3% postoperatively, with a gradual recovery in upper limb activity (as a percentage of preoperative levels), most notably between postoperative days 1 and 2 (mean, 45.3% versus 56%, $p<0.05$). Upper limb activity was significantly greater on the untreated side compared to the surgically treated side after week 1 (mean, 75.8% vs. 62.3%; $p<0.0005$) and week 2 (mean, 91.6% vs. 77.4%; $p<0.005$). Construct validity has been demonstrated because the trend of postoperative upper limb activity is as expected (i.e., postoperative decline followed by a gradual return to baseline). In addition, the upper limb activity data can differentiate between various surgical procedures, providing more support for this claim. Concurrent validity has been demonstrated through a significant negative moderate correlation between upper limb activity and DASH questionnaires ($R = -0.506$; $p < 0.05$). This study demonstrated the feasibility and validity of WAMs to objectively measure postoperative upper limb activity after breast surgery.

10.4 The use of Wearable Activity Monitors in Acute Postoperative Setting – Comparison between Axillary Lymph Node Dissection and Sentinel Lymph Node Biopsy

To build on chapter 5, a larger cohort of patients (n=56) undergoing ALND and SLNB were recruited to further validate the use of WAMs in acute postoperative setting with a specific hypothesis. The results demonstrated that patients who underwent ALND experienced significantly worse upper limb activity compared with those who underwent SLNB in week 2 (median 66.4% versus 72.7%, $p=0.015$). Subgroup analysis revealed significantly lower upper limb activity in Mx-ALND versus Mx-SLNB

(median 70.5% versus 90.3%, p=0.015) in week 2. The negative effects on the upper limb caused by SLNB were still considerable and lasted longer than anticipated up to 2 weeks following surgery. This discovery is significant as it suggests the potential for extended morbidity even in de-escalated surgical procedures. It is essential to thoroughly investigate adjunct methods (e.g axillary reverse mapping), non-invasive alternatives (e.g ultrasound), or consider the possibility of safely omitting nodal mapping altogether to reduce the incidence of upper limb complications successfully and safely.

10.5 The use of Wearable Activity Monitors in Complex Surgery – Comparison between Simple Mastectomy, Deep Inferior Epigastric Perforator and Implant-Based Reconstruction

Chapter 6 focused on the application of WAMs in a complex surgical setting (n=48) comparing the 2 most common breast reconstruction procedures (DIEP and IBR) and simple mastectomy in an extended follow up (>6 months). The collection of prospective, longitudinal post-operative data in this patient cohort using WAMs was novel, providing unique insight into the upper limb recovery process. The significant finding from this study was that patients undergoing DIEP procedures experienced a significantly greater reduction of gross upper limb activity as a percentage of pre-operative activity compared with Mx and IBR patients across week 1 (Median: 40.1% versus 62.1% versus 61.8%; p<0.001) and week 2 (Median: 60.1% versus 77% versus 83.9%; p<0.001). In the long-term follow-up, the average activity had reached or exceeded their baseline levels for all operative procedures, Mx = 113.9%, IBR = 98%, and DIEP = 102.9%. Multivariate analysis showed that DIEP surgery was an independent factor that influence upper limb activity in week 1 (F=4.796, p=0.043) and 2 (F=7.306, p=0.015) whereas adjuvant immunotherapy (F=11.153, p=0.004) was an independent predictor for upper limb activity at greater than 6 months postoperatively. The methodology was also able to identify patients who were non-adherent to expected trajectories in the setting of post-operative complications. This study provides significant insights into a novel objective assessment of upper limb activity that have been underreported in the literature following breast reconstruction.

10.6 Short-term Upper Limb Activity as Predictor of Long-term Upper Limb Functional Outcome as measured by WAMs

Application of WAMs proved useful in a prospective long-term follow-up study (median: 21 months) of patients undergoing breast and axillary surgery (n=39). The results suggest that the upper limb activity two weeks after surgery ($\beta=0.552, p<0.001$) and preoperative activity level ($\beta=-0.368, p=0.004$) were independent predictors of long-term upper limb activity. This information highlights the importance of quantifying preoperative activity and early upper limb activity which can be used to identify individuals who require additional rehabilitation support. Furthermore, the findings indicated that merely 59% of patients were able to regain their initial activity levels in the long run. WAMs may complement the current PROMs as predictive tools that can help identify patients in need of extra support in their recovery and may promote self-directed rehabilitation.

10.7 The use of Wearable Activity Monitors in Breast Cancer Patients: Patient Perspectives

Finally, a qualitative study was conducted, utilising semi-structured feedback interviews, to get insight into the perceptions of breast cancer patients regarding WAMs and wearable technologies. The study demonstrated that there was a general acceptance of this technology as an objective tool to monitor upper limb activity following breast surgery. The findings of this qualitative study will inform the design of future systems, further improving usability and the implementation of WAMs in healthcare settings, as well as the potential for developing a personalised rehabilitation programme.

10.8 Future Work

These studies make important progress in tackling clinical challenges related to subjective evaluations of upper limb morbidity and optimising postoperative recovery by assessing and utilising WAMs to objectively monitor upper limb activity in the immediate postoperative period and in the long-term. Even though it has its own limitations, as discussed in chapter 3, it has been demonstrated that WAMs are capable of measuring and differentiate upper limb activity levels following different types of breast

and axillary surgeries. The objective data on preoperative activity and short-term upper limb activity have been demonstrated to be predictors of long-term upper limb activity following surgery. The studies illustrated the benefits of WAMs in predicting patients who require additional care pre- and post-surgery and facilitating in-hospital and post-discharge monitoring. Nevertheless, further research is required before the clinical implementation of this relatively new technology in the NHS.

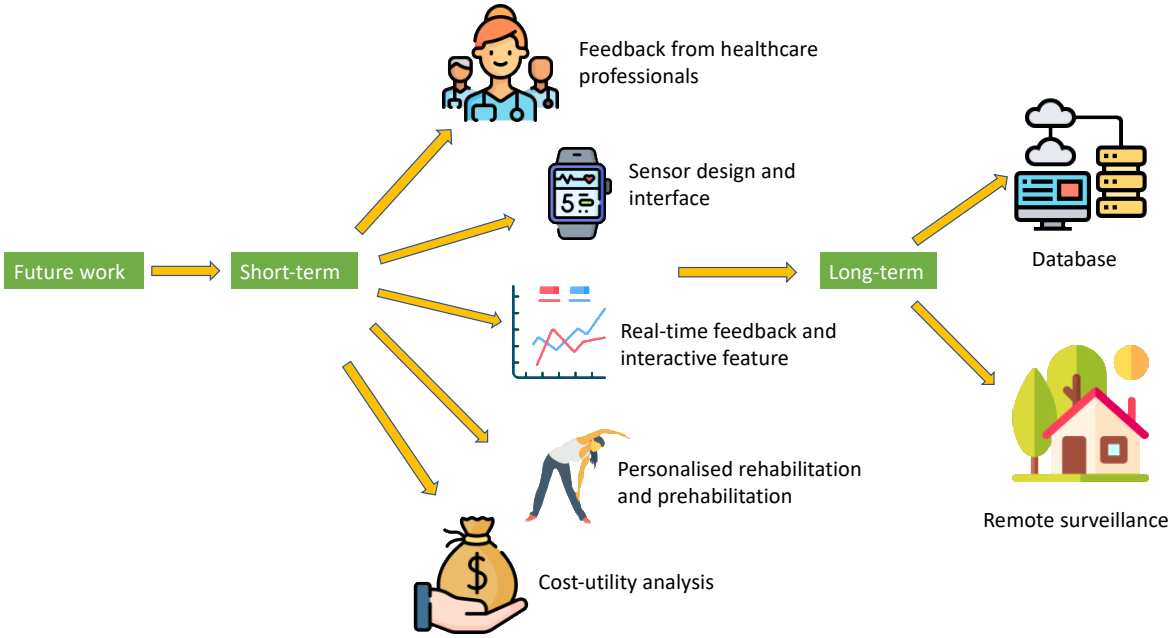


Figure 10-1 Future work to investigate the application of WAMs following breast and axillary surgery in the short-term and long-term. WAM, wearable activity monitor.

10.8.1 Further Research

10.8.1.1 *Short-term*

Following feedback from breast cancer patients in chapter 9, it is necessary to make modifications in order to meet specific requirements expected by the patients. Furthermore, input from medical professionals is essential for conducting more in-depth assessments of how surgeons and the healthcare team plan to incorporate WAMs into patient monitoring, as a predictive tool, and the potential to develop self-directed rehabilitation within the ERAS programme in the future studies. This includes determining the most effective ways to utilise WAMs in different settings, such as the hospital or home follow-up.

It is vital to make improvements to the hardware to ensure the accuracy and reliability of the WAMs. There are evidently many options for improving the technical capabilities of the tri-axial accelerometers used in this thesis, some of which have been discussed. For example, the inclusion of machine learning models to differentiate between functional (i.e., task-specific arm movements) and non-functional arm movements (e.g., arm swing while walking). This would help reduce the overestimation of upper limb activities.[257] Recently, several other wearable sensors have emerged, such as Kirigami-based sensors that have been recently developed,[353] or IMU sensors that have been improved or modified to improve the detection of upper limb movements. These advancements present potential avenues for additional investigation in future research.

In addition to developing WAM as an outcome and predictive tool, the ultimate aim is to develop a tool that could be used to monitor and predict outcomes that could also be incorporated as an adjunct tool for rehabilitation programmes, as discussed in chapter 9. Further improvement should also include real-time data feedback. This feedback can be accessed directly on the device or potentially viewed on a computer by clinicians or a portable tablet. Engaging in collaboration with engineers in the department or industry partners would facilitate the integration of sleek designs and data interfaces that are similar to those already present in consumer goods like AppleWatch and FitBit. After completing the design and testing of the new device, the next phase would involve initiating a pilot study to assess the usability of this new sensor. This will guarantee that the WAM is operating according to the appropriate standard, that patients fully understand the data presented by the WAM, and that any technical challenges can be completely resolved. This new device can then be tested in a large cohort of breast cancer patients in an appropriately powered study on a more frequent or continuous basis following surgery in order to identify the recovery plateau of different breast surgical procedures.

As well as providing an objective tool to assess and monitor patients, wearables have also demonstrated the potential to positively influence behaviour, improve patient engagement with treatment as well as reduce anxiety and worry.[740] The feedback scoring system and the interactive feature (e.g. traffic light system, vibration, visual feedback or motivational messages) should be further investigated to identify

the most optimal system for empowering and encouraging positive behaviour. Wearable systems have specific goals as an intervention, specifically to improve the effectiveness and frequency of self-directed treatment by providing patients with feedback and a sense of self-empowerment and responsibility. An interactive feedback system called OnTrack Rehab, incorporated into smartwatches, is currently being investigated in a feasibility study by another PhD student from my research group to help support postoperative upper limb rehabilitation of breast cancer patients undergoing axillary surgery. Another technical hurdle involves the integration of WAMs into electronic health records and the regular workflow in the NHS pathway. The successful integration of this device into clinical care requires the collaboration of several stakeholders, such as clinicians, software designers, industrial partners, IT department, and the NHS management. Subsequently, an RCT could be conducted, consisting of two groups. One group would receive a structured exercise programme along with WAMs that could monitor activity levels, offer motivational feedback, and set personalised goals. The other group would receive standard clinical care and WAMs that only monitors physical activity. After the completion of this study, a power calculation could be performed to determine the necessary power for a large multi-centre RCT.

In addition, a prior study demonstrated that breast cancer patients who are active prior to their surgery have a faster physical recovery as reported by the patients 3 weeks post breast cancer surgery.[631] Prehabilitation also known as preventative rehabilitation is relatively new within the breast cancer surgery sphere. According to MacMillan Cancer Support, prehabilitation assists individuals with cancer in preparing for treatment, incorporating areas such as physical activity, nutrition, emotional well-being, alcohol reduction, and smoking cessation.[741] In recent years, an increasing number of studies have been conducted to examine the practicality of prehabilitation intervention in this specific group of patients.[742] In order to provide comprehensive care for individuals with breast cancer prior to treatment, it is important to include upper limb assessment and therapy as part of prehabilitation where WAMs could be adopted, as upper limb dysfunction is a common consequence of treatment. Future randomised controlled trials ought to investigate a multimodal prehabilitation programme that meets the physical,

emotional, social, spiritual, and informational requirements of individuals diagnosed with breast cancer at all stages of the disease.

The adoption of healthcare technology is predominantly dependent upon their cost. To accurately assess the economic value of a technology or intervention on a patient, it is necessary to do a cost-utility analysis. Quality-adjusted life years (QALYs) are commonly used to quantify this. QALYs are determined by multiplying the change that occurs in quality of life by the number of years during which that quality of life will be experienced. The NHS employs a threshold range of £20000 to £30000 per QALY for the implementation of standard technology appraisals.[743] If the treatment meets or falls below the specified limit, it will typically be approved. In general, those that surpass it will be rejected. However, it is crucial to acknowledge that the threshold is not a fixed point, and the NHS has occasionally authorised treatments that exceed the threshold.[743] Hence, it is imperative to do a health economic analysis in order to ascertain the cost-effectiveness of incorporating this wearable technology into clinical practice.

10.8.1.2 Long-term

Previous study using the UK Biobank activity data of 96000 individuals have shown that engaging in any form of physical activity is beneficial for one's health, but engaging in more intense activity offers even larger advantages.[744] Equivalent to the UK Biobank data, a comprehensive database of physical activity might be established, encompassing detailed, anonymised health and genetic data from numerous breast cancer survivors across different age groups. This publicly accessible database has the potential to be utilised by researchers globally and make a significant contribution to the progress of modern medicine and treatment. It can facilitate scientific breakthroughs aimed at improving the survival rates and quality of life of individuals who have overcome breast cancer.

Furthermore, the potential clinical value of using WAMs is not simply derived from the improvement of patient outcomes, but also from the possibility of reducing resource demand during postoperative

surveillance with appropriate medico social support. WAMs have the potential to revolutionise patient management by identifying, preventing, or minimising post-surgical complications and by transferring suitable care services from the hospital to community settings without compromising patient safety in line with the NHS Long-Term Care plan.[272] Conducting continuous assessments via remote surveillance could provide a more economical approach to triaging and determining the necessity of specialist appointments. This is expected to improve the accessibility of clinic appointments for urgent situations on short notice, and potentially decrease the number of visits to Accident & Emergency departments.

10.9 Concluding Remarks

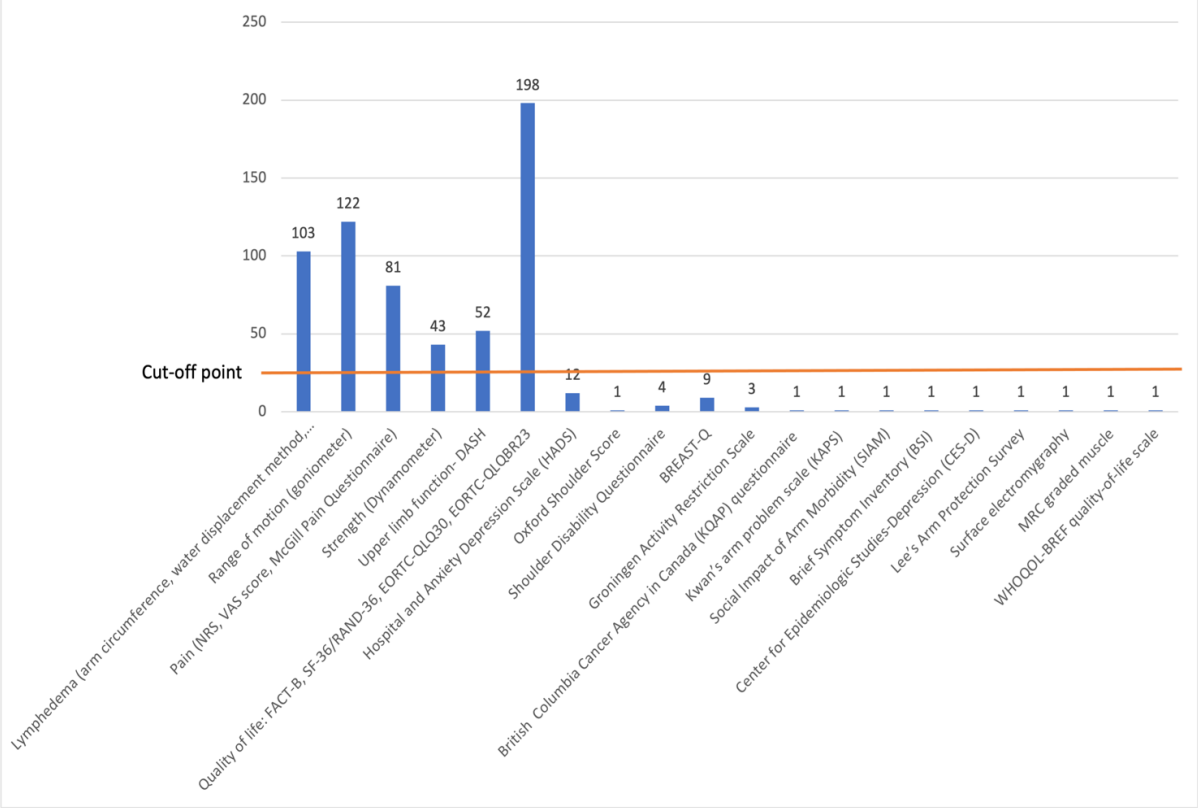
This thesis has demonstrated the potential use of WAM as an objective tool to measure upper limb activity following breast cancer surgery. The meta-analysis discussed in chapter 2 illustrated that the treatment of breast cancer may result in upper limb morbidities, including pain, lymphoedema, reduced range of motion, and reduced strength, all of which have a detrimental effect on HRQoL. Upper limb activity could be measured as a surrogate marker of these upper limb morbidities. Overall, WAMs have the potential to distinguish the upper limb activity levels between patients and healthy individuals, measure the progress of upper limb activity after various types of breast cancer and reconstructive breast surgery, and identify patients who need further support based on their activity levels. Utilising this technology may improve communication between patients and clinicians, empowering patients to actively participate in their healthcare team and play a crucial role in their own recovery by following a personalised rehabilitation programme. Although further advances are required in wearable technology research both generally and within the breast surgery setting, the utilisation of such technology adjuncts is a key avenue for exploration, especially given the significant relationship between physical activities and improved surgical outcomes.

11 Appendices

Appendix 1. Search keywords

Search	Keywords
Breast cancer	breast adj3 cancer* OR breast adj3 carcinoma* OR breast adj3 tumo?r* OR mamma* adj3 carcinoma* OR mamma* adj3 neoplasm* OR breast adj3 neoplasm* OR mamma* adj3 cancer* OR mamma* adj3 tumo?r* OR (subject heading)
Upper limb	upper limb* OR upper bod* OR (shoulder* or arm* or underarm* or elbow* or hand* or wrist*) OR upper extremit* OR (subject heading)
Function	(joint characteristics and functions) OR (movement (physiology)) OR (move* or function* or motion* or rotat* or strength* or disabilit* or impair* or dysfunction*) OR limit* OR (subject heading)
Surgery	surger* OR operate or operation* OR mastectom* OR lumpectom* OR reconstruct* OR (wide local excision* or wide excision* or WLE) OR breast resection* OR breast amput* OR (subject heading)
Axilla	(axilla* adj3 dissect*) OR axilla* OR (axilla* adj3 treat*) OR (axilla* adj3 clear*) OR (axilla* adj3 excis*) OR (underarm* or under arm* or armpit*) OR (lymph nod* adj3 excis*) OR (lymph nod* adj3 clear*) OR (lymph nod* adj3 resect*) OR (lymph nod* adj3 dissect*) OR (lymph nod* adj3 remov*) OR lymph nod* biops* OR (subject heading)
Radiotherapy	radiotherap* OR (external beam and (radiation or radiotherapy or irradiation)) OR (three dimensional and (radiation or radiotherapy or irradiation)) OR (3d and (radiation or radiotherapy or irradiation)) OR (three dimensional conformal radiation therapy) OR (whole breast and (radiation or radiotherapy or irradiation)) OR (cancer adjuvant therapy) OR (adjuvant chemoradiotherapy) OR (subject heading)

Appendix 2. Six outcomes extracted based on the most common findings from reviewed studies



Outcomes measured in the literature. The six most-commonly reported outcomes were extracted. Cut-off point refers to >25 studies. Most commonly reported outcomes were lymphoedema, range of motion, pain, strength, upper limb function, and quality of life. Y-axis represents the number of studies with specific outcomes and x-axis represents the outcome reporting. (Numerical Rating Scale, NRS; Visual Analogue Scale, VAS; Disability of Arms, Shoulder and Hand, DASH; Functional Assessment of Cancer Therapy – Breast, FACT-B; 36-Item Short Form Survey, SF-36; European Organization for Research and Treatment of Cancer core quality of life, EORTC QLQ-C30; Breast cancer specific module, QLQ-BR23; Medical Research Council, MRC graded muscle; World Health Organization Quality of Life, WHOQOL-Bref)

Appendix 3. Methods of Outcome Reporting

Outcome	Measurement Tool and Definition
Lymphoedema	Arm volume/circumference: More than 5%, >10%, or >200mL difference in volume (compared to baseline and/or contralateral limb) measured by water displacement method,[745] tape measurement and perometry; or >2cm difference at any site on the upper extremity using tape circumferential measurements[106,132,746-749] (compared to baseline and/or contralateral limb); Bioimpedance spectroscopy analysis: measurement increased by 10% or more compared to baseline or if impedance ratio is more than three standard deviations than normative data.[750]
Pain	Any pain (mild, moderate, severe, intermittent or persistent) measured by Visual Analogue Scale (VAS), numerical rating scale (NRS), McGill Pain Questionnaire, Brief Pain Inventory-Short Form[751-754]
Range of motion	Goniometer: Restriction in shoulder movement of more than 10 degrees, 15 degrees, 20 degrees or 25 degrees for each movement in comparison to contralateral arm or baseline measurement;[104,106,131] or the limit for reduced mobility is set at 5% for flexion and abduction, and 10% for internal and external rotation as recommended by the American Academy of Orthopaedic Surgeons;[755] or range of motion impairment less than 80° for rotation and less than 170° for abduction; or using a scale from 0 to 3 (0, no motion restriction; 1, minor restriction; 2, moderate restriction; and 3, severe restriction).[144]
Strength	Dynamometer: Assessment of external rotators, internal rotators, abductors and adductors using a protocol described by Donatelli *et al.,*[280] or as recommended by The Americans Society of Hands Therapists.[756]
Upper limb function	Disability of Arms, Shoulder and Hand (DASH) questionnaire.[185]
Quality of life	Functional Assessment of Cancer Therapy - Breast (FACT-B),[757] 36-Item Short Form Survey (SF-36),[758] European Organization for Research and Treatment of Cancer core quality of life (EORTC QLQ-C30)[759] and breast cancer specific module (QLQ-BR23) questionnaires.[275]

Appendix 4. All studies reported the impact of SLNB and/or ALND on upper limb morbidities.

Author	Design	Treatment/ Participants/Follow up	Measurement instruments in outcome	Main findings
Abdelhamid 2020	RCT	98 (Group A: 49 ARM + positive preservation ALND vs Group B: 49 conventional ALND) Follow up: Pre-surgery, 6 months, 12 months and 24 months	Lymphoedema (arm circumference/volume) ROM	• For group A: At 6 months, 12 months and 24 months post-op, the LR was 4.35%, 6.5% and 6.5% respectively • For group B: At 6 months, 12 months and 24 months post-op, the LR was 11.6%, 13.9% and 20.9% respectively • For group A: At 6 months, 12 months and 24 months post-op, the reduced ROM rate was 19.6%, 17.4% and 13.04% respectively • For group B: At 6 months, 12 months and 24 months post-op, the reduced ROM rate was 23.3%, 18.6% and 13.9.9% respectively
Arraras 2018	Longitudinal cohort study	138 (13 ALND, 82 SLNB, 28 no axillary surgery) + radiotherapy Follow up: 3 years	EORTC QLQ-30 EORTC QLQ-BR23	• The ALND group scored lower (15-20 points) on the future perspective item than the other two axillary treatment groups at follow-up • No differences in pre- and post-treatment assessments across the different axillary treatment groups
Armer 2019	Longitudinal prospective study	488 (neoadjuvant chemotherapy followed by ALND)	Lymphoedema (arm circumference/volume)	• LR at 3 years by ≥10% volume increase was 60.3% (95% CI 55.0–66.2%) and by ≥2 cm-circumference increase was 75.4% (95% CI 70.8–80.2%)

		Follow up: pre surgery, 1-2 weeks post-surgery and semi-annually for 36 months		• 3-year cumulative incidence of lymphedema and heaviness was 26.0% (95% CI 21.7–31.1%) and 30.9% (95% CI 26.3–36.3%), respectively
Ashikaga 2010	RCT	1975 ALND, 2008 SLNB Follow up: baseline, 1 week, 2/3 weeks after surgery, every 6 months during the 3 year follow up	Lymphoedema - volume ROM- goniometer	• Shoulder abduction deficits ≥ 10% peaked at one week for the ALND (75%) and SLNB (41%) • Arm volume differences ≥ 10% at 36 months in ALND (14%) and SLNB (8%) • Numbness and tingling peaked at 6 months for the ALND (49%, 23%) and SLNB (15%, 10%)
Ballal 2018	Retrospective review of prospective study	745 (Group A – receiving SLNB only; Group B – primary ALND (with or without SLNB); and Group C – ALND as a second, separate procedure within 6 weeks of a positive SLNB) Follow up: 6 months, 12 months post-surgery	Lymphoedema - arm circumference/volume ROM-goniometer	• Overall LR: 8.2% at 12 months • No difference in LR between immediate or delayed ALND (17.8 vs 8.6%, p= 0.092) • Post-operative shoulder elevation, odds ratio (OR) = 0.390, 95% confidence interval (CI) = (0.218, 0.698) and abduction, OR = 0.437 (95% CI = (0.271, 0.705) reduced after ALND. No difference between immediate or delayed.

Beaulac 2002	Retrospective Cohort study	151 (ALND + Mastectomy or BCS) Follow up: Mean 4.8 ± 0.2 years after surgery	Lymphoedema -arm volume (water displacement) ROM- goniometer Strength- hydraulic hand dynamometer FACT-B	• Total LR: 27.8% • Mastectomy or BCS patients had similar LR • Women with lymphedema in both surgical groups scored significantly lower on 4 of the 5 subsections than women without lymphedema, even after adjusting for other factors influencing HRQoL
Beek 2019	RCT	94 (46 standard ALND versus 48 ARM+ALND) Follow up: pre-surgery, 6 months, 12 months and 24 months	Lymphoedema -arm volume (water displacement) + arm circumference ROM	• For standard ALND: At 6 months, 12 months and 24 months post-op, the LR was 21.4%, 23.4% and 32.3% respectively • For ARM+ALND: At 6 months, 12 months and 24 months post-op, the LR was 25%, 9.1% and 22.5% respectively • For standard ALND: 24 months post-op, the reduced ROM rate was 10% • For ARM+ALND: At 24 months post-op, the reduced ROM rate was 9%

Belmonte 2018	Prospective cohort study	68 SLNB 44 ALND Follow up: at baseline (pre-surgery) and at the first and fifth year post-surgery.	Strength – dynamometer ROM- goniometer Lymphoedema – physician monitor SF-36 FACT-B	• ALND group had significant loss of strength for IR (1.39 kg, p=0.001) and significant arm volume increase (132.45 mL, p=0.031) at 5 years. • ALND group had a greater number of patients with IR strength loss (38.7% vs. 13.6%, p=0.012) and a greater number of lymphoedema requiring treatment (33.3% vs. 3.4%, p<0.001) than the SLNB group. • A loss of strength for shoulder ER, shoulder ROM, and HRQoL in Physical and Arm domains persisted at 5 years in both SLNB and ALND.
Bogusevisious 2013	Prospective case-control study	48 breast conserving surgery with SLNB vs ALND Follow up: before surgery and after 1, 3, 6, 12, and 36 months	EORTC QLQ-C30 and QLQBR23	• Emotional functioning and cognitive functioning were significantly better in the SLNB group than ALND group at the 12-month follow-up (86.7 vs 72.4, p<0.05) • SLNB scored sexual functioning significantly better at 3 (79.2 vs 53.1, p<0.05), 12 (80 vs 62.9, p<0.05), and 36-month (82.5 vs 73.8, p<0.05) follow-ups than ALND group. • The score on the arm symptom subscale was significantly worse at 1 (40.9 vs 19.1, p<0.05), 6 (30.6 vs 13.7, p<0.05),

				and 36- (31.7 vs 13.6, p<0.05) month follow-ups in the ALND than SLNB group.
Bruce 2014	Cohort study	362 (any treatment) Follow up: 4 and 9 months after surgery	Pain (Numerical Rating scale)	• Independent predictors of CPSP at 4 months included younger age and acute postoperative pain (odds ratio [OR] 1.34, 95% confidence interval [CI] 1.12 to 1.60), whereas preoperative psychological robustness (OR 0.70, 95% CI 0.49 to 0.99), a composite variable comprising high dispositional optimism, high positive affect, and low emotional distress, was protective.
Button 2010	Observational study	58 (autologous latissimus dorsi flap (ALD) breast reconstruction (22 quilted vs 36 non-quilted donor site techniques) Follow up: pre-operatively and at 8 post-operative time-points (up to 3 years after reconstruction)	DASH	• Strong correlation between DASH scores at 3 months and long-term function up to 3 years after surgery (r=0.66, p<0.0003) • Higher post-operative DASH scores correlated significantly with pre-operative DASH (r=0.58) and BMI (r=0.36).
Blackburn 2018	Cohort study	159 (LD flap reconstruction) Follow up: Mean time since reconstruction 62 (28.9 days)	DASH EQ-5D	• LD reconstruction had an impact on shoulder function and some ADL, which impacted not only on the women but also family and significant others.

Cattelani 2018	non-randomised clinical trial	86 (Submuscular (group 1) vs preprectoral breast implant (group 2)) Follow up: mean 12 months, with a minimum of 4 and a maximum of 22 months.	DASH	• Compared to group 2 patients, group 1 patients showed less postoperative pain and faster upper limb functional recovery
Chrischilles 2019	Cohort study	833 breast cancer survivors (any treatment) Follow up: Mean follow up 22.1 (5.4) months after diagnosis	QuickDASH FACT-B	• Patients who had post-mastectomy radiation and chemotherapy experienced significantly worse upper extremity dysfunction and HRQoL • Patients with lower income, lower health literacy and prior diabetes, arthritis or shoulder diagnoses had worse upper extremity disability
DeGroef 2016	Longitudinal study	100 sentinel node negative patients Follow up: pre-surgery and 1 year post op	Lymphoedema – arm circumference/volume Pain (VAS) ROM (Dr Ripstein Plurimeter-V gravity	• 8% of sentinel node-negative breast cancer patients had lymphedema • 50% of patients had pain, 30% had an impaired ROM, 8% had a decreased handgrip strength and 49% had an impaired shoulder function

			reference analogue inclinometer) DASH Strength (dynamometer)	• Pain, shoulder range of motion, strength and shoulder dysfunctions changed significantly over one year ($p<0.001$).
Del Bianco 2008	RCT	341 patients randomized to the ALND group and 336 to the SLNB group Follow up: every 6 months after surgery and yearly thereafter up to 24 months	Lymphoedema – arm circumference/volume Pain (NRS) SF-36	• 6 months after surgery, the SLNB group had significantly less lymphoedema (OR 0.37, p= 0.005), movement restrictions (OR 0.47, p=0.005), pain (OR 0.52, p=0.006) and numbness (OR 0.65, p=0.016) with respect to the ALND group. • Lymphoedema was significantly reduced (OR 0.48, p=0.03) at 12 months and numbness ($p<0.0001$) remained significantly less frequent in the SLNB arm at all time points.
Devoogdt 2011	Cohort study	49 (mastectomy vs BCS + ALND) Follow up: 3.4 years after surgery	ROM (goniometer) Pain – VAS Arm lymphoedema – arm circumference	• At long term, 31% of the patients experienced impaired shoulder mobility, 18% developed lymphoedema, 79% had pain and 51% mentioned impaired daily activities. • Between 3 months and 3.4 years after surgery, impaired shoulder mobility decreased from 57% to 31%. The incidence of lymphoedema increased from 4% to 18%. Patients experienced an equal amount of pain but fewer problems with daily activities. • At 3.4 years, no significant differences between mastectomy and breast-conserving procedure were found.

Di Sipio 2009	Cohort study	316 (regional vs rural breast cancer survivors) Follow up: 12 months	DASH FACT-B	• In age-adjusted analyses, mean HRQoL scores of regional breast cancer survivors were comparable to their rural counterparts 12 months post-diagnosis (122.9, 95% CI: 119.8, 126.0 vs. 123.7, 95% CI: 119.7, 127.8; p>0.05). • Irrespective of residence, younger (<50 years) women reported lower HRQoL than older (50+ years) women (113.5, 95% CI: 109.3, 117.8 vs. 128.2, 95%CI: 125.1, 131.2; p<0.05) • Women who received chemotherapy, reported two complications post-surgery, had poorer upper-body function than most, reported more stress, reduced coping, who were socially isolated, had no confidante for social- emotional support, had unmet health care needs, and low health self-efficacy reported lower HRQoL scores.
Donker 2014	RCT	2402 ALND, 2404 axillary RT Follow up: 1, 2 and 5 years	Lymphoedema - arm circumference/volume	• Clinical sign of lymphoedema in the ipsilateral arm was noted significantly more often after ALND than after axillary radiotherapy at 1 year (28% vs 15%, p<0.0001), 3 years (23% vs 14%, p=0.003), and 5 years (23% vs 11%, p<0.0001). • Arm circumference increase >10% of the ipsilateral upper or lower arm, or both was noted significantly more often after ALND than after axillary radiotherapy at 5 years (13% vs 5%, p=0.0009)
Duff 2001	Cohort study	100 (64 mastectomy, 36 BCS + axillary clearance)	Lymphoedema – arm volume ROM- goniometer	• 10 % patients had significant arm swelling at 1 year. • Reduced arm movements were noted in the first week after operation but had returned to normal at 6 months.

		Follow up: At least 1 year (pre-op, day 5, 6 months, 1 year, 2 years)		
Eyjolfsdottir 2017	Cross-sectional	15 (mastectomy and LD flap reconstruction) Follow up: pre-op, 1,6,12 months post op	Pain (NRS) ROM (goniometer) Strength (dynamometer)	• At 12 months post-operatively, patients had achieved full range of shoulder movement, when compared to pre-operative values. • Muscle strength in flexion–extension–internal rotation was significantly (p= 0.01) reduced on the operated side at 12 months post-operatively.
Faisal 2019	RCT	48 (24 standard ALND – control group vs 24 ARM+ALND – study group) Follow up: Pre-surgery and 6 months post-surgery	Lymphoedema - arm circumference/volume	• LR in control group – 16.7% • LR in study group – 4.2%
Fougo 2011	RCT	106 (Group 1 – Assigned to axillary lymphadenectomy n=49. Group 2 – Assigned to observation n=57) Follow up: 6, 12, 24 and 48 months after surgery	Lymphoedema – arm circumference/volume ROM	• The % of patients with morbidity and who had more than two complications was significantly higher in Group I • LR in group 1 was significantly higher than group 2 at 36 (38.3% vs 7%, p=0.001) months • Shoulder dysfunction in group 1 was significantly higher than group 2 at 36 (23.4% vs 3.6%, p=0.005) months

Francis 2006	Cohort study	155 (41 SLNB, 105 ALND, 9 no axillary surgery) Follow up: 12 months after surgery	Lymphoedema - arm circumference/volume	• LR at 12 months: total (68%), SLNB (17%), ALND (47%)
Freitas-Silva 2010	Cross-sectional	BCS (n = 44) or MRM and IBR (n = 26)	Lymphoedema – arm circumference/volume SF-36 ROM-goniometer	• No differences in prevalence of lymphoedema • Restricted IR: 32% in the BCS group vs 12% MRM and IBR group (OR: 7.23; p = 0.03 following adjustment for potential confounding factors) • No difference in QoL or satisfaction with surgery between the two groups
Gosselink 2003	Cohort study	76 (45 BCS with axillary dissection or 31 MRM)	Lymphoedema – arm circumference/volume ROM (goniometer) Pain (VAS)	• MRM patients had more limitations in shoulder mobility than BCS patients (shoulder flexion: 150 degrees vs. 126 degrees, respectively, p=0.0001) after 3 months • Upper limb ADL was significantly impaired: MRM patients suffered from greater functional disabilities than BCS patients, ADL score 2.7 and 1.8, respectively (p= 0.037) at 3 months • Patients with axillary radiation experienced greater disability of shoulder mobility and ADL • 2.5% patients with LE at 3 months

Golshan 2003	Retrospective study	125 (48 ALND, 77 SLNB) +/- chemotherapy +/- radiotherapy Follow up: Minimum 1 year after surgery	Lymphoedema – arm circumference/volume	• LR: ALND 27% and SLNB 2.6%
Glassey 2008	Prospective observational study	22 (17 delayed LD flap, 5 immediate LD flap) Follow up: preoperatively, 6 weeks, 6 months and 1 year postoperatively	ROM – goniometer DASH Pain (VAS)	• ROM: Initial loss of the majority of ROM at 6 weeks after surgery, but the ROM at 6-month and 1-year had increased slightly compared with preoperative values • DASH: Initial deterioration in function 6-week and 6-month postoperatively but DASH score returned to preoperative baseline at 1 year • Pain: Initial increase in pain at the 6-week and 6-month but decreased at 1-year when compared with preoperative assessment
Haid 2002	Cohort study	140 had ALND, 57 had SLNB Follow up: mean 18 (5–30) months	Lymphoedema – arm circumference/volume	• No significant difference in HRQoL for both groups • Significant difference in overall complaints: (49% ALND group vs 19.3% SLNB group), pain (ALND: 47% vs SLNB: 19.3%), perceived limitation of motion (ALND: 43.5% vs. SLNB: 8.8%), numbness on the inner aspect of the affected arm (ALND: 49% vs SLNB: 0%), lymphoedema (ALND: 27.1% vs SLNB: 3.5%), disability in activities of daily living (ALND: 50% vs SLNB: 12.3%)
Han 2012	Cohort study	97 (SLNB vs ALND)	Lymphoedema – arm circumference	• 6 months: total (1%), SLNB (0%), ALND (1%)

		Follow up: mean 9.6± 4.3 months (range, 3- 24 months)		
Hau 2013	Cross-sectional	688 (randomised between the control arm of 50 Gy in 25 fractions to the whole breast and the boost arm of 45 Gy in 25 fractions to the whole breast followed by a 16 Gy in eight fraction electron boost)	EORTC QLQ-C30	• At 10 years, multivariable modelling showed that arm pain had the greatest impact on QoL (95 % CI 6–19).
Hojris 2000	RCT	84 (post mastectomy RT + systemic treatment vs systemic treatment alone) Follow up: median length of follow-up from mastectomy was 9 years (range 6–13 years)	Lymphoedema – arm circumference/volume	• Lymphoedema: 14% of the irradiated patients vs 3% of the non-irradiated patients (NS) • Slightly decreased shoulder morbidity in 45% of the irradiated women vs 15% of the non-irradiated patients, but moderate or more severe impairment was seen in only 5% of the irradiated patients and in none of the non-irradiated patients (p=0.004) • 17% of the irradiated patients and 2% of the non-irradiated patients found that impairment of shoulder movement caused symptoms (p=0.001)
Husen 2006	Cohort study	370 (Group A, SLNB only), (Group B, SLNB followed by a complete ALND during the first (and only) operation),	Lymphoedema-arm circumference	• Lymphoedema : 4% in SLNB group, 19% in ALND group and 34% in ALND (2-step procedure)

		(Group C, SLNB only in the first procedure, and a complete ALND in a second procedure) Follow up: 23.5 months	Pain, lymphoedema, numbness, reduced mobility, reduced strength, fatigue-questionnaire	• Pain: 16% in SLNB group, 38% in ALND group and 52% in ALND (2-step procedure)
Jassim 2013	Cross-sectional	239 (any treatment) Follow up: early after diagnosis (≤1 year since diagnosis), transitional period (>1 and ≤5years since diagnosis) and long-term survivors (>5 to ≤10 years).	EORTC QLQ-C30 and QLQBR23	• Mean score for global health of 63.9 (95% CI 61.21-66.66). • Among functional scales, social functioning scored the highest (Mean 77.5 [95% CI 73.65-81.38]) whereas emotional functioning scored the lowest (63.4 [95% CI 59.12-67.71]). • The most distressing symptom on the symptom scales was fatigability (Mean 35.2 [95% CI 31.38-39.18]).
Johansson 2001	Cohort study	90 women undergoing axillary dissection combined with mastectomy or segmental resection Follow up: pre-op and monthly for 6 months with 1 and 2 year follow ups	Lymphoedema - volume (water displacement method) ROM (goniometer) Strength (dynamometer)	• There were significant differences in lymphoedema between the ART and NRT groups at the 1- and 2-year follow-ups ($p<0.05$) and ($p<0.02$), respectively. • At 1 and 2 months, there were no differences between the groups at any ROM. At 3 months, the ART group had reduced mobility in abduction ($p=0.003$) and flexion ($p=0.017$), and at 6 months, they had reduced mobility in external rotation ($p=0.021$).

				• At 6 months, 1 year, and 2 years, isometric muscle strength in the flexors, adductors, and internal rotators of the shoulder decreased significantly in the entire group.
Kingsmore 2005	Retrospective cohort study	2122 women treated for invasive breast cancer Follow up: Median 8 years since diagnosis	Lymphoedema – Objective assessment by clinician	• LR: SLNB (20/146, 5%); ALND (69/1099, 6%) • LR: Axillary radiotherapy only (4/92, 4%) • Addition axillary radiotherapy to SLNB and ALND increased the LR: SLNB + ART (26/230, 11%), ALND + ART (17/123, 14%) p<0.001)
Koehler 2018	Longitudinal prospective cohort study	36 (AWS vs non AWS) Follow up: at 2, 4, and 12 weeks and 18 months following breast cancer surgery	Lymphoedema – arm circumference/volume, bioimpedance spectroscopy (BIS), and trunk tissue dielectric constant measurements ROM (goniometer) Pain (VAS) DASH	• No statistical group differences between the AWS and non-AWS groups related to upper extremity percent volume difference (F=0.07, p 0.79) • The AWS group had statistically impaired abduction active ROM (F=4.5, p=0.005) and passive ROM (F=3.6, p=0.02) at 2 and 4 weeks but not at subsequent visits • Shoulder flexion AROM was statistically lower in the AWS group compared to the non-AWS group at 2 weeks (p<0.05) but not subsequent visits • Both AWS and non-AWS groups had a decrease in DASH scores from 2 weeks to 12 weeks, but at 18 months the AWS group had an increase in DASH scores while the non-AWS group had a continued decrease in DASH scores

Kootstra 2013	Longitudinal cohort study	110 (SLNB vs ALND) Follow up: pre-surgery (T0) and 6 weeks after surgery (T1), 7 years later (T2)	ROM (goniometer) Strength (dynamometer) Lymphoedema - arm circumference	• ROM (excluding external rotation), abduction strength, and arm volume were all reduced 7 years after surgery compared to pre-surgery levels • Those with ALND demonstrated 70% greater forward flexion disability, increased arm volume, and clinically relevant impairments than women with SLNB (41%) • The strongest predictors of long-term shoulder–arm function are shoulder–arm function at 6 weeks following surgery and age
Kopec 2013	RCT	744 (SLNB vs ALND). Women who had sentinel node–negative breast cancer were enrolled in the HRQoL component of NSABP B-32 Follow up: 6 months after surgery	ROM (goniometer) Lymphoedema - volume (water displacement method) DASH survey	• 1/3 experienced reduced ROM • 1/3 avoided the use of the arm 6 months after surgery • Limitations in work and other regular activities were reported by 1/4 • In multivariable analyses with a global HRQoL score as a continuous variable, significant predictors of HRQoL were ROM ($p<0.001$) and neuropathy ($p<0.001$)
Kuehn 2000	Cohort study	396 (breast conserving therapy or mastectomy including axillary dissection)	Lymphoedema – arm circumference/volume ROM (goniometer) Strength – five-point score	• Total LR: 22.7% • 115 patients (29.0%) declared ‘arm symptoms’ as their most important problem • Mean restriction of 21◦ for abduction and 12◦ for forward flexion compared to the contralateral arm are statistically significant (Wilcoxon test, $p<0.001$).

		Follow up: mean 34 months (median 32, range 6–96) after surgery		• Restriction of isometric strength of at least one score point was observed in 172 (43.4%) of patients • 24 patients (56.6%) had no measurable reduction of arm strength compared to the contralateral arm
Kuwajerwala 2013	RCT	199 (SLNB vs SLNB+ immediate ALND or completion ALND) Follow up: every 6 months up to 24-36 months	Lymphoedema – arm volume	• LR for node-positive SLNB+ALND was 10.3% and node-negative SLNB+ ALND was 6.8% • Comparison between immediate and completion ALND lymphedema was not statistically significant (10.3% vs. 14.3%, p= 0.65).
Leidenius 2005	Cohort study	92 SLNB only or 47 ALND Follow up: 3 years post op	Lymphoedema – arm circumference/volume ROM (goniometer) Pain (VAS)	• Breast pain in SLNB and ALND (39% vs 28%, p=NS) respectively • Arm pain more common after ALND than SLNB (30% vs 12%, p=0.0045) • LR after ALND: 6% and 0% after SLNB, p=0.0172. • The ipsilateral shoulder flexion restricted in 16 (34%) ALND patients and in 15 (16%) SLNB patients, p=0.0175.
Lopez Penha 2011		145 breast cancer patients (any treatment) Follow up: >5 years post surgery	Lymphoedema – water displacement method, arm circumference	• LR using arm circumference: 23/145 (16%) - SLNB: 24/76 (32%) and ALND: 37/69 (54%) • LR using water displacement method: 11/145 (7.6%)

Lorek 2019	Cohort study	303 patients (SLNB procedure in combination with wide local excision (WLE), simple mastectomy or autonomous SLNB procedure) Follow up: mean 25.5 months	ROM (goniometer)	• Restricted mobility: 3 patients (1.5%) after WLE and 6 patients (5.6%) after simple mastectomy. • Lymphoedema: 2 patients (1%) after WLE and 7 patients (6.5%) after simple mastectomy.
Lucci 2007	RCT	891 randomly assigned to SLNB + ALND (n = 445) or SLNB alone (n = 446) Follow up: 1 year	Lymphoedema – arm circumference/volume Lymphoedema (reported subjectively)	• Adverse surgical effects reported in 70% (278 of 399) of patients after SLNB + ALND and 25% (103 of 411) after SLNB alone (p<0.001) • Patients in the SLNB + ALND group had more wound infections (p<0.0016), seromas (p<.0001), and paresthesia (p<.0001) than those in the SLNB-alone group • The difference between the two lymphoedema groups, assessed by arm measurements at 30 days (p=0.36), 6 months (p=0.22), and 1 year (p=0.078) • LR at 1 year (subjective report) were 13% (37 of 288) after SLNB + ALND and 2% (six of 268) after SLNB alone (p<or= 0.0001).
Lumachi 2009	Cohort study	Group A (n=54) SLNB alone; Group B (n=48) SLNB followed by ALND using	Lymphoedema – arm circumference/volume	• Total LR, 15/205 (7%); SLNB, 2/54 (4%); ALND, 13/151 (9%)

		ultrasound scissors (harmonic scalpel); Group C (n=53), ALND using ultrasound scissors; Group D (n=50) traditional ALND dissection Follow up: Median 22 months (range 18-28 months)		
Lee 2018	cohort study	30 (transverse rectus abdominis myocutaneous (TRAM) flaps after mastectomy (MTX + TRAM) and patients who underwent mastectomy only (MTX)) Follow up: Mean follow up was 62.1+/-39.5 months	Pain (VAS) Strength (myometer)	• no significant differences in VAS, restricted ROM, rotator cuff disease, muscle strength, shoulder function scores or scapula tilt on physical examination
Mansel 2006	RCT	1031 patients randomized: 515 SLNB, 516 ALND	Lymphoedema – Arm volume FACT-B+4	• Moderate/severe lymphoedema reported more often in ALND than SLNB at 1, 3, 6, and 12 months after surgery (e.g 5% versus 13% at 12 months; all $p<0.001$) • There was statistically significantly more impairment of shoulder flexion and abduction on the ipsilateral side when comparing ALND to SLNB at 1 month after surgery ($p=0.004$ and 0.001, respectively).

		Follow up: 1, 3, 6, and 12 months after surgery		• HRQoL and arm functioning scores were statistically significantly better in the SLNB group throughout (all p≤0.003).
Martin da Silva 2014	Cross-sectional	82 (breast-conserving surgery (quadrantectomy or tumorectomy), and ALND at 3 levels) Follow up: mean time since surgery was 5.78 years (± 4.60).	FACT-B QuickDASH survey ROM (goniometer) Lymphoedema – arm circumference/volume	• LR: 28% but did not impair QoL or functional capacity • Deficit of 13.6% in shoulder flexion ROM ipsilateral to surgery, 17.2% in abduction ROM and 25.1% in external rotation ROM • Deficit in shoulder ROM was evidenced on contralateral side, with 4.9% in flexion ROM, 6.4% in abduction ROM and 4.5% in external rotation ROM • The mean functional capacity correlated with HRQoL had a negative impact on physical well-being (p<0.001), family well-being (p= 0.012), emotional well-being (p <0.001), functional well-being (p <0.001), breast subscale (p= 0.18), FACT-B TOI (p<0.001), FACT-G TOTAL (p<0.001).
Mathew 2006	Retrospective review	312 in Group 1 (SLNB) and 194 in Group 2 (ALND) Follow up: 2 years after surgery	Lymphoedema – arm circumference	• Total LR (31/506, 6%); SLNB (7/312, 2.2%); ALND (24/194, 12.3%)
McCarthy 2012	RCT	69 implant reconstruction (ADM vs submuscular tissue expander/implant)	Pain (VAS)	• No differences between the two groups in pain in the immediate post-operative period (p=0.19) and pain during the expansion phase (p=0.65)

McDuff 2019	Cohort study	2171 (1,232 underwent a lumpectomy and 1,034 underwent a mastectomy; 199 patients had no axillary surgery performed, 1520 received a SLNB, and 547 received ALND) Follow up: 4 years median follow up	Lymphoedema – arm circumference/volume	• 5-year cumulative incidence of lymphoedema was 13.7% • Significant factors associated with lymphoedema on multivariable analysis were high preoperative BMI, ALND and RLNR • Those receiving ALND with RLNR experienced the highest 5-year rate of lymphoedema (31.2%), followed by ALND without RLNR (24.6%), followed by SLNB with RLNR (12.2%)
McLaughlin 2008	Prospective observational cohort study	936 (SLNB alone vs SLNB followed by ALND) Follow up: Median 5 years after surgery	Lymphoedema – arm circumference	• Total LR (86/936, 9%); SLNB (31/600, 5%); SLNB+ALND (55/336, 16%)
Monleon 2016	Cohort study	112 (44 underwent ALND and 68 SLNB) Follow up: pre-surgery, and at 1, 6 and 12 months after surgery	Strength (dynamometer)	• Internal rotator strength decreased significantly after ALND in the first month, and did not return to pre-surgery levels after one year of follow-up, with a mean difference of 2.26 kg (p=0.011); no significant loss of strength for patients treated with SLNB • The loss of shoulder ROM was only significant in the first month for the ALND group.

				• The ALND surgery and having had physical/occupational therapy during follow-up were factors associated with strength loss
Nagel 2003	Cohort study	106 (mastectomy or breast conserving therapy with complete axillary dissection +/- adjuvant RT) Follow up: median follow-up of 14.3 months (range 4- 25 months).	Lymphoedema - arm circumference/volume ROM (goniometer) Pain (VAS)	• 13 patients (12.6%) had lymphoedema • Significant relation between adjuvant radiotherapy and lymphoedema (p=0.001, OR 37.2) • 39 out of 106 patients (37%) had reduced ROM • 9 out of 11 who had RT (82%) had a restriction in anteflexion and abduction
Nesvold 2008	Cohort study	263 (MRM vs BCS + ALND) Follow up: median of 47 months (range 32-87) post-surgery	Lymphoedema – arm circumference/volume ROM (goniometer)	• 20% lymphoedema in MRM group vs 8% in BCS group (p=0.02) • In multivariate analysis, lymphoedema was associated with a higher number of metastatic axillary lymph nodes [OR1.14, p=0.02], MRM [OR 2.75, p=0.04] and increasing BMI [OR 1.11, p=0.01] • 24% had a restricted ROM in shoulder flexion in MRM compared to 7% in the BCS group (p=0.01) • Shoulder pain reported by 32% in MRM group and by 12% in BCS group (p=0.001) • Increasing observation time, MRM, and increasing BMI were significantly associated with impaired arm/shoulder function

Olson 2008	Cross-sectional	1,003 patients with SLNB metastasis had immediate (n=425) or delayed (n=578) complete ALND (part of American College of Surgeons Oncology Group (ACOSOG) trials Z0010 and Z0011). Follow up: 30 days, 6 months and 1 year after surgery	ROM (goniometer) Lymphoedema – arm circumference/volume	• Patients who received immediate ALND had more axillary paraesthesia (51% vs. 35%; p<0.0001) and impaired ROM (49% vs. 36%; p<0.0001) at 30 days than those who received delayed ALND • Impaired ROM observed at 30 days improved significantly at 6 months and 1 year, with no difference noted between groups • Patients who underwent delayed ALND had more lymphoedema at 6 months (13% vs 10%; p=not significant) but this difference did not remain at 1 year
Ozcinar 2012	Prospective observational cohort study	218 patients, patients surgically treated for early-stage breast Follow up: median 64 months	Lymphoedema – arm circumference/volume	• LR at 64 months was 7.3%. (BCS: 11.1%, 4.2% and 0.5%; Mastectomy: 15.0%, 3.2% and 1.4%; SLNB: 8.0%, 1.9% and 0.5%; ALND: 18.0%, 5.3% and 1.4%; RT: 14.7%, 6.3% and 1.4%; without RT: 11.4%, 2.1% and 0.5% at mid-term, late period and late period without mid-term lymphoedema respectively) • When mid-term and late term lymphoedema were excluded, only 4 patients developed lymphoedema at late period, with lymphoedema rate of 1.8%. • Factors affecting lymphoedema in late period were ALND (p=0.005) and RT(p<0.001)
Paim 2008	Cross-sectional	96 women treated for breast cancer at an outpatient service (who underwent SLNB or ALND)	ROM (goniometer) Lymphoedema – arm circumference/volume	• The most common complications were pain (57%), impaired shoulder strength (57%), and fibrosis (54%), impaired shoulder ROM (46%) and lymphoedema (17%)

		Follow up: unknown	FACT-B Pain - Short Form and McGill Pain Questionnaire	• The incidence of impaired shoulder flexion (p= 0.01) and lymphoedema (p=0 .002) was higher in ALND group • Winged scapula (8.4%) only occurred in the ALND group • HRQoL was significantly correlated with pain (r=0.53, p=0.000) and impaired shoulder strength in flexion (r=0.4; p= 0.000) and abduction (r=0.5, p=0.000)
Paiva 2013	Cross-sectional	250 women being treated for breast cancer Follow up: beyond or within 5 years	Lymphoedema – arm circumference/volume	• LR: 112/250 (44.8%) • Shoulder joint mobility, restrictions on abduction movements, internal and external rotation, and anterior shoulder adduction were significantly associated with lymphoedema (p<0.001)
Peintinger 2003	Prospective study	56 SLNB (25 patients receiving the SLNB only (Group I) vs 31 patients who underwent the standard level I and II ALND (Group II) when intraoperative frozen section showed metastatic disease) Follow up: before surgery (t1), 1 week after discharge (t2) and 9–12 months after surgery (t3).	ROM (goniometer) McGill Pain EORTC QLQ-C30 and BR23	• Arm/shoulder pain reported in 36% of patients after SLNB in comparison to 68% receiving ALND • Numbness reported in 4% of patients in the SLNB group vs 19.3% after ALND • Abduction, flexion and horizontal adduction of the affected arm show significant impairment after ALND

Perez 2018	Observational and cross-sectional	28 women - undergoing surgery and adjuvant treatment of breast cancer Follow up: at least 6 months post treatment	Lymphoedema – arm circumference/volume Strength – dynamometer DASH survey	• When surgery was performed on the non-dominant side, a significant difference (p=0.001) was seen between the affected and unaffected sides • Electromyographic activity of women who had nondominant side surgery showed a significant difference in the flexor muscles of the wrist and fingers (p=0.001) when compared to the unaffected upper limb
Rietman 2004	Retrospective study	55 patients who underwent a modified radical mastectomy or a segmental mastectomy with ALND Follow up: Mean follow-up was 2.7 years	Lymphoedema – arm circumference/volume ROM (goniometer) Pain (VAS) Strength (dynamometer)	• The most frequent complications: Pain (60%) and reduction of grip-strength (40%) • The prevalence of impaired ROM and lymphoedema was 9–16% and 15% respectively • Radiotherapy and chemotherapy were significant factors in the prediction of impaired ROM
Rietman 2006	Prospective cohort study	204 patients (SLNB or ALND) Follow up: pre-surgery and 2 years after surgery	Pain (VAS) EORTC QLQ-C30 and QLQBR23	• Patients experienced significantly less perceived disability in ADL and worsening of HRQoL after SLNB compared with ALND • RT to the axilla predicts an additional decrease in shoulder ROM and increase of arm volume
Ronka 2005	Cohort study	83 patients – SLNB or ALND +/- adjuvant therapies	Lymphoedema – arm circumference/volume ROM (goniometer)	• 10% in SLNB group and 22% ALND group had impaired flexion of the ipsilateral shoulder (not significant) at 1 year after surgery

		Follow up: before surgery and again 2 weeks and 3, 6 and 12 months after surgery	Pain (VAS)	• Muscle weakness was reported more often by patients in the ALND group compared to SLNB (42% vs 19%; p= 0.014) at 1 year after surgery • A similar increase in the arm circumference was observed in both patient groups 1 year after surgery (80% vs 86%, p=0.084) • Arm morbidity affected work (p=0.004), hobbies (p=0.003) and daily life in general (p=0.002) more often in the ALND group than in patients who underwent SLNB
Roy 2018	RCT	1544 patients - sALND restricted to cases with positive SLN biopsy (test arm, n = 774) versus SLN biopsy followed by sALND (control arm, n = 770). Follow up: up to 5 years	Pain	• Pain: 27.3% in systematic ALND and 13.4% in ALND restricted to positive SLN
Sagen 2014	Prospective longitudinal cohort	391 (ALND and SLNB group) Follow up: 2.5 years	Lymphoedema – arm circumference/volume Strength – dynamometer Pain (VAS) ROM (goniometer)	• More complications after ALND than with SLNB after 2.5 years ($p<0.05$); arm lymphoedema (17% vs 3%), grip strength reduction (12% vs 2%), and shoulder abduction-provoked pain (increase of 6% vs decrease of 50%). • At 2.5 years, the prevalence of women in paid work had fallen significantly from 79 to 66 % ($p<0.05$) in the ALND group and from 68 to 61 % ($p<0.05$) in the SLNB group

Schrenk 2000	Cohort study	35 had ALND of Level I and II and 35 had SLNB Follow up: Mean follow-up 15.4+/- 6.2 months (range 4 – 28 months)	Lymphoedema – arm circumference/volume Pain (VAS) ROM – Scale 0 to 3	• Significant increase from pre-op to post op measurement was found in the greatest dimension of the arm (upper arm and forearm) in patients after ALND compared to SLNB (p=0.0001) • Significantly more pain in the operated arm after ALND (p=0.0001) compared to SLNB • 6 patients in the ALND group reported minor but significantly decreased arm mobility (p=0.011)
Soares 2014	Cross-sectional	200 women with invasive breast cancer who underwent breast-conserving surgery (n = 165) or mastectomy (n = 35) with ALND Follow up: mean 35 months from surgery	Lymphoedema – arm circumference/volume ROM (goniometer) Pain (Yes/no)	• Lymphedema was found in 7 (3.5%) of patients. • Paraesthesia was observed in 106 (53%) of patients. • Reduced ROM was observed in 48 (24%) of the patients • Pain was reported by 55 (27.5%) of patients
Sowa 2017	Cohort study	18 LD flap + RT	ROM (goniometer) Strength (dynamometer)	• ROM measurements at 3 months post-surgery showed significant decreased in both flexion and abduction by 7.1% and 9.2% and at 3 years post-surgery by 4.7% and 5.7%

		Follow up: before surgery, and at 3 and 6 months, and 1 and 3 years		• The muscle strength measurements at 3 months post-surgery showed statistically significant decreased in adduction and in medial rotation by 30.7 and 25.9% and at 3 years post-surgery by 36.4 and 20.4%.
Sun 2014	Cross-sectional	407 (254 underwent BCS, 122 underwent total mastectomy and 31 underwent total mastectomy with reconstruction Follow up: 49 months (mean) follow up following surgery	EORTC QLQ-C30 EORTC QLQ-BR23	• BCS showed better outcomes than women in the total mastectomy and reconstruction after total mastectomy groups with respect to emotional–social function, nausea/vomiting, financial difficulty, body image, arm symptoms and self-esteem. • Patients in the reconstruction after total mastectomy group had significantly better outcomes on the sexual scale and arm symptoms than the total mastectomy group.
Tengrup 2000	Cohort study	110 consecutive partial mastectomy and axillary dissection Follow up: baseline, once a year for up to 5 years after the operation	Lymphoedema – arm circumference/volume ROM (goniometer) Pain (VAS)	• 21/110 (19%) developed lymphoedema, 17/75 (22%) in the radiotherapy group and 4/35 (12%) in the group without radiotherapy • 54/110 (49%) of the patients had reduced shoulder mobility, and of these, 44/75 (57%) were in the radiotherapy group and 10/35 (30%) in the group without radiotherapy • 31% of patients were still perceiving some pain five years after the operation

van Huizum 2016	Cohort study	12 (LD flap reconstruction) Follow up: mean of 3.5 years after surgery	DASH Strength - Dynamometer	• The mean total DASH score among the patients (16.51+/-15.46) was significantly higher than the mean of the controls (2.73+/-4.63) • Decrease of shoulder strength for extension ($p<0.05$), adduction ($p<0.05$), and internal rotation ($p<0.05$) of on the operated side compared to the non-operated • 19% higher scores for overall torque of the motions performed by the latissimus muscle, on the non-operated side
Veronesi 2003	RCT	516 patients: SLNB and ALND (axillary dissection group) or SLNB followed by ALND if positive sentinel node (sentinel node group) Follow up: at 6 months and 24 months after surgery	Lymphoedema – arm circumference ROM – Mobility scale from 0 to 100 Pain (Questionnaire)	• LR at 24 months: 12/100 (12%) in ALND and 0/100 (0%) in SLNB • Arm mobility <80% at 24 months: 21/100 (21%) in ALND, 0/100 (0%) in SLNB • Sporadic pain at 24 months: 34/100 (34%) in ALND and 7/100 (7%) in SLNB • Continuous pain at 24 months: 5/100 (5%) in ALND and 1/100 (1%) in SLNB
Voogd 2003	Cohort study	332 ALND Follow up: Mean time after surgery 4.2 years	Lymphoedema – arm circumference ROM (goniometer)	• 26% had LE or reduced abduction • These patients with LE and reduced abduction had a greater difficulty performing house chores, were more likely to have discontinued hobbies, felt more disabled, and were more likely to have treatment from a physiotherapist.
Wernicke 2011	Cohort study	265 (lumpectomy and either SLNB or SLNB and ALND	Lymphoedema – arm circumference	• Total LR: (45/223, 20%); SLNB (5/108, 5%); SLNB+ALND (40/115, 35%)

		Follow up: Median follow-up 9.9 years	ROM (assessed by clinicians)	• Statistically significant decreased range of motion in the ipsilateral shoulder (p< 0.0001) in ALND compared to SLNB
Wernicke 2013	Cohort study	226 women (lumpectomy, either SLNB or SLNB+ALND) Follow up: median follow-up 9.9 years	Lymphoedema – arm circumference/volume ROM (goniometer)	• The only chronic complications at 10 years were decreased shoulder ROM 46/111 (41.4%) in SLNB and 92/115 (80.0%) in ALND (p<0.0001), paraesthesia 12/111 (10.8%) in SLNB and 39/115 (33.9%) in ALND (p<0.0001), and lymphoedema assessed by patients 10/111 (10.0%) in SLNB and 39/115 (33.9%) in ALND (p<0.0001). • Clinicians identified chronic lymphedema in 6/111 (5.4 %) of the SLNB and 21/115 (18.3%) of the ALND cohorts, respectively (p<0.0001).
Wetzig 2017	RCT	1088 randomised to SNBM with ALND if the sentinel node was positive or RAC preceded by sentinel-node biopsy. Follow up: at 1, 6, and 12 months, and annually for 5 years	Lymphoedema – arm circumference/volume	• Only 28 patients (3.3%) had a corrected increase of arm volume [15% from baseline (RAC 5.0% vs. SNBM 1.7% at 5 years) • Significant predictors of lymphoedema were surgery type (RAC vs. SNBM), obesity, diabetes, palpable tumour, and weight gain exceeding 10% of baseline value
Wilke 2006	Prospective cohort study	5327 patients (SLNB)	Lymphoedema – arm circumference/volume	• At 6 months, 8.6% of patients experienced axillary paraesthesia, 3.8% had restricted ROM, and 6.9% developed proximal upper extremity lymphoedema

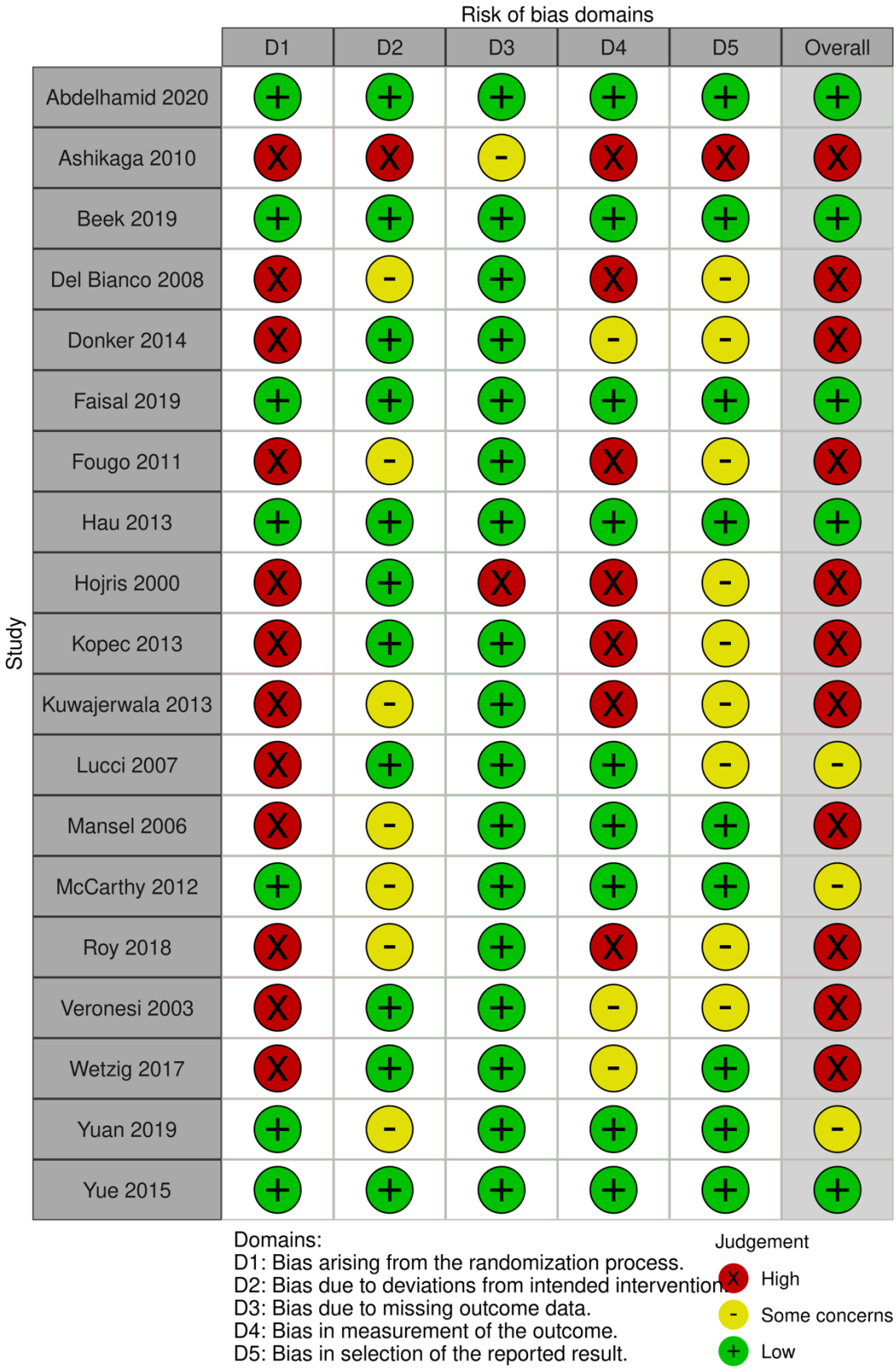
		Follow up: 30 days and 6 months after surgery	ROM (goniometer)	• A decreasing age for axillary paraesthesia, increasing BMI, and increasing age for upper extremity lymphoedema were all significant predictors of surgical complications at 6 months
Winters 2016	Cohort study	206 implant-assisted latissimus dorsi (LDI) and autologous latissimus dorsi (ALD) flap breast reconstructions Follow up: 2-3 years after surgery	EORTC QLQ-C30, QLQBR23, and FACT-B	• Patients in both surgical groups showed improvements in emotional scales, but worse physical functioning, social well-being, body image and anxiety. • At 3 years, younger women experienced worse physical well-being than older women ($P = 0.006$), and chemotherapy was associated with worse arm symptoms ($P = 0.005$)
Woo 2018	Prospective observational study	430 reconstructions (223 expander-implant, 44 LD flap, and 163 DIEP flap) Follow up: 52 months on average (range 24 to 120 months)	ROM (goniometer)	• Expander-implant (OR 2.15, p=0.010) and the LD flap (OR 6.27, p< 0001) were significant risk factors for shoulder morbidity, compared to the DIEP flap • Old age (p=0.041), presence of tumor-positive lymph nodes (p=0.014), and neoadjuvant chemotherapy (p=0.002) were independent risk factors for the development of shoulder morbidity
Yang 2015	Prospective cohort study	191 (LD flap) Follow up: baseline, 3 months, 12 months (t2) and 24 months (t3) after surgery.	DASH	• DASH score was 7.1+/-4.2 before surgery and increased significantly to 20.3+/-5.1 at 3 months after surgery and 27.1+/-5.4 at 12 months after surgery; but decreased to 11.6+/-3.8 at 24 months after surgery (not statistically

				significantly different from baseline to 24 months after surgery) • Upper-limb impairment recovered with time after breast cancer surgery; however, upper-limb function related activity and participation were reduced through 2 years after surgery
Yuan 2019	RCT	558 ARM+ALND (study group) versus 665 standard ALND Follow up: Pre-surgery, 3 months, 6 months, 12 months, 24 months, 36 months	Lymphoedema -arm volume (water displacement)	• For group ARM+ALND: At 3 months, 6 months, 12 months, 24 months and 36 months post-op, the LR was 2.6%, 2.9%, 3.1%, 3.3% and 3.3% respectively • For group standard ALND: At 3 months, 6 months, 12 months, 24 months and 36 months post-op, the LR was 6.9%, 10.8%, 12%, 14% and 15.3% respectively
Yue 2015	RCT	127 standard ALND (control group) versus 138 ARM+ALND (study group) Follow up: Pre-surgery, 6 months, and annually for 3 years	Lymphoedema – arm circumference/volume	• For control group, LR was 33.07% (median follow up: 20 months) • For study group, LR was 5.93% (median follow up: 20 months)
Zhou 2019	Cohort study	60 (32 patients were assigned in the LD group, and 28 in the conventional BCS	ROM (inclinometer) DASH	• no significant difference in muscle strength, ROMs of the shoulder or DASH scores between LD and CCS groups

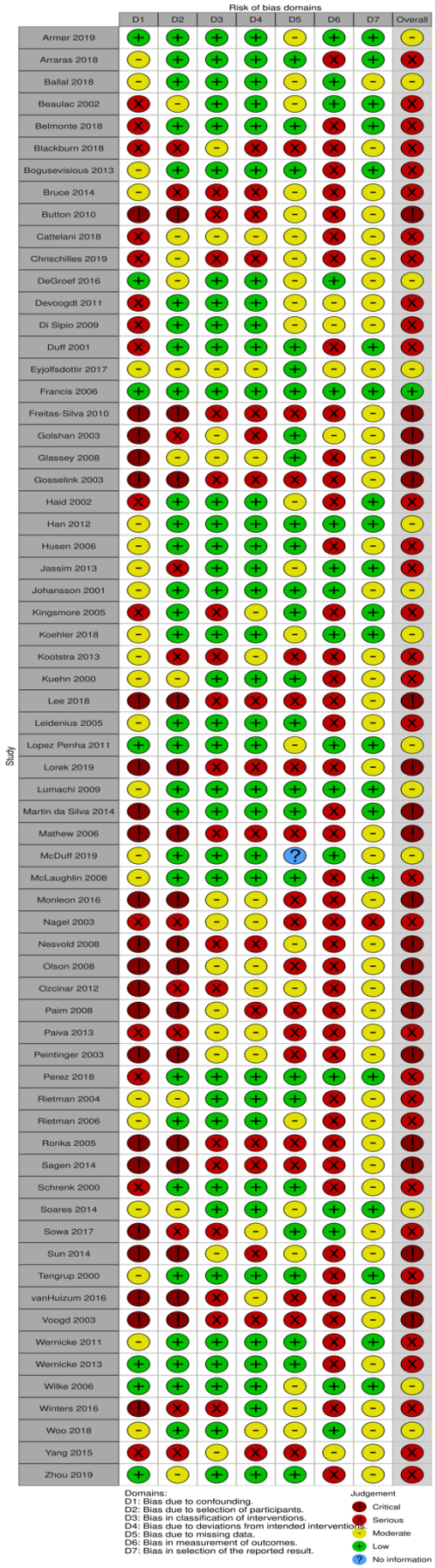
		(CCS) group) Follow up: 1 year post surgery		

RCT, randomised-controlled trial; SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection; RLNR, regional lymph node radiation; LR, lymphoedema rate; LE, lymphoedema; SA, scapula alata; IR, Internal rotator/rotation; ER, external rotator/rotation; HRQOL, health related quality of life; ROM, range of motion; BCS, breast conserving surgery; MRM, modified radical mastectomy; IBR, immediate breast reconstruction; RT, radiotherapy; OL, operated limb; HL, healthy limb; AWS, axillary web syndrome; PM, partial mastectomy; UBF, upper body function; BC, breast cancer; IDDD, Deterioration in Daily Living Activities in Dementia; ASP, arm/shoulder problems; ALN, axillary lymph node; SNBM, sentinel node-based management; RAC, routine axillary clearance; ABPI, Accelerated partial breast irradiation - 30 Gy in five daily fractions; WBI, whole breast irradiation - 50 Gy in 25 fractions, plus a 10 Gy in 5 fractions tumour bed boost; DVH, dose-volume histograms; CPSP, chronic post-surgical pain; UED, upper extremity disability; POD, postoperative day; PPSP, Persistent postsurgical pain; CSS, Constant Shoulder Score; PWB, Physical well-being; CON, closure without flap fixation; FFeS, flap fixation using sutures; FF-G, flap fixation using an adhesive tissue glue; PPBR, pre-pectoral breast reconstruction; IORT, intraoperative radiotherapy; EBRT, external beam whole breast radiotherapy; CF-WBI, conventionally fractionated whole-breast irradiation; HF-WBI, hypofractionated whole-breast irradiation; BCTOS, Breast Cancer Treatment Outcome Scale; BIS, Body Image Scale; EWB, emotional well-being; SWB, social & family well-being; CR, conventional radiotherapy; TT, hypofractionated tomotherapy; TM, total mastectomy; TM-R, immediate reconstruction after total mastectomy; ADM, acellular dermal matrices; NRT, no radiotherapy; BRT, only breast radiotherapy; LD, latissimus dorsi; DIEP, Deep Inferior Epigastric Perforator; ART, breast and axilla radiotherapy; DASH, Disabilities of Arm, Shoulder and Hand Questionnaire; VAS, Visual analogue scale; BMI, body mass index; BIS, bioimpedance spectroscopy; ARM, axillary reverse mapping; TLE, transient lymphoedema; PLE, persistent lymphoedema

Appendix 5. ROB-2 Tool Risk of Bias Assessment



Appendix 6. ROBINS-I Tool Risk of Bias Assessment



Appendix 7. Breast Cancer Now - Exercises After Breast Surgery



Why do I need to do these exercises after my breast surgery?

These exercises can help you regain arm and shoulder movement after surgery and radiotherapy for breast cancer.

Muscles and joints can seize up very quickly if they're not used, so it's important to do these exercises as part of your daily routine.

The exercises can also help:

- Improve symptoms that may be caused by tight scars and cording (when a build-up of scar tissue causes blood vessels to become stuck, and you feel as if you have a tight cord running down your affected arm)
- Prevent long-term problems with arm and shoulder movement, posture and stiffness
- Reduce the risk of lymphoedema (swelling of the arm, hand, breast or chest area caused by a build-up of lymph fluid)

If you're worried about any of these, speak to your breast care nurse or physiotherapist as soon as possible. You should also contact your breast care nurse or physiotherapist as soon as possible if you:

- Had shoulder problems before your surgery
- Develop symptoms of cording after surgery
- Develop a seroma (a collection of fluid that forms under a wound after an operation) after surgery

Who are the exercises suitable for?

The exercises have been developed with the help of breast surgeons, breast care nurses and physiotherapists.

The exercises are suitable for people who have had:

- Breast surgery
- Lymph node removal
- Radiotherapy

If you've recently had a breast reconstruction, or any other type of surgery, talk to your surgeon, breast care nurse or physiotherapist before you start any exercises. You should always follow their advice.

When should I start the exercises?

Ideally, you should start these exercises before your surgery. This is so you can begin to build up flexibility and movement in your arm and shoulder before surgery.

You should then aim to begin the exercises again the day after your surgery.

If you feel unable to start the exercises within a couple of days of your surgery, speak to your breast care nurse or physiotherapist.

Don't worry if you can't manage to do all the exercises every time. You may find the exercises harder at certain times of your treatment, for example during radiotherapy. Do as much as you feel you can but try to do something every day.

How should the exercises feel?

You should not feel pain when doing the exercises. However, a stretching or pulling sensation is normal. The more you do the exercises, the easier they should become.

Always do the warm-up at the start and the cool-down at the end of each session to help avoid injury and prevent stiffness.

You may be advised to take some pain relief before doing the exercises.

If at any time you become concerned about your range of movement or level of discomfort, speak to your breast care nurse or physiotherapist.

When to stop the exercises

Stop doing the exercises and speak to your surgeon, physiotherapist or breast care nurse as soon as possible if you have:

- A seroma
- A wound infection or problems with your wound healing
- Pain that gets worse during these exercises or continues once you've finished them

Start the exercises again when your surgeon, physiotherapist or breast care nurse says it's safe to do so.

How long should I continue doing the exercises?

If you've had surgery

If you've had surgery, keep doing the exercises until you've got back the range of movement you had before your operation. Continue doing the exercises if you're going to have radiotherapy, as they will help your shoulder flexibility.

If you've had radiotherapy

If you've had radiotherapy, it's a good idea to do the exercises for as long as you're still feeling tightness and stiffness.

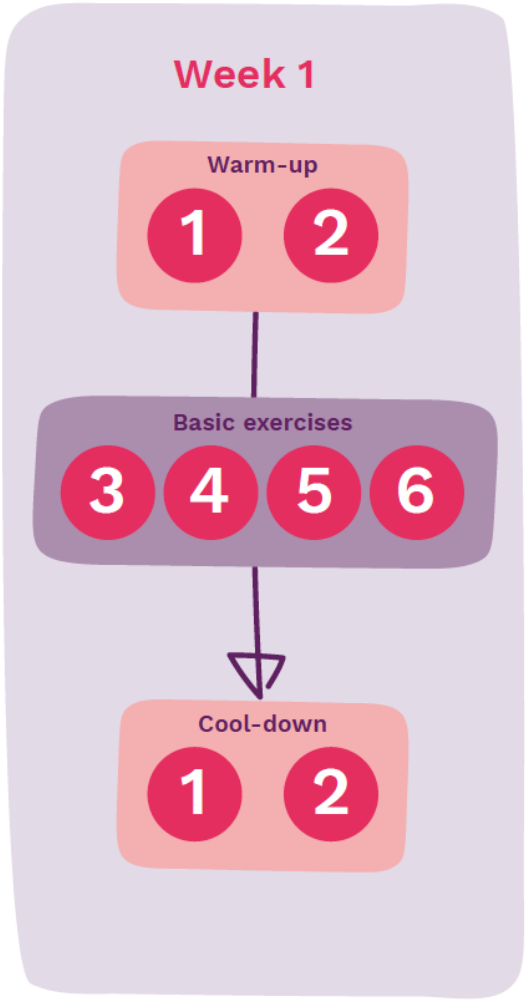
Arm stiffness and weakness can happen after radiotherapy. So continue doing the exercises, or some form of stretching, to maintain your range of movement and use of your arm.

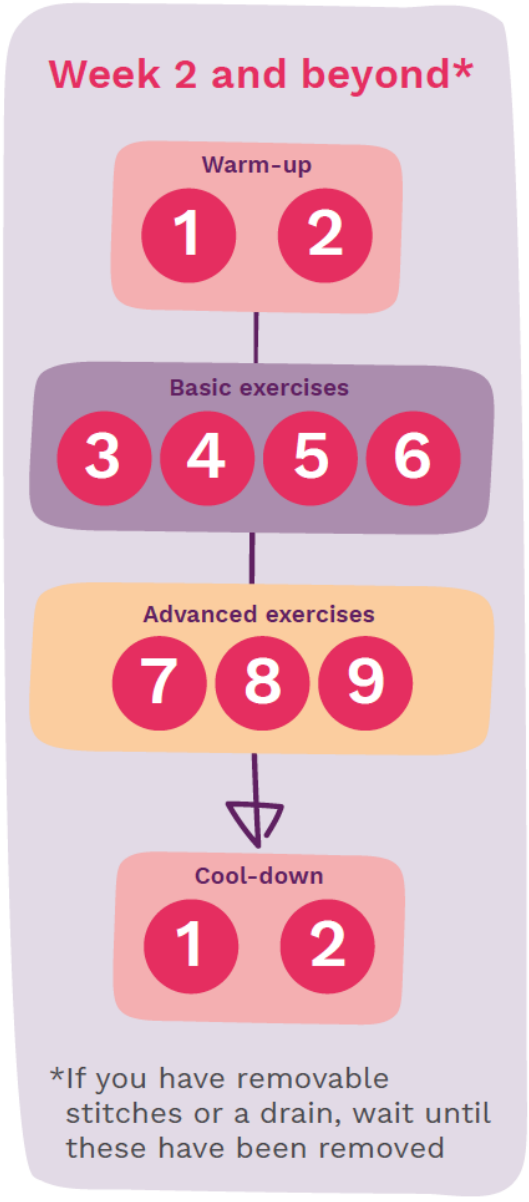
Talk to your breast care nurse or physiotherapist if:

- You're having difficulty getting your range of movement back
- You're not sure how long to continue the exercises
- You have concerns about your recovery after surgery

When to do the exercises

- Repeat each exercise 5 times before moving on to the next one
- Try to do the exercises 3 times a day (morning, around midday and evening) for the first 3 months
- After 3 months, and once you have regained usual movement in your arm, continue exercises 1, 3 and 6 once a day to help reduce discomfort and stiffness in the future





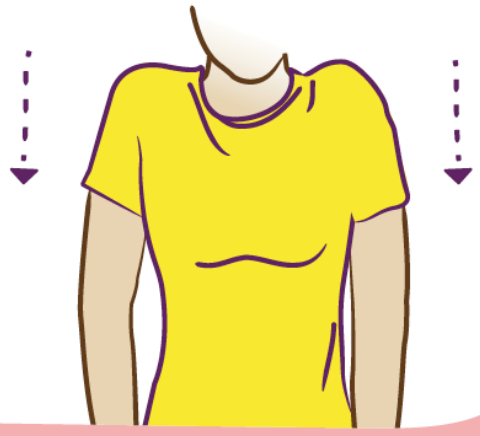
Warm-up and cool-down

Read the information on the other side of the leaflet before you start, especially the section called “When to stop the exercises”.

1

Shoulder shrugs

- Keep your arms loose and relaxed by your sides
- Shrug your shoulders up towards your ears and lower gently back down



2

Shoulder circling

- Keep your arms loose and relaxed by your sides
- Shrug your shoulders up towards your ears, then circle them back and down



Basic exercises

You can do these exercises sitting down or standing up.

During the first week after surgery, do not raise your arms above shoulder level (90 degrees) when doing these exercises.

3

Bent arm forwards

- Bend your elbows and rest your hands lightly on your shoulders
- Raise both your arms forward so they are at right angles to your body
- Lower your elbows slowly



4

Bent arm sideways

- Rest your hands on your shoulders, but this time raise your elbows out to the sides
- Lower your elbows slowly



5 Back scratching

- Hold your arms out to the sides and bend your arms from the elbow
- Slowly reach up behind your back to just under your shoulder blades
- Slowly lower your arms back down to your sides



6 Winging it

- Place your hands behind your head with your elbows pointing forwards
- Bring your elbows back so they're pointing out to the sides, then return to the starting position



Advanced exercises

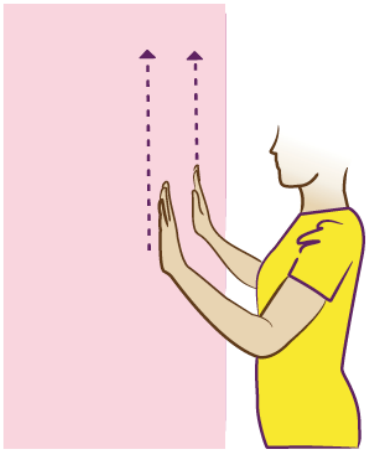
7

Wall climbing

Step 1

With your feet apart, stand close to and facing a wall. Put both hands on the wall at shoulder level.

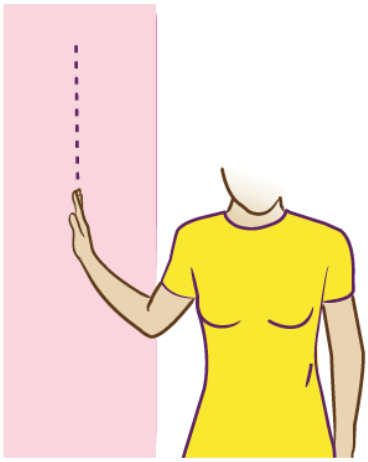
- Looking straight ahead, gradually work your hands up the wall – sliding them or using your fingers to climb. Get as far as you can, to feel a stretch but not pain
- Hold here and count to 10
- Slide your hands back to shoulder level before repeating the exercise



Try to get higher each time.

Step 2

- Stand sideways with your affected side nearest the wall
- Put your hand on the wall, keeping your elbow bent and your shoulders relaxed
- Look straight ahead and gradually creep your hand up the wall as far as you can, allowing your elbow to straighten
- Hold here and count to 10, then lower your hand back down



8 Arm lifts

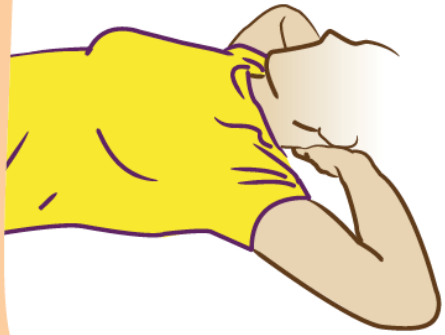
- Lie on the bed or floor with a cushion or pillow to support your head
- Take three or four really deep breaths and concentrate on relaxing your shoulders so they are not hunched up towards your ears
- Clasp your hands together or hold onto a stick or broom handle. Keep your elbows straight and lift your arms up and over your head as far as you feel comfortable
- Hold them here and count to 10, then lower your arms slowly. You may find it useful to put a pillow behind you to support your arms until you're able to get them further back



Alternative

If you have difficulty lying down – for example because of breathlessness – you can do this exercise in a sitting position, leaning back in your chair.

9 Elbow push



- Lie on your back with your hands behind your head and your elbows out to the sides
- Gently push your elbows downwards into the bed or floor as far as is comfortable
- Hold and count to 10, then relax

Alternative

If you have difficulty lying completely flat, you can do this exercise with your head and upper back propped on a few pillows. As you get more comfortable, try to reduce the number of pillows you are using.

Appendix 8. Ethics approval documents

Health Research Authority

London - Bromley Research Ethics Committee

Level 3, Block B
Whitefriars
Lewins Mead
Bristol
BS1 2NT

Tel: 0207 104 8063

Please note: This is the favourable opinion of the REC only and does not allow the amendment to be implemented at NHS sites in England until the outcome of the HRA assessment has been confirmed.

15 January 2021

Ms Aliza Abeles
10th Floor, QEQM Building
St Mary's Hospital, Praed Street
Paddington, London
W2 1NY

Dear Ms Abeles

Study title:	**The Step Home Trial: Utilising Physical Activity Data in the Acute Post-operative Setting**
REC reference:	**15/LO/1038**
Amendment number:	**SA5**
Amendment date:	**6th January 2021**
IRAS project ID:	**177761**

The above amendment was reviewed on 12 January 2021 by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*	
Completed Amendment Tool [BRACELET substantial amendment 5]	SA5	06 January 2021	
Interview schedules or topic guides for participants [Semi-structured interview topic guide v1]	1	02 December 2020	
Participant consent form [Healthy Volunteer Consent form v1]	1	02 December 2020	
Participant consent form [Patient Consent form v5]	5	02 December 2020	
Participant information sheet (PIS) [Healthy volunteers info sheet v1]	1	02 December 2020	
Participant information sheet (PIS) [Patient info sheet v5]	5	02 December 2020	
Research protocol or project proposal [BRACELET Protocol v3]	3	02 December 2020	
Research protocol or project proposal	3		

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

Working with NHS Care Organisations

Sponsors should ensure that they notify the R&D office for the relevant NHS care organisation of this amendment in line with the terms detailed in the categorisation email issued by the lead nation for the study.

Amendments related to COVID-19

We will update your research summary for the above study on the research summaries section of our website. During this public health emergency, it is vital that everyone can promptly identify all relevant research related to COVID-19 that is taking place globally. If you have not already done so, please register your study on a public registry as soon as possible and provide the HRA with the registration detail, which will be posted alongside other information relating to your project.

Statement of compliance

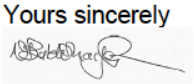
The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at: https://www.hra.nhs.uk/planning-and-improving-research/learning/

IRAS Project ID - 177761:	**Please quote this number on all correspondence**

Yours sincerely



pp

Dr Koula Asimakopoulou (Chair)

Chair

E-mail: bromley.rec@hra.nhs.uk

Enclosures:	*List of names and professions of members who took part in the review*
Copy to:	*Ms Aliza Abeles*

London - Bromley Research Ethics Committee

Attendance at Sub-Committee of the REC meeting on 12 January 2021

Committee Members:

Name	*Profession*	*Present*	*Notes*	
Mrs Frances Riggs	Retired Deputy Head Teacher	Yes		
Dr Jacqueline Tavabie (Vice-Chair)	General Practitioner	Yes		

Also in attendance:

Name	*Position (or reason for attending)*	
Nina Bakhshayesh	Approvals Administrator	

NHS
Health Research Authority

London - Bromley Research Ethics Committee

Temple Quay House
2 The Square
Temple Quay
Bristol
BS1 6PN

23 August 2022

Ms Aliza Abeles
10th Floor, QEQM Building
St Mary's Hospital, Praed Street
Paddington, London
W2 1NY

Dear Ms Abeles

Study title:	**The Step Home Trial: Utilising Physical Activity Data in the Acute Post-operative Setting**
REC reference:	**15/LO/1038**
Amendment number:	**Substantial amendment 6**
Amendment date:	**10 August 2022**
IRAS project ID:	**177761**

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Completed Amendment Tool [Amendment tool]	Substantial amendment 6	10 August 2022
Research protocol or project proposal [Protocol]	Version 4	10 August 2022

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

Working with NHS Care Organisations

Sponsors should ensure that they notify the R&D office for the relevant NHS care organisation of this amendment in line with the terms detailed in the categorisation email issued by the lead nation for the study.

Amendments related to COVID-19

We will update your research summary for the above study on the research summaries section of our website. During this public health emergency, it is vital that everyone can promptly identify all relevant research related to COVID-19 that is taking place globally. If you have not already done so, please register your study on a public registry as soon as possible and provide the HRA with the registration detail, which will be posted alongside other information relating to your project.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

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We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at: https://www.hra.nhs.uk/planning-and-improving-research/learning/

IRAS Project ID - 177761:	**Please quote this number on all correspondence**

Yours sincerely

pp. Bsearle

Chair

E-mail: bromley.rec@hra.nhs.uk

Enclosures:	*List of names and professions of members who took part in the review*
Copy to:	*Ms Aliza Abeles*

London - Bromley Research Ethics Committee

Attendance at Sub-Committee of the REC meeting on 23 August 2022

Committee Members:

Name	*Profession*	*Present*	*Notes*
Mr Colin Allies	General Manager (Retired)	Yes	
Mrs Helen Jane Wood (chaired the meeting)	Solicitor, Chair of the Board of Trustees of Myelopathy.org	Yes	

Also in attendance:

Name	*Position (or reason for attending)*
Bethany Searle	Approvals administrator

Utilising Physical Activity data in the Peri-operative setting

Department of Surgery and Cancer, Imperial College London
Version 4, Date 10/08/2022, IRAS: 177761

Contact
Dr Richard Kwasnicki
Department of Surgery and Cancer
10th Floor QEQM building
St Mary's Hospital
Praed Street
London W2 1NY United Kingdom

Email: rmk107@imperial.ac.uk

Sponsor: Imperial College London

Insurance and Indemnity: Imperial College London

Aims

1. To assess how post-operative physical activity levels correlate with patient recovery and duration of stay following elective surgical operations.
2. To investigate the utility of physical activity data to the post-operative surgical team as part of standard patient observations

Background

The importance of patients ambulating following their surgery has long been recognised as an important factor for post-operative recovery. From the reduction of chest infection and venous thromboembolism, to promoting the maintenance of muscle mass, activity following surgery is an essential component of the enhanced recovery after surgery (ERAS) paradigm.[760] In our pre-trial questionnaire from a multidisciplinary cohort of clinicians at an enhanced recovery workshop 85% of respondents thought that physical activity post operatively was highly important (LCA ERAS event – unpublished data).

Furthermore, physical activity is also used as a marker for assessing recovery after an operation. When a surgical team reviews patients on the post-operative ward round they frequently seek the patient's physical activity status, which is then used in conjunction with other observations (e.g. heart rate, blood pressure, temperature) and patient examination to assess a patient's progress and plan for their discharge home.

Hospitals use technology in a variety of ways to monitor patients, these include more invasive methods (e.g. oesophageal Doppler monitoring for cardiac output) as well as less invasive methods of

observations (e.g. pulse oximeter for heart rate and oxygen saturation measurements, electronic blood pressure monitors). Currently, however, there is no valid objective measure for physical activity, and responses with regard to how a patient's activity is progressing is subjective and can be variable.

Recent advances in technology have led to the emergence of wearable devices that are small and minimally invasive with the ability to monitor not only the basic baseline observations (heart rate, temperature etc.) but also to monitor physical activity levels.[761] The integration of Bluetooth and other wireless technologies have improved communication and interfacing with smart devices such as mobile phones and tablet computers. Such technologies provide a very realistic platform to facilitate the collection and collation of large amounts of data which can be processed and presented to the surgical team to allow objective analysis of patients post-operatively and aid decision-making.

Some groups have begun to investigate activity levels using wearable sensors, for example monitoring of physical activity in patients undergoing ambulatory pH monitoring, [762] and the development of an objective mobility assessment tool using a wearable motion sensor after lower limb reconstruction.[763] However, there has been minimal objective information gained with regard to inpatient activity and how this correlates both with the duration of hospital stay and longer term outcomes.

One study, [764] looking at day case laparoscopic cholecystectomy patients used accelerometery data to monitor physical activity levels one week before and one week following surgery. They found that the majority of patients did not return to their baseline activity level until at least one week following surgery. A further study, [593] looking at cardiac surgery in-patients showed a correlation between the number of steps a patient took each day following surgery and their length of hospital stay.

This study will provide further evidence for the usability and utility of wearable sensors in the surgical setting. It will provide supporting evidence for surgeons to confidently analyse and assess patients in hospital, allowing for safe and expedient discharge home as well as identify high-risk patients who are likely to require extra support and surveillance in the community setting.

Hypotheses

1. Inpatient physical activity is a predictor of length of stay
2. Physical activity data has important utility as an objective measurement for surgical teams

Methods

Trial Design

A single-centre observational study will be conducted at Imperial College NHS healthcare Trust (UK). The work will be split into two phases.

Phase One

250 patients due for elective surgical procedures will be recruited from Imperial College NHS Healthcare Trust outpatient general surgical clinics. Potential participants will be given a participant information sheet and then time to consider whether they wish to participate. If patients wish to participate they will have the opportunity to ask questions before signing a consent form.

At the pre-operative assessment (1-2 weeks prior to operation) participants will be given a wrist-worn motion sensor (AX3 accelerometer, Axivity, Newcastle upon Tyne, UK) together with an information sheet to explain how and when they must wear it. The participants will also be given up to 3 health surveys including Short Form 36, DASH, and EQ5D to complete as well as a prepaid envelope to return the sensors and questionnaires if patients are not seen by researchers in the hospital post-surgery.

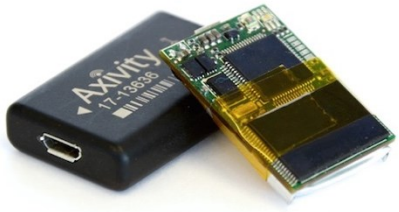


Figure 1. Axivity AX3 logging accelerometer

The AX3 is an ADXL345 tri-axial accelerometer manufactured by Analog Devices, weighing 11g and contains a non-volatile flash memory chip linked by a USB enabled microcontroller. A temperature sensor, ambient light sensor, real time clock (RTC) and lithium polymer battery are also integrated into the sealed polycarbonate puck. The product is compliant with the Directive 2004/108/ EC; (CE marked). The product has been tested to BS EN 61000-6-1:2007 and BS EN 61000-6-3:2007.



Figure 2. Axivity AX3 accelerometer worn on the wrist.

Participants will be asked to wear the wrist-worn sensor at all times (it is showerproof) except if they are swimming or taking a bath, and will be advised to go about their normal daily activity. The patient will continue to wear the sensor on admission and throughout their hospital stay. It will be collected back just prior to discharge or they may return it via a pre-paid envelope if the patient does not stay as an in-patient or is not seen whilst an in-patient.

At follow-up clinic, 2-3 weeks post-operatively, patients will be asked to complete up to 3 health surveys including Short Form 36, DASH, and EQ5D to complete. These may be repeated at a later date.

Staff (theatre, recovery and ward) will be briefed before patient recruitment is started and there will be a feedback period for both staff and patients early in the data collection period to ensure that there are no issues with patient safety or any other concerns that need to be addressed. The first 5 patients will be asked to complete a feedback form at their follow-up patient clinic in order to identify any issues or concerns early on in the data collection period.

The SF-36[765], which has been validated as a measure of post-operative recovery, [766] assesses eight health concepts including physical activity, mental health and general health perceptions. The questionnaire yields scores (0-100) for each concept which are then combined to produce a physical component score and a mental component score.
The EQ5D survey is another measure of quality of life, consisting of 6 questions. The Disabilities of the Arm, Shoulder and Hand (DASH) questionnaire is a measure of arm function which may be reduced after surgery.

Documentation of daily activities: Among the patients recruited into the study, those who feel comfortable using a smartphone will be invited to download an application developed by the research team, and use it to record the activities performed during each day, selecting them from a predefined list of activities that are of interest to the study. The application will record the starting and finishing time for each activity. No other data will be recorded or provided to the research team through this application

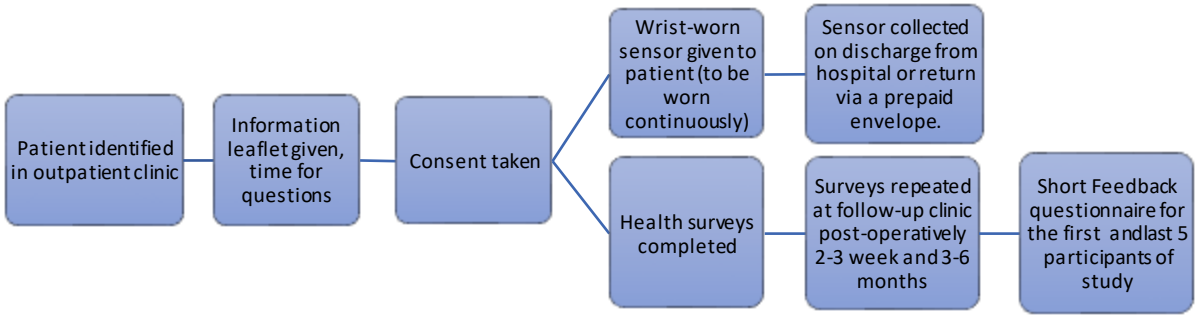
Some of the patients may be invited to take part in a semi-structured interview. The session may last for 45-60 minutes. The session will be done either face to face (when the participant attends their follow up clinic), by telephone calls or video calls. The patients will be risk-stratified and additional face to face meeting will be avoided for patients with high risk. If the interview is done face to face, members of the research team will wear personal protective equipment (PPE) and follow the protocol as per Public Health of England guidance. The session will be recorded and will be stored on a secure encrypted database and will be completely anonymised.

Inclusion	**Exclusion**
Undergoing elective surgical operative procedure	Unable to mobilise independently
	Have medical condition characterized by movement disorder e.g. Parkinson's Disease
	Unable to understand and complete the SF-36 (unless interpreter present) or lack capacity to consent
	Psychological Disorder
	Aged less than 18

Consenting

The principal researcher will take consent (following an initial verbal consent by the surgeon indicating the patient's agreement to be contacted by the researcher as well as for their records to be viewed by the researcher). The patient will have time in the clinic to read the information sheet, ask any questions and decide if they wish to participate. If the patient is happy then written consent will be taken (including consenting to fully understanding the participant information sheet).

Participant schedule



Outcome measures

Primary outcomes

- Pre and post-operative (inpatient) physical activity levels
- Length of stay

Secondary:

- Self-reported quality of life: SF-36 score, broken down into physical and mental component scores, EQ5D score, DASH score
- 30 day readmission
- Complications: Wound infection, chest infection, abdominal/pelvic collection, deep vein thrombosis/pulmonary embolism, myocardial infarction, need for reoperation/further procedure

Patient demographics will be collected via medical records. This includes medical history (including surgical history, comorbidities) and biometrics such as age, gender, weight, height.

Data Analysis

The sensor data will be analysed using software compatible with the specific accelerometer sensor. The processing that is carried out provides more easily understandable and manageable values for both statistical analysis and graphical representation of results.

SPSS (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY) will be used to analyse the data.

Data we will collect includes

- Overall physical activity level
- Frequency and duration of bursts of physical activity
- Intensity levels of activity each hour and day
- Patient activity behaviour – times of day activity occurs

Data we will analyse

- Correlation between pre-operative +/- post-operative activity levels and length of stay – Spearman Rank Correlation
- Correlation between the difference between pre-op and post-op activity levels and length of stay - Spearman Rank Correlation
- Correlation between physical activity levels and the SF-36 score, 30 day readmission rates and complications - Spearman Rank Correlation

Healthy volunteer recruitment

A group of up to 20 participants will be identified by advertising the study between students at Imperial College London. Participants (healthy volunteers) who feel comfortable using a smartphone will be invited to download an application developed by the research team, and use it to record the activities performed during each day, selecting them from a predefined list of activities that are of interest to the study. The mobile application will record the starting and finishing time for each activity. No other data will be recorded or provided to the research team through this application.

Exclusion criteria for participation in the study will be recent surgery or other impairment that might limit mobility of the upper limb. A dedicated informed consent form has been created for this group of participants. After signing the informed consent, participants will be given two wrist-worn sensors and will follow the same data collection protocol as the NHS patients, No data from clinical questionnaires will be collected from this group.

Phase Two (optional)

10-15 patients will be recruited and will follow the exact same participant schedule.

The LG Watch Urbane 2nd Edition Verizon W200V will be used instead of the AX3 axivity sensor. This is a watch which can tell the time but can also monitor and display the patient's physical activity as it contains an accelerometer, gyroscope and barometer.

The watch has been modified by Google to include only the necessary functions for this study, this saves battery power and allows the watch to require less charging. Patients will be taught how to change between the different functions of the watch if they so wish, but they will not be asked to use any functions specifically. Participants will have to charge the watch once a day, and are asked to wear it at all times except in the shower, bath or when swimming as it is not water resistant. Each watch will be set up anonymously with just an ID number and no patient identification details.

A semi-structured feedback session will take place at the first clinic follow-up after the operation. The patients will be asked to fill in a questionnaire/feedback survey to help us understand how patients view this data and its uses. We will also ask them to fill in a 'system usability scale' This is a validated technology survey used to assess how easily a technology can be used by participants. If the patient has any extra comments there will be space on the feedback questionnaire to leave these, alternatively any comments they make verbally will be noted by the researcher. Clinicians (doctors, nurses, physiotherapists) will be asked to look at the data via an app/website both at the time of inpatient stay and on discharge. We will then ask the members of the team to fill in a questionnaire/feedback survey and the 'System usability scale' in order to find out the utility of the data and what clinical teams think about the usability of the data. Again extra comments and feedback can be documented on the feedback questionnaire or given verbally to the researcher.

Ethical Approval

The Chief Investigator has obtained approval from the NRES Committee London Bromley. The study has also been submitted for Site Specific Assessment (SSA) at Imperial College Healthcare NHS Trust. The study will be conducted in accordance with the recommendations for physicians involved in research on human subjects adopted by the 18th World Medical Assembly, Helsinki 1964 and later revisions.

Confidentiality

The Chief Investigator will preserve the confidentiality of participants taking part in the study and is registered under the Data Protection Act.

11.1

Indemnity

Imperial College London holds negligent harm and non-negligent harm insurance policies which apply to this study.

Sponsor

Imperial College London will act as the main Sponsor for this study. Delegated responsibilities will be assigned to the NHS trusts taking part in this study.

Funding

Imperial College London are funding this study.

Audits

The study may be subject to inspection and audit by Imperial College London under their remit as sponsor and other regulatory bodies to ensure adherence to GCP and the NHS Research Governance Framework for Health and Social Care (2nd edition).

Publication Policy

We intend to publish the results of this study in high quality peer-reviewed international journals and at a similar standard conferences. In addition if the results could lead to improvement in clinical practice we would look to cite the publication or provide a separate summary for relevant clinical bodies, including advisers of local protocol.

Clinical Impact of Research

This study will provide objective evidence of a link between physical activity and length of hospital stay. This will act as a clear rationale for developing a system to provide activity observations for doctors. Giving hospital staff access to patient activity data has potential utility for surgeons, physicians and other allied healthcare professionals. As technology progresses further, collection of all patient 'observations' is likely to become possible using wearable devices.

Summary

This project will provide supporting evidence for surgeons to confidently, and safely, expedite patient discharge from hospital. This boasts advantages financially, freeing up bed space, and also to the patients themselves, both physically and psychologically. Furthermore, it may help to identify those at high-risk who require extra support in the community setting.

Appendices

A. Phase One

a. Participant Information sheet V5
b. Patient Consent form V5
c. Healthy Volunteer Information sheet V1
d. Healthy Volunteer Consent form V1
e. Semi-structured Interview Topic guide
f. Patient Feedback form V1.1
g. Clinician Information sheet V1.2
h. Clinician Consent form V1.2
i. Clinician Feedback form V 1.1

B. Phase Two
a. Participant Information sheet V2.2
b. Patient Consent form V1.2
c. Patient Feedback form V1.1
d. Clinician Information sheet V1.2
e. Clinician Consent form V1.2
f. Clinician Feedback form V1.1

C. SF-36 Questionnaire, EQ5D and DASH surveys
D. System Usability Scale

Selected References

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3. Kwasnicki RM, Ley Greaves R, Ali R, Gummett PA, Yang GZ, Darzi A, et al. Implementation of objective activity monitoring to supplement the interpretation of ambulatory esophageal PH investigations. Diseases of the esophagus : official journal of the International Society for Diseases of the Esophagus / ISDE. 2015.

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EQ-5D-5L

Health Questionnaire

English version for the UK

Under each heading, please tick the ONE box that best describes your health TODAY.

MOBILITY

I have no problems in walking about ❑
I have slight problems in walking about ❑
I have moderate problems in walking about ❑
I have severe problems in walking about ❑
I am unable to walk about ❑

SELF-CARE

I have no problems washing or dressing myself ❑
I have slight problems washing or dressing myself ❑
I have moderate problems washing or dressing myself ❑
I have severe problems washing or dressing myself ❑
I am unable to wash or dress myself ❑

USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*

I have no problems doing my usual activities ❑
I have slight problems doing my usual activities ❑
I have moderate problems doing my usual activities ❑
I have severe problems doing my usual activities ❑
I am unable to do my usual activities ❑

PAIN / DISCOMFORT

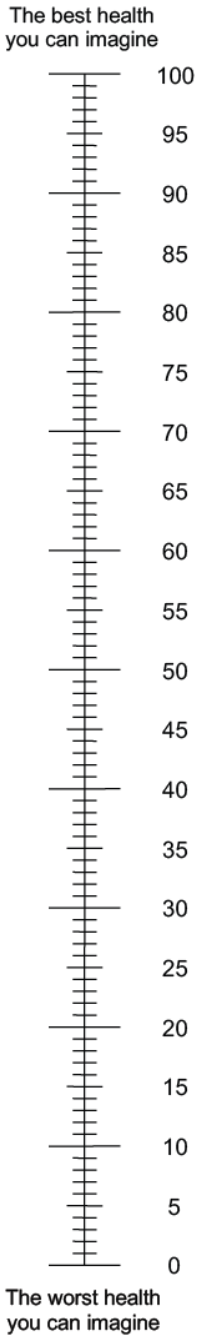
I have no pain or discomfort ❑
I have slight pain or discomfort ❑
I have moderate pain or discomfort ❑
I have severe pain or discomfort ❑
I have extreme pain or discomfort ❑

ANXIETY / DEPRESSION

I am not anxious or depressed ❑
I am slightly anxious or depressed ❑
I am moderately anxious or depressed ❑
I am severely anxious or depressed ❑
I am extremely anxious or depressed ❑

- We would like to know how good or bad your health is TODAY.
- This scale is numbered from 0 to 100.
- 100 means the best health you can imagine.
  0 means the worst health you can imagine.
- Mark an X on the scale to indicate how your health is TODAY.
- Now, please write the number you marked on the scale in the box below.

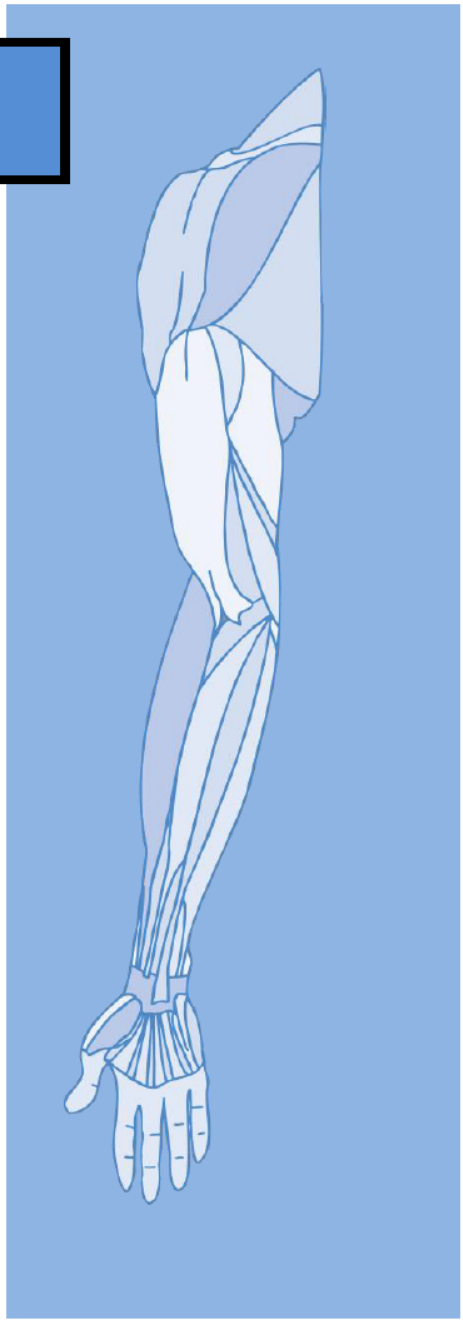
YOUR HEALTH TODAY = ☐



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DISABILITIES OF THE ARM, SHOULDER AND HAND – British English

THE DASH



INSTRUCTIONS

This questionnaire asks about your symptoms as well as your ability to do certain activities.

Please answer every question, based on your condition in the last week, by circling the appropriate number.

If you did not do an activity in the last week, please give your best guess which response would be most accurate.

It doesn't matter which hand or arm you use to do the activity; please answer based on your ability regardless of how you do the task.

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British English translation courtesy of: Prof Alison Hammond[1], Dr Yeliz Prior[1], Prof Sarah Tyson[2]
[1] Centre for Health Sciences Research, University of Salford;
[2] Centre for Long term Conditions Research, University of Manchester, UK.

DISABILITIES OF THE ARM, SHOULDER AND HAND – British English

Please rate your ability to do the following activities in the last week by circling the number below the appropriate response.

	NO DIFFICULTY	*MILD DIFFICULTY*	*MODERATE DIFFICULTY*	*SEVERE DIFFICULTY*	*UNABLE*
1 Open a tight or new jar	1	2	3	4	5
2 Write	1	2	3	4	5
3 Turn a key	1	2	3	4	5
4 Prepare a meal.	1	2	3	4	5
5 Push open a heavy door	1	2	3	4	5
6 Place an object on a shelf above your head	1	2	3	4	5
7 Do heavy household jobs (e.g. wash windows, clean floors)	1	2	3	4	5
8 Garden or outdoor property work	1	2	3	4	5
9 Make a bed	1	2	3	4	5
10 Cary a shopping bag or briefcase	1	2	3	4	5
11 Carry a heavy object (over 10 lbs/ 5kgs)	1	2	3	4	5
12 Change a lightbulb overhead	1	2	3	4	5
13 Wash or blow dry your hair	1	2	3	4	5
14 Wash your back	1	2	3	4	5
15 Put on a jumper	1	2	3	4	5
16 Use a knife to cut food	1	2	3	4	5
17 Recreational activities which require little effort (e.g. card playing, knitting, etc)	1	2	3	4	5
17 Recreational activities which require you to take some force or impact through your arm, shoulder or hand (e.g. golf, hammering, tennis etc)	1	2	3	4	5
18 Recreational activities in which you move your arm freely (e.g. playing Frisbee, badminton etc)	1	2	3	4	5
20 Manage transport needs (getting from one place to another)	1	2	3	4	5
21 Sexual activities	1	2	3	4	5

	NOT AT ALL	SLIGHTLY	MODERATELY	Quite a bit	Extremely
22 During the past week, *to what extent* has your arm, shoulder or hand problem interfered with your normal social activities with family. friends, neighbours or groups? *(circle number)*	1	2	3	4	5

	NOT LIMITED AT ALL	SLIGHTLY LIMITED	MODERATELY LIMITED	VERY LIMITED	UNABLE
23 During the past week, were you limited in your work or other regular daily activities as a result of your arm, shoulder or hand problem? *(circle number)*	1	2	3	4	5

Please rate the severity of the following symptoms in the last week *(circle number)*	NONE	MILD	MODERATE	SEVERE	EXTREME
24 Arm, shoulder or hand pain	1	2	3	4	5
25 Arm, shoulder or hand pain when you do any specific activity	1	2	3	4	5
26 Tingling (pins and needles) in your arm, shoulder or hand	1	2	3	4	5
27. Weakness in your arm, shoulder or hand	1	2	3	4	5
28 Stiffness in your arm, shoulder or hand	1	2	3	4	5

	NO DIFFICULTY	MILD DIFFICULTY	MODERATE DIFFCULTY	SEVERE DIFFCULTY	SO MUCH DIFFICULTY THAT I CAN'T SLEEP
29 During the past week, how much difficulty have you had sleeping because of the pain in your arm, shoulder or hand? *(circle number)*	1	2	3	4	5

	STRONGLY DISAGREE	DISAGREE	NEITHER AGREE OR DISAGREE	AGREE	STRONGLY AGREE
30 I feel less capable, less confident or less useful because of my arm, shoulder or hand problem *(circle number)*	1	2	3	4	5

DASH DISABILITY/SYMPTOM SCORE = [(sum of n responses)–1] x 25 (where n is the number of completed responses)
n

A DASH score may not be calculated if there are greater than 3 missing items.

3

DISABILITIES OF THE ARM, SHOULDER AND HAND – British English

WORK MODULE (OPTIONAL)

The following questions ask about the impact of your arm, shoulder or hand problem on your ability to work (including home-making if that is your main work role).

Please indicate what your job / work is: _____

❑ I do not work (you may skip this section).

Please circle the number that best describes your physical ability in the past week. Did you have any difficulty:

	NO DIFFICULTY	*MILD DIFFICULTY*	*MODERATE DIFFICULTY*	*SEVERE DIFFICULTY*	*UNABLE*
1. Doing your work in your usual way?	1	2	3	4	5
2. Doing your usual work because of arm, shoulder or hand pain?	1	2	3	4	5
3. Doing your work as well as you would like?	1	2	3	4	5
4. Spending your usual amount of time doing your work?	1	2	3	4	5

SPORTS/PERFORMING ARTS MODULE (OPTIONAL)

The following questions relate to the impact of your arm, shoulder or hand problem on playing *your musical instrument or sport or both*. If you play more than one sport or instrument (or play both), please answer with respect to that activity which is most important to you.

Please indicate the sport or instrument which is most important to you: _____

❑ I do not play a sport or an instrument. (You may skip this section).

Please circle the number that best describes your physical ability in the past week. Did you have any difficulty:

	NO DIFFICULTY	*MILD DIFFICULTY*	*MODERATE DIFFICULTY*	*SEVERE DIFFICULTY*	*UNABLE*
1. Playing your instrument or sport in your usual way?	1	2	3	4	5
2. Playing your musical instrument or sport because of arm, shoulder or hand pain?	1	2	3	4	5
3. Playing your instrument or sport as well as you would like?	1	2	3	4	5
4. Spending your usual amount of time practising or playing your instrument or sport?	1	2	3	4	5

Scoring the optional modules: add up the assigned values for each response;
Divide by 4 (number of items); subtract 1; multiple by 25.
An optional module score may <u>not</u> be calculated if there are any missing items.

Site: Imperial College Healthcare NHS Trust
Patient Hospital Number:
Subject Identification Number for this trial:

CONSENT FORM

Version 5, Date 02/12/2020

Title of Project:
Utilising Physical Activity Data in the Peri-operative Setting

Name of Principal Investigator:
Dr Richard Kwasnicki
Department of Surgery and Cancer
10th Floor QEQM building
St Mary's Hospital
Praed Street
London W2 1NY United Kingdom

Email: rmk107@ic.ac.uk

Please initial box

1. I confirm that I have read and understand the information sheet dated 02/12/2020 version 5 for the above study and have had the opportunity to ask questions. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that sections of any of my medical notes may be looked at by responsible individuals from Imperial College, the NHS Trust or from regulatory authorities where it is relevant to my taking part in this research. ☐

4. I give permission for these individuals to access my records that are relevant to this research. ☐

5. I give/do not give **(delete as applicable)** consent for information collected about me to be used to support other research in the future, including those outside of the EEA. ☐

6. I agree to take part in the above study. ☐

7. I agree to the audio/video-recording of my interview after I complete the study if I am invited. ☐

8. I agree to record the starting and finishing time of specific activities of interest to the study through a smartphone application if I am invited. I understand that no personal data, other than the starting and finishing time of the activities will be recorded by the application and provided to the research team. ☐

_____	_____	_____
Name of Participant	Date	Signature
_____	_____	_____
Name of Person taking consent	Date	Signature

(if different from researcher)

_____	_____	_____
Researcher	Date	Signature

(COPIES: 1 for participant, 1 for researcher, 1 for medical notes

PARTICIPANT INFORMATION SHEET

Research Study Title: Utilising Physical Activity data in the Peri-operative setting

Version 5, 02/12/2020

Contact
Dr Richard Kwasnicki
10th Floor QEQM Building
St Mary's Hospital
Praed Street
London W2 1NY
United Kingdom
Email: rmk107@imperial.ac.uk

REC reference: 15/LO/1038
IRAS project ID: 177761

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take your time to decide whether or not you wish to take part.

Thank you

Summary

Why?

We are researching how peoples' activity levels change before and after surgical operations. This is important to help us understand how people recover from operations and to help doctors make decisions about these patients in the future.

What?

We are asking participants to wear a light wrist-worn activity monitor/sensor to measure how much movement and activity they undergo daily both before and after their operations.
The activity monitor will be worn for two weeks at home before the operation, and in the hospital after the operation.

Who?

Anyone undergoing a surgical procedure is eligible to take part in this study.

Where?

This study is being conducted at Imperial College Healthcare NHS Trust.

1. What is the purpose of the study?

We are interested in seeing how patients' movement and activity levels change around the time of surgical procedures.

The movements of study participants will be measured using a light wrist-worn activity monitor/sensor. This will help doctors to understand how people recover from operations and will help us to make decisions in the future about patients after they have had surgical procedures.

2. Why have I been chosen?

You have been invited to take part in this study because you are undergoing a surgical procedure at Imperial College Healthcare NHS Trust.

3. Do I have to take part?

You can decide whether or not to take part. If you decide to take part you will be asked to sign a consent form. You are still free to withdraw at any time without giving a reason.

Not participating or withdrawing from this study will not affect your current clinical care or any future clinical care.

4. What will happen to me if I take part?

Please see the following timetable:

1	You have received this participant information sheet and have time to ask any questions in the initial outpatient clinic appointment
2	You will come to the normal pre-admission clinic that all patients attend before their operation. At this point you will have the opportunity to ask any questions to the researcher before you decide whether or not to take part. If you are happy to participate you will be asked to read and sign a consent form.
3	Once you have signed the consent form you will be asked to complete one or more surveys (including SF-36, EQ5D and DASH)
4	You will be given a small and light wrist-worn activity monitor/sensor to wear. This should be worn continuously on your wrist (it is showerproof) except if you go swimming or take a bath. Please continue to go about your normal daily activity. Some participants may be asked to record the activities performed during each day using a smartphone application, selecting them from a predefined list of activities that are of interest to the study. You may choose to install the application provided on your personal device, or use one provided by the research team. The application will record the starting and finishing time for each activity. No other data will be recorded or provided to the research team through this application.
5	You will be admitted to the hospital on the day of surgery. Please continue to wear the sensor while you are in the hospital. The activity monitor/sensor will be collected from you at your post operative appointment. **It is essential that you return the activity monitor/sensor to the researchers at the end of the study.** **If the device is broken, lost or stolen please contact the researcher as soon as possible and we will try to replace it with a new device.**
6	You will attend the usual follow-up clinic 2-3 weeks after the operation. At this time we will ask you to complete another health survey. You will also be asked to fill in a short feedback form to ensure any issues or concerns are addressed early on in the study. If you have concerns or worries at any other time please contact Dr Richard Kwasnicki (as above).

The total amount of time that you will wear the activity monitor/sensor will be 2-6 weeks. You will be involved in the study for approximately 6 weeks, until you have been seen in the outpatient clinic for follow-up and have repeated the questionnaire forms. At this point you will no longer be involved in the research.

You will meet a researcher on 2-3 occasions. The first time will be at your regular outpatient clinic after you have seen the surgical team. You will then meet again at the pre-admission clinic for a formal consent form to be signed, as well as being given the wrist-worn activity monitor/sensor. At your post-operative appointment the researcher will collect the activity monitor/sensor from you.

Taking part in this study in no way changes or affects the standard of clinical care you will receive now or in the future.

It is highly unlikely that you will lose mental capacity during the study. However, should you do so, we will take you out of the study. If data has been collected before this, we may still use the data in the study to make sure that we present the actual data collected.
Participating in the study does **NOT** increase chances of losing capacity. There are no risks associated with participation.

Some of you may be invited to participate in an interview after you complete the study in order for us to collect feedback about your experiences after surgery and your opinions about the use of wearable sensors. The session may last for 45-60 min. The interview will be done either face to face (when you attend your follow up clinics), by telephone calls or video calls. The session will be recorded and will be stored on a secure encrypted database and the recording will be pseudo anonymised through a coding system.

6. What happens to the data collected?

The data collected from the activity monitor is the amount and type of activity done throughout the day. Other data we will collect in this study will include the operation you are having, other medical conditions you suffer from and how you recover both in hospital and at home after the operation. This information will be used only by the researchers in this project.

Data collected will be stored on a secure encrypted database. The data will be pseudoanonymised through a coding system. The data will be processed to give the investigators a more manageable value of physical activity for each participant. **Important**: **none of the data collected from the study will be used to influence your clinical management**. You will receive the same care whether you participate or not. The smartphone application will record the starting and finishing time for each activity. No other data will be recorded or provided to the research team through this application.

The interviews will be recorded, transcribed and stored on a secure encrypted database. Transcription services will be outsourced to an agency that Imperial College usually uses for their transcription requirements. The recordings will be pseudo-anonymised through a coding system.

7. What are the possible benefits and disadvantages/risks of taking part?

Benefits

There are no specific benefits to taking part in this study. However, participants may find some satisfaction knowing that they are participating in research that is likely to help improve decision making by doctors in the future.

Disadvantages/risks

The wrist-worn activity monitor/sensor is a CE approved device and is completely safe. The monitor/sensor does not affect any other electrical equipment that you might carry.

We will not ask you to attend any extra clinics or meetings above normal standard care.

We understand that taking part in a research study can lead to increased anxiety, and as such we would like to invite you to call the support number on this information sheet should you have any concerns.

8. What will happen if I don't want to carry on with the study?

The decision to take part in this study is entirely voluntary and you can change your mind at any time. Any decision you take to withdraw from the study will not affect the care you receive now or in the future.
If you do withdraw from the study information already collected may still be used.

9. What if something goes wrong?

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation, but you may have to pay your own legal costs. The normal National Health Service complaints mechanisms will still be available to you.

If you are still not satisfied with the response, you may contact the Imperial AHSC Joint Research Office.

10. Will my participation in this study be kept confidential?

All information collected about you during the course of the research is strictly confidential. Any information about you which leaves the clinic will have your name and details removed.

11. What will happen to the results of the research study?

The results of the research will be analysed and published in scientific journals. No individual participants will be identifiable from any report or publication. We will happily provide you with a copy of the results after publication upon request.

12. Who is organising and funding the research?

The research is being organised and funded by Imperial College London.

13. Who has reviewed the study?

This study has been reviewed and approved by the Research Ethics Committee NRES committee London – Bromley.

14. How will we use information about you?

Imperial College London is the sponsor for this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. Imperial College London will keep your personal data for:

- 10 years after the study has finished in relation to data subject consent forms.
- 10 years after the study has completed in relation to primary research data.
- The tapes/recordings of patient interviews will be retained for 10 years and the patient identifiable data will be pseudo anonymised through a coding system.

15. Legal basis

As a university we use personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use your data in the ways needed to conduct and analyse the research study.

Health and care research should serve the public interest, which means that we have to demonstrate that our research serves the interests of society as a whole. We do this by following the UK Policy Framework for Health and Social Care Research

16. International Transfers

There may be a requirement to transfer information to countries outside the European Economic Area (for example, to a research partner). Where this information contains your pseudo anonymised data, Imperial College London will ensure that it is transferred in accordance with data protection legislation. If the data is transferred to a country which is not subject to a European Commission (**EC**) adequacy decision in respect of its data protection standards, Imperial College London will enter into a data sharing agreement with the recipient organisation that incorporates EC approved standard contractual clauses that safeguard how your data is processed.

17. Sharing your information with others

For the purposes referred to in this privacy notice and relying on the bases for processing as set out above, we may share pseudo anonymised data with certain third parties.

- Other College employees, agents, contractors and service providers (for example, suppliers of printing and mailing services, email communication services or web services, or external transcribers or suppliers who help us carry out any of the activities described above). Our third party service providers are required to enter into data processing agreements with us. We only permit them to process your data for specified purposes and in accordance with our policies.

18. Complaint

If you wish to raise a complaint on how we have handled your personal data, please contact Imperial College London's Data Protection Officer via email at dpo@imperial.ac.uk, via telephone on 020 7594 3502 and/or via post at Imperial College London, Data Protection Officer, Faculty Building Level 4, London SW7 2AZ.

If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO). The ICO does recommend that you seek to resolve matters with the data controller (us) first before involving the regulator.

19. Contact Richard Kwasnicki (details above) for further information and support OR for independent advice please contact:

Patient Advice and Liaison Service (PALS)
Ground floor of Queen Elizabeth the Queen Mother (QEQM) wing, St Mary's Hospital. Open Monday to Friday, from 10.00 to 16.00
PALS address: PALS manager, Ground floor, Clarence wing, St Mary's Hospital, London W2 1NY **Telephone:** 020 3312 7777, Monday to Friday from 09.00 to 17.00 **Text phone:** 07962 985118 **Fax:** 020 3312 1753 **Email:** pals@imperial.nhs.uk

THANK YOU FOR PARTCIPATING IN THE STUDY !

Participants will be given a copy of the consent form and information sheet for their own records.

Informed Consent Form for Adults with Capacity

Version 1, Date 02/12/2020

Site: Dep. Mechanical Engineering, Imperial College London
Subject Identification Number for this trial:

Study Protocol Number:

Title of Project:
Utilising Physical Activity Data in the Peri-operative Setting

Name of Researcher:
Prof. Ferdinando Rodriguez y Baena
Department of Mechanical Engineering
Room 718, City and Guilds Building
Imperial College London
London, SW7 2AZ, UK

Email: f.rodriguez@imperial.ac.uk

		Please initial box
1.	I confirm that I have read and understand the subject information sheet dated.....02.12.20..... version .....1..... for the above study and have had the opportunity to ask questions which have been answered fully.	☐
2.	I understand that my participation is voluntary and I am free to withdraw at any time, without giving any reason and without my medical care or legal rights being affected.	☐
3.	I give permission for these individuals to access my records that are relevant to this research.	☐
4.	I give/do not give **(delete as applicable)** consent for information collected about me to be used to support other research in the future, , including those outside of the EEA.	☐
5	I give / do not give **(delete as applicable)** for my pseudo anonymised data to be sent to other organisations, including these outside of the EEA	☐
6.	I consent to take part in the above study.	☐
7.	I give/do not give (delete as applicable) consent to record the starting and finishing time of specific activities of interest to the study through a smartphone application if I am invited. I understand that no personal data, other than the starting and finishing time of the activities will be recorded by the application and provided to the research team.	☐

8. I give/do not give (delete as applicable) consent to being contacted to potentially taking part in other research studies. ☐

_____	_____	_____
Name of Subject	Signature	Date
_____	_____	_____
Name of Person taking consent	Signature	Date

1 copy for subject; 1 copy for Principal Investigator;

PARTICIPANT INFORMATION SHEET (non-NHS)

Research Study Title: Utilising Physical Activity data in the Peri-operative setting

Version 1, 02/12/2020

Contact
Prof. Ferdinando Rodriguez y Baena
Department of Mechanical Engineering
Room 718, City and Guilds Building
Imperial College London
London, SW7 2AZ, UK

Email: f.rodriguez@imperial.ac.uk

REC reference: 15/LO/1038
IRAS project ID: 177761

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take your time to decide whether or not you wish to take part.

Thank you

Summary

Why?

We are researching how peoples' activity levels change before and after surgical operations. This is important to help us understand how people recover from operations and to help doctors make decisions about these patients in the future. As part of this research we are also collecting data from healthy student volunteers, to use as reference and to help us develop analytical tools.

What?

We are asking participants to wear a light wrist-worn activity monitor/sensor to measure their movement and activity throughout the day. Participants are also being asked to document the start and finish time of a set predefined activities, using a smartphone application.
The activity monitor will be worn for two weeks at home, or as otherwise agreed with the researcher.

Who?

Anyone who has not had recent surgery and does not have any impairments that might limit upper limb mobility is eligible to take part in this study.

Where?

This study is being conducted at the Department of Mechanical Engineering, Imperial College London.

1. **What is the purpose of the study?**

The movements of study participants will be measured using a light wrist-worn activity monitor/sensor. These data will be used to develop tools that will allow us to automatically recognise the activities performed during the day and provide information on the quality of upper limb mobility.

We are interested in seeing how patients' movement and activity levels change around the time of surgical procedures.

This will help doctors to understand how people recover from operations and will help us to make decisions in the future about patients after they have had surgical procedures. We are also collecting data from healthy volunteers, to use as reference and to help us develop analytical tools.

2. **Why have I been chosen?**

You have been invited to take part in this study because you are a student at Imperial College London, you have not had recent surgery and do not have any impairments that might limit upper limb mobility.

3. **Do I have to take part?**

You can decide whether or not to take part. If you decide to take part you will be asked to sign a consent form. You are still free to withdraw at any time without giving a reason.

Not participating or withdrawing from this study will not affect your relationship with Imperial College London.

4. **What will happen to me if I take part?**

Please see the following timetable:

1	You have received this participant information sheet and have time to review it fully.

2	After reviewing this participant information sheet you will have the opportunity to ask any questions to the researcher before you decide whether or not to take part. If you are happy to participate you will be asked to read and sign a consent form.
3	Once you have signed the consent form you may be asked to complete a general survey.
4	You will be given a small and light wrist-worn activity monitor/sensor to wear. This should be worn continuously on your wrist (it is showerproof) except if you go swimming or take a bath. Please continue to go about your normal daily activity. You will be asked to do certain activities of daily living e.g brushing your teeth, eating with a fork and knife. You will also be asked to indicate the time at which you start and finish certain activities using a smartphone application. You may choose to install the application provided on your personal device, or use one provided by the research team. The application will record the starting and finishing time for each activity. No other data will be recorded or provided to the research team through this application.
5	You will return the activity monitor/sensor after two weeks, or as otherwise agreed upon with the research team. At this stage you may be asked to complete a feedback survey. **It is essential that you return the activity monitor/sensor to the researchers at the end of the study.** **If the device is broken, lost or stolen please contact the researcher as soon as possible and we will try to replace it with a new device.**

The total amount of time that you will wear the activity monitor/sensor will be approximately 2 weeks. You will meet a researcher on 2 occasions. The first time will be at your initial meeting for a formal

consent form to be signed, as well as being given the wrist-worn activity monitor/sensor. At your second appointment the researcher will collect the activity monitor/sensor from you.

Taking part in this study in no way changes or affects your relationship with Imperial College London.

5. What happens to the data collected?

The data collected from the activity monitor is the amount and type of activity done throughout the day. This information will be used only by the researchers in this project.

Data collected will be stored on a secure encrypted database. The data will be pseudo anonymised through a coding system. The data will be processed to give the investigators a more manageable value of physical activity for each participant. The smartphone application will record the starting and finishing time for each activity. No other data will be recorded or provided to the research team through this application.

6. What are the possible benefits and disadvantages/risks of taking part?

Benefits

There are no specific benefits to taking part in this study. However, participants may find some satisfaction knowing that they are participating in research that is likely to help improve decision making by doctors in the future.

Disadvantages/risks

The wrist-worn activity monitor/sensor is a CE approved device and is completely safe. The monitor/sensor does not affect any other electrical equipment that you might carry.

We understand that taking part in a research study can lead to increased anxiety, and as such we would like to invite you to call the support number on this information sheet should you have any concerns.

7. What will happen if I don't want to carry on with the study?

The decision to take part in this study is entirely voluntary and you can change your mind at any time. Any decision you take to withdraw from the study will not affect your relationship with Imperial College London.

If you do withdraw from the study information already collected may still be used.

8. **What if something goes wrong?**

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation, but you may have to pay your own legal costs. The normal Student Complaints Procedure will still be available to you.

If you are still not satisfied with the response, you may contact the Imperial AHSC Joint Research Office.

9. **Will my participation in this study be kept confidential?**

All information collected about you during the course of the research is strictly confidential. Any information about you which leaves the College will have your name and details removed.

10. **What will happen to the results of the research study?**

The results of the research will be analysed and published in scientific journals. No individual participants will be identifiable from any report or publication. We will happily provide you with a copy of the results after publication upon request.

11. **Who is organising and funding the research?**

The research is being organised and funded by Imperial College London.

12. **Who has reviewed the study?**

This study has been reviewed and approved by the Research Ethics Committee NRES committee London – Bromley

13. How will we use information about you?

Imperial College London is the sponsor for this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. Imperial College London will keep your personal data for:

- 10 years after the study has finished in relation to data subject consent forms.
- 10 years after the study has completed in relation to primary research data.

14. Legal basis

As a university we use personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use your data in the ways needed to conduct and analyse the research study.
Health and care research should serve the public interest, which means that we have to demonstrate that our research serves the interests of society as a whole. We do this by following the UK Policy Framework for Health and Social Care Research

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There may be a requirement to transfer information to countries outside the European Economic Area (for example, to a research partner). Where this information contains your pseudo anonymised data, Imperial College London will ensure that it is transferred in accordance with data protection legislation. If the data is transferred to a country which is not subject to a European Commission (**EC**) adequacy decision in respect of its data protection standards, Imperial College London will enter into a data sharing agreement with the recipient organisation that incorporates EC approved standard contractual clauses that safeguard how your data is processed.

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For the purposes referred to in this privacy notice and relying on the bases for processing as set out above, we may share pseudo anonymised data with certain third parties.

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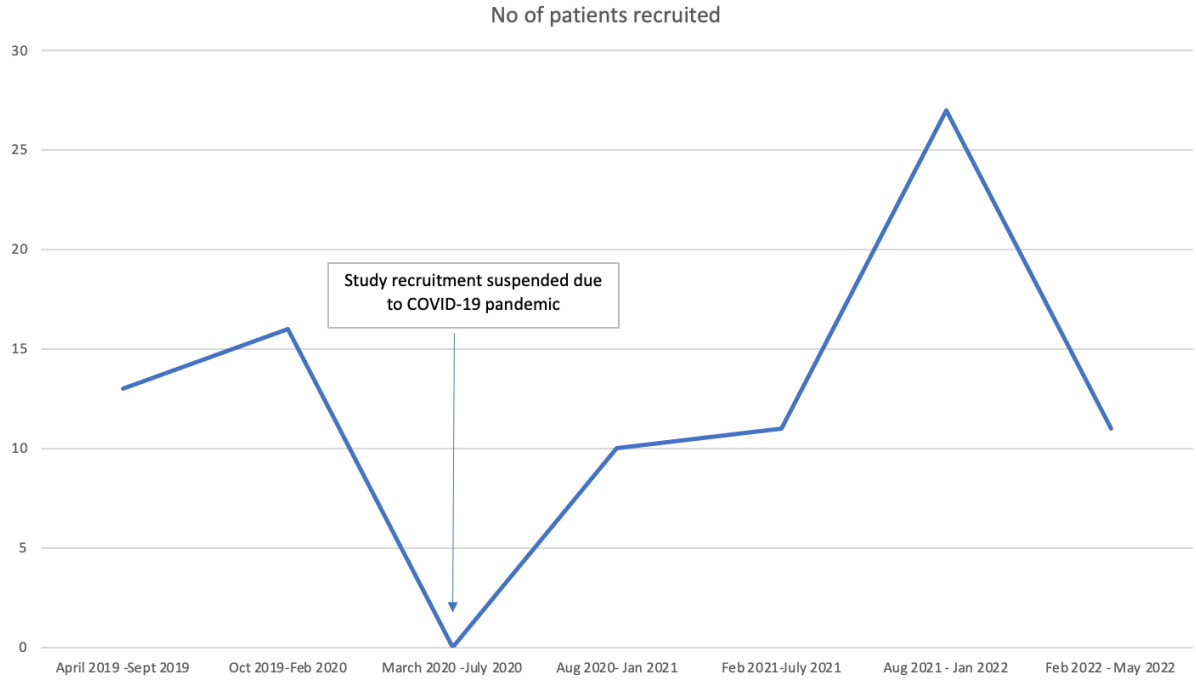
If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO). The ICO does recommend that you seek to resolve matters with the data controller (us) first before involving the regulator.

18. **Contact Ferdinando Rodriguez y Baena (details above) for further information and support.**

THANK YOU FOR PARTICIPATING IN THE STUDY !

Participants will be given a copy of the consent form and information sheet for their own records.

Appendix 9. Number of patients recruited from April 2019 to May 2022



Number of patients recruited from April 2019 to May 2022. The study recruitment was suspended between March 2020 and July 2020 due to the COVID-19 pandemic.

Appendix 10. List of comorbidities – chapter 5

Comorbidities	**n (%)**
Hypertension	10 (25.6)
Hypothyroidism	7 (17.9)
Hyperparathyroidism	1 (2.6)
Hypercholesterolaemia	7 (17.9)
Chronic kidney disease	1 (2.6)
Rheumatoid arthritis	1 (2.6)
Dilated cardiomyopathy	1 (2.6)
Diabetes	3 (7.7)
Atrial fibrillation	2 (5.1)
Depression	2 (5.1)
Osteoarthritis	1 (2.6)
Ischaemic heart disease	1 (2.6)
Bipolar	1 (2.6)
Asthma	1 (2.6)
Diverticular disease	1 (2.6)
Anaemia	1 (2.6)
Fibroid	1 (2.6)
Renal calculus	1 (2.6)
Transient ischaemic attack	2 (5.1)
Endometriosis	2 (5.1)
Obesity	2 (5.1)
Epilepsy	1 (2.6)
Irritable bowel syndrome	4 (10.3)
Osteopenia	1 (2.6)
Previous subdural haemorrhage	1 (2.6)
Previous Pulmonary embolism	1 (2.6)
Previous transabdominal bilateral salpingoophorectomy	1 (2.6)
HIV	1 (2.6)
Previous laparotomy for upper gastrointestinal perforation	1 (2.6)
Parathyroid adenoma	1 (2.6)
Previous tonsillectomy	1 (2.6)
Sickle cell trait	1 (2.6)
Previous parathyroidectomy	1 (2.6)

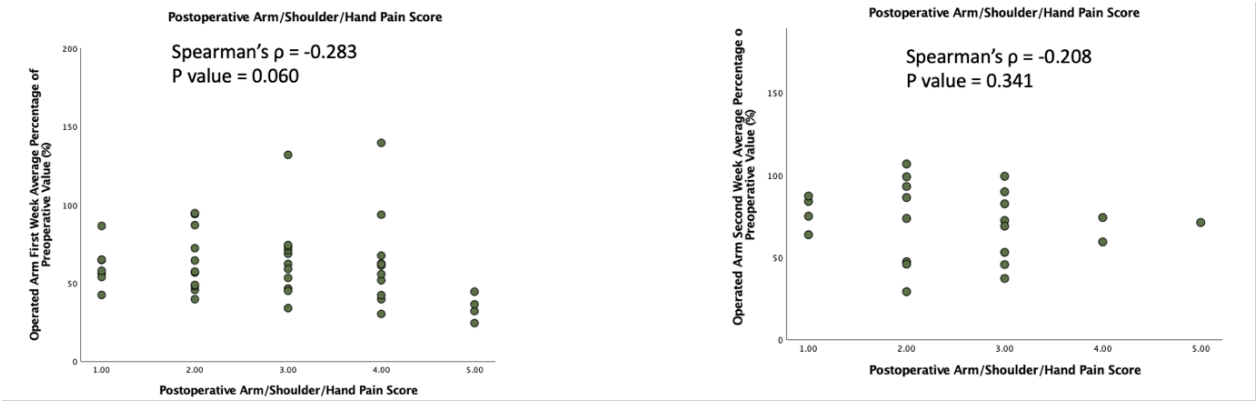
Appendix 11. List of comorbidities – chapter 6

Co-morbidities	**n (%)**
Hypertension	12 (21.4)
Hypothyroidism	9 (16.1)
Hyperparathyroidism	1 (1.8)
Hypercholesterolaemia	7 (12.5)
Rheumatoid arthritis	1 (1.8)
Diabetes	3 (5.4)
Atrial fibrillation	1 (1.8)
Depression	4 (7.1)
Anxiety	1 (1.8)
Obstructive sleep apnoea	1 (1.8)
Osteoarthritis	1 (1.8)
Ischaemic heart disease	1 (1.8)
Bipolar	1 (1.8)
Asthma	4 (7.1)
Colitis	1 (1.8)
Diverticular disease	1 (1.8)
Anaemia	1 (1.8)
Transient ischaemic attack	1 (1.8)
Bronchiectasis	2 (3.6)
Gallstone	1 (1.8)
Rectocele	1 (1.8)
Obesity	1 (1.8)
Epilepsy	1 (1.8)
Multiple sclerosis	1 (1.8)
Irritable bowel syndrome	1 (1.8)
Previous aneurysm	1 (1.8)
Lung cancer – previous lobectomy	1 (1.8)
Interstitial lung disease	1 (1.8)
Previous cholecystectomy	1 (1.8)
Previous transabdominal bilateral salpingoophorectomy	1 (1.8)
Previous hysterectomy	1 (1.8)
HIV	1 (1.8)
Previous laparotomy for upper gastrointestinal perforation	1 (1.8)
Parathyroid adenoma	1 (1.8)
Sickle cell trait	1 (1.8)
Previous parathyroidectomy	1 (1.8)

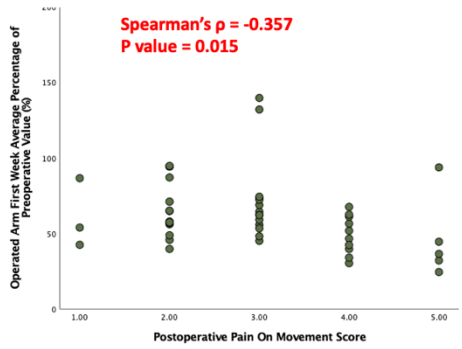
Appendix 12. Surgically treated side only - Comparison of simple mastectomy (Mx) + sentinel lymph node biopsy (SLNB) vs Mx + axillary lymph node dissection (ALND) at week 1 and week 2 [excluding patients without drains]

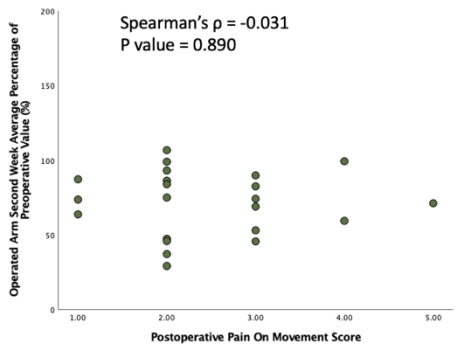
Week	Mx-SLNB (Median %)	Mx-ALND (Median %)	p value
1	**52.8**	**55.0**	**0.321**
2	**81.6**	**69.1**	**0.023**

Appendix 13. Correlation of physical activity with pain score in week 1 and week 2



Appendix 14. Correlation of physical activity with pain score on movement/specific activities in week 1 and week 2





Appendix 15. Analgesia requirements for patients who had DIEP and Mx (+ axillary surgeries)

DIEP patients were found to have a higher analgesia requirement (need as required analgesia at least once on top of the regular analgesia) compared to Mx patients (44% vs 20%).

Appendix 16. List of comorbidities – chapter 7

Comorbidities	**n (%)**
Hypertension	12 (25)
Hypothyroidism	6 (12.5)
Hypercholesterolaemia	4 (8.3)
Chronic kidney disease	1 (2.1)
Rheumatoid arthritis	1 (2.1)
Diabetes	3 (6.3)
Atrial fibrillation	1 (2.1)
Depression	4 (8.3)
Anxiety	1 (2.1)
Obstructive sleep apnoea	1 (2.1)
Osteoarthritis	1 (2.1)
Ischaemic heart disease	1 (2.1)
Osteoporosis	1 (2.1)
Bipolar	1 (2.1)
Ulcerative colitis	1 (2.1)
Asthma	5 (10.4)
Colitis	1 (2.1)
Diverticular disease	1 (2.1)
Anaemia	2 (4.2)
Fibroid	1 (2.1)
Renal calculus	1 (2.1)
Bronchiectasis	1 (2.1)
Gallstone	1 (2.1)
Rectocele	1 (2.1)
Obesity	1 (2.1)
Multiple sclerosis	1 (2.1)
Irritable bowel syndrome	2 (4.2)
Varicose vein	1 (2.1)
Previous subdural haemorrhage	1 (2.1)
Previous aneurysm	1 (2.1)
Previous Pulmonary embolism	1 (2.1)
Lung cancer – previous lobectomy	1 (2.1)
Previous cholecystectomy	2 (4.2)
Previous transabdominal bilateral salpingoophorectomy	1 (2.1)
Previous hysterectomy	1 (2.1)
HIV	1 (2.1)
Previous laparotomy for upper gastrointestinal perforation	1 (2.1)
Gastroesophageal reflux disease (GORD)	1 (2.1)
Hiatus hernia	1 (2.1)

Appendix 17. Comparison of deep inferior epigastric perforator (DIEP) vs mastectomy (Mx) vs implant-based reconstruction (IBR) (excluding patients without drains)

Post-operative week	**DIEP (Median %)**	**Mx (Median %)**	**IBR (Median %)**	**p value**
Week 1	48.74	66.75	62.20	<0.001
Week 2	72.11	82.35	86.52	<0.001

Appendix 18. Surgically treated side versus control side for deep inferior epigastric perforator (DIEP), mastectomy (Mx) and implant-based reconstruction (IBR)

Surgery	Follow up	Week 1	Week 2	19 months
DIEP	**Operated: Median (%)**	38.89	61.28	105.7
	IQR	29.98	41.73	30.4
	Control: Median (%)	43.09	51.57	95.6
	IQR	32.44	33.74	30.9
p value		0.036	0.375	0.273
Mx	**Operated: Median (%)**	56.14	72.07	109.2
	IQR	35.52	40.03	25.9
	Control: Median (%)	66.55	81.43	111.9
	IQR	41.94	44.41	46.4
p value		0.020	0.020	0.333
IBR	**Operated: Median (%)**	52.40	79.80	104.2
	IQR	25.62	42.09	24.9
	Control: Median (%)	62.38	88.88	98.7
	IQR	33.80	46.61	11.0
p value		0.128	0.118	0.715

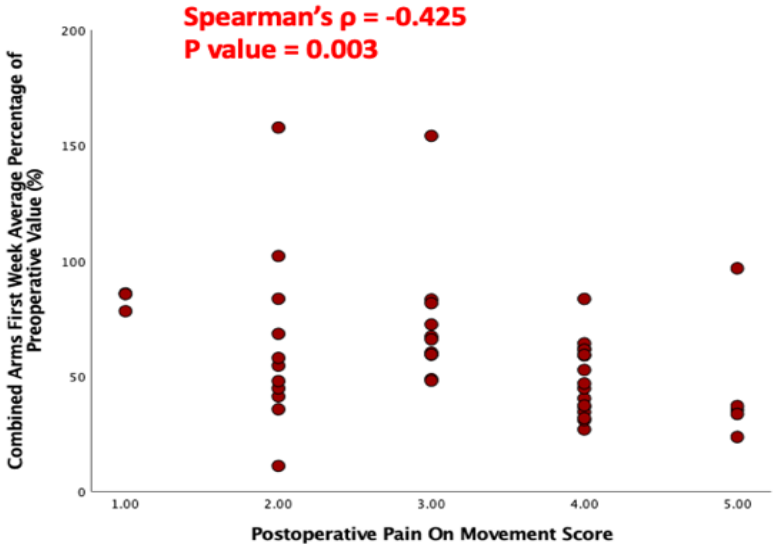
Appendix 19. Univariate analysis

Post-operative	Week 1		Week 2		>6 months	
Independent variable	**Spearman's Rank Coefficient**	**P value**	**Spearman's Rank Coefficient**	**P value**	**Spearman's Rank Coefficient**	**P value**
Age	0.104	0.483	-0.007	0.963	0.044	0.842
BMI (BMI≥25 versus BMI<25)	n/a	0.181	n/a	0.520	n/a	0.710
Comorbidity score (CCI≥5 versus CCI<5)	n/a	0.347	n/a	0.324	n/a	0.766
Stage 1	n/a	0.291	n/a	0.125	n/a	0.699
Stage 2	n/a	0.391	n/a	0.146	n/a	0.291
Stage 3	n/a	0.188	n/a	0.281	n/a	0.451
DIEP	n/a	0.004**	n/a	0.038*	n/a	0.462
Mx	n/a	0.037*	n/a	0.349	n/a	0.352
IBR	n/a	0.376	n/a	0.188	n/a	0.779
SLNB	n/a	0.324	n/a	0.501	n/a	0.571
ALND	n/a	0.112	n/a	0.583	n/a	0.052
Neoadjuvant radiotherapy	n/a	0.527	n/a	0.226	n/a	n/a
Neoadjuvant chemotherapy	n/a	0.129	n/a	0.849	n/a	0.069
Neoadjuvant endocrine therapy	n/a	0.297	n/a	0.065	n/a	0.038*
Neoadjuvant immunotherapy	n/a	0.537	n/a	0.548	n/a	0.132
Adjuvant radiotherapy	n/a	0.250	n/a	0.967	n/a	0.011*
Adjuvant chemotherapy	n/a	0.849	n/a	0.896	n/a	0.100
Adjuvant endocrine therapy	n/a	0.009**	n/a	0.031*	n/a	0.014*
Adjuvant immunotherapy	n/a	0.013*	n/a	0.019*	n/a	0.563

Univariate analysis was carried out to identify an association between age, BMI, co-morbidity score, stage, DIEP, Mx, IBR, type of axillary surgery, neoadjuvant radiotherapy, neoadjuvant chemotherapy, neoadjuvant endocrine therapy, neoadjuvant immunotherapy, adjuvant radiotherapy, adjuvant chemotherapy, adjuvant endocrine therapy, adjuvant immunotherapy and upper limb activity levels. Spearman's Rank Correlation Test was carried

out to identify any significant correlations between age and upper limb activity levels. A Mann-Whitney U test was carried out to identify significant differences in upper limb activity levels between BMI subgroups, comorbidity subgroups, stage, DIEP, Mx, IBR, type of axillary surgery, neoadjuvant radiotherapy, neoadjuvant chemotherapy, neoadjuvant endocrine therapy, neoadjuvant immunotherapy, adjuvant radiotherapy, adjuvant chemotherapy, adjuvant endocrine therapy and adjuvant immunotherapy. Upper limb activity was expressed as a percentage of pre-operative value. BMI groups have been split into those with a body mass index (BMI) <25 and those with a BMI ≥ 25. Age-adjusted Charlson Comorbidity Index (ACCI) <5 and those with an ACCI ≥ 5.
*** $p<0.001$, ** $p<0.01$, * $p<0.05$

Appendix 20. Correlation of physical activity with pain score on movement/specific activities at week 1



Appendix 21. List of comorbidities – chapter 8

Co-morbidities	**n (%)**
Hypertension	5 (12.8)
Hypothyroidism	6 (15.4)
Hypercholesterolaemia	3 (7.7)
Depression	3 (7.6)
Anxiety	2 (5.1)
Obstructive sleep apnoea	1 (2.6)
Osteoarthritis	1 (2.6)
Asthma	2 (5.1)
Colitis	1 (2.6)
Anaemia	1 (2.6)
Fibroid	1 (2.6)
Renal calculus	1 (2.6)
Transient ischaemic attack	1 (2.6)
Bronchiectasis	2 (5.1)
Gallstone	1 (2.6)
Rectocele	1 (2.6)
Obesity	1 (2.6)
Irritable bowel syndrome	2 (5.1)
Osteopenia	1 (2.6)
Varicose vein	1 (2.6)
Previous Pulmonary embolism	1 (2.6)
Interstitial lung disease	1 (2.6)
Previous cholecystectomy	1 (2.6)
Previous transabdominal bilateral salpingoophorectomy	1 (2.6)
Previous hysterectomy	1 (2.6)
Parathyroid adenoma	1 (2.6)
Previous parathyroidectomy	1 (2.6)
Gastroesophageal reflux disease (GORD)	1 (2.6)
Hiatus hernia	1 (2.6)

Appendix 22: Semi-structured interviews

Length: 45-60min

Introduction

Thank you for agreeing to participate in this interview. We are interviewing you to better understand what patients think about wearable activity monitors and how we can improve the way we provide care for breast cancer survivors who develop arm impairment. So there are no right or wrong answers to any of our questions, we are interested in your own experiences. Participation in this study is voluntary and your decision to participate, or not participate, will not affect the care you currently receive from Imperial College Healthcare NHS Trust. The interview should take approximately one hour depending on how much information you would like to share. With your permission, I would like to audio record the interview because I don't want to miss any of your comments. All responses will be kept confidential. This means that anonymised interview responses will only be shared with research team members and we will ensure that any information we include in our report does not identify you as the respondent. You may decline to answer any question or stop the interview at any time and for any reason. Are there any questions about what I have just explained? May I turn on the digital recorder?

Establishing Rapport

Before we begin, it would be nice if you could tell me a little bit about yourself. Tailor a question here to specific person and/or situation. For example: "What do you do? Have you been doing the job for a long time? Does it involve physical activities?

Post breast cancer surgery/treatment experience

Can you tell me about your post breast surgery treatment experience?

Prompts: Did you experience any arm impairment post-treatment? Were there any activities that you used to be able to do before surgery/treatment that you are not able to do now? Did you need to get help/assistance to do your daily activities in the last few weeks and months? Did you expect to have an arm impairment? Did you have to do any lifestyle changes?

Prompts: Did you have any problems returning to work?

Prompts: Did you receive any advice from physiotherapists, breast specialist nurses or clinicians about what to do with your arms post-surgery/treatment? Did you receive a leaflet/pamphlet about what exercises to do? If so, how useful or not useful were they in helping you to go about with your daily activities and routine?

Prompts: What were your particular concerns about your health (ie managing arm impairment, managing pain, employment issues,fatigue/tiredness, sadness/depression, ability to participate in social life, quality of life, ability to participate in personal relationships, etc).

Patient experiences with wearable sensors

Can you tell me your experience wearing the wearable sensors?

Prompts: Have you ever used wearable sensors previously (e.g Apple Watch, FitBit)? Are you aware about wearable sensors prior to this study?

Prompts: Would you wear the wearable sensors again?

Prompts: Was there anything you liked about the wearable sensors? Was there anything you didn't like about the wearable sensors?

Prompts: What is the practicality of using wearable sensors? Is it wearable? Is it comfortable? What do you think of the design?

Prompts: Does it interfere with other devices on your wrists?

Prompts: What improvements can be done to the wearable sensors?

Patient is going to be shown their individualised recorded data

What are your thoughts about the data that we present here?

Prompts: Will you change or not change the way you behave if we give you feedback such as this? What if the feedback is given to you immediately while you are wearing the wearable sensors?

Prompts: Is this data useful or not useful?

Prompts: How do you think this data should be presented to you?

Patient opinions about standardised pathway to recognise patients with arm impairment and personalised rehab programme?

In your opinion, what do you think is the best way to identify patients with complications after breast cancer treatment?

Prompts: Do you think wearable sensors are useful or not useful to monitor recovery after breast cancer treatment? Can wearable sensors encourage patients to do physical activities?

Prompts: What other ways can be done to identify these complications from your experience?

Sensor-based scoring system

What are your thoughts if we develop a scoring system based on wearable sensors so we can identify patients who need intervention early?

Prompts: Do you think the wearable sensors data will/will not improve communication between patients and healthcare team?

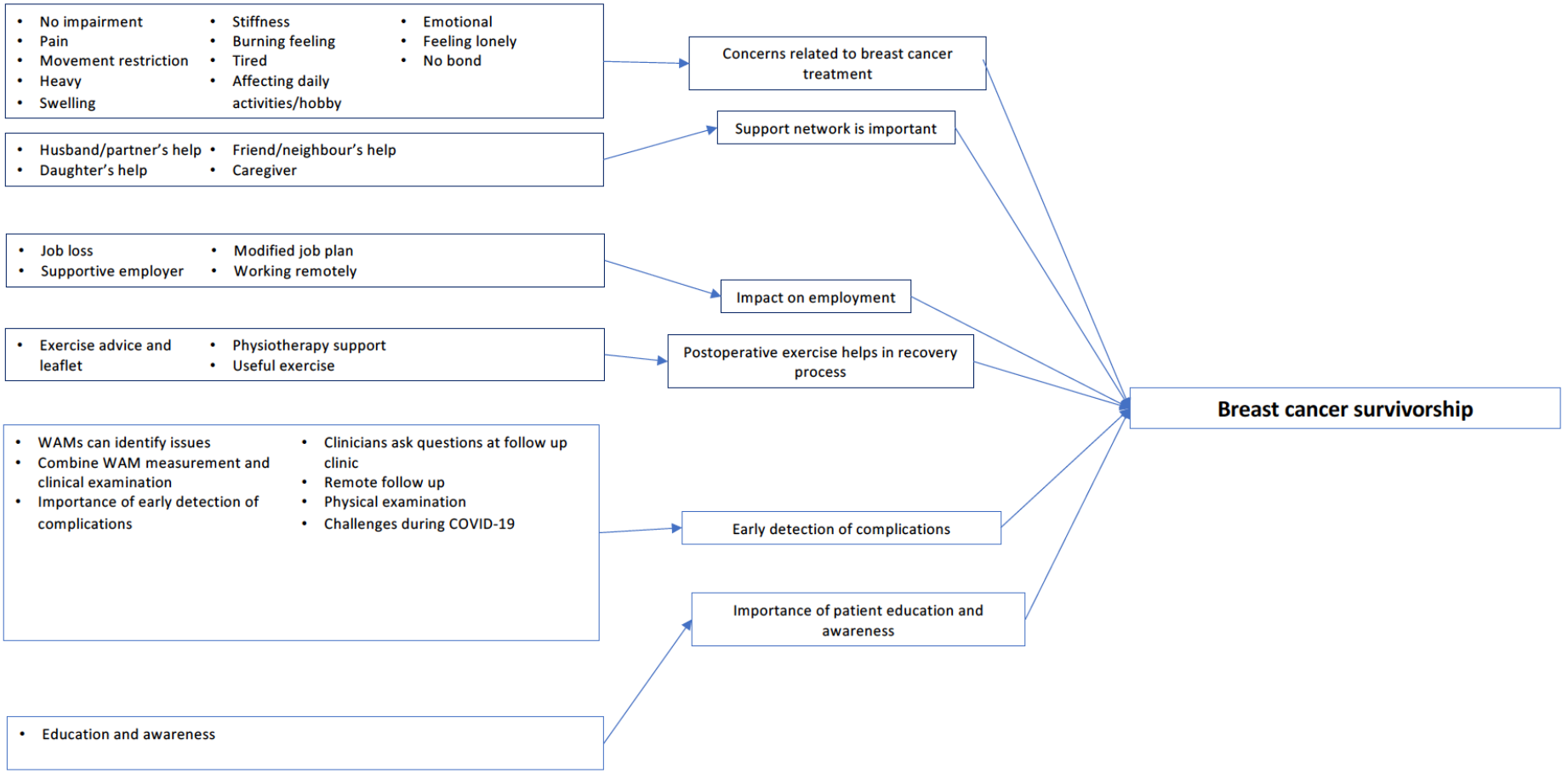
Prompts: What do you think should be included in the scoring system apart from the data that we collect using wearable sensors? Pain? Arm swelling? Perception limitation of daily activities?

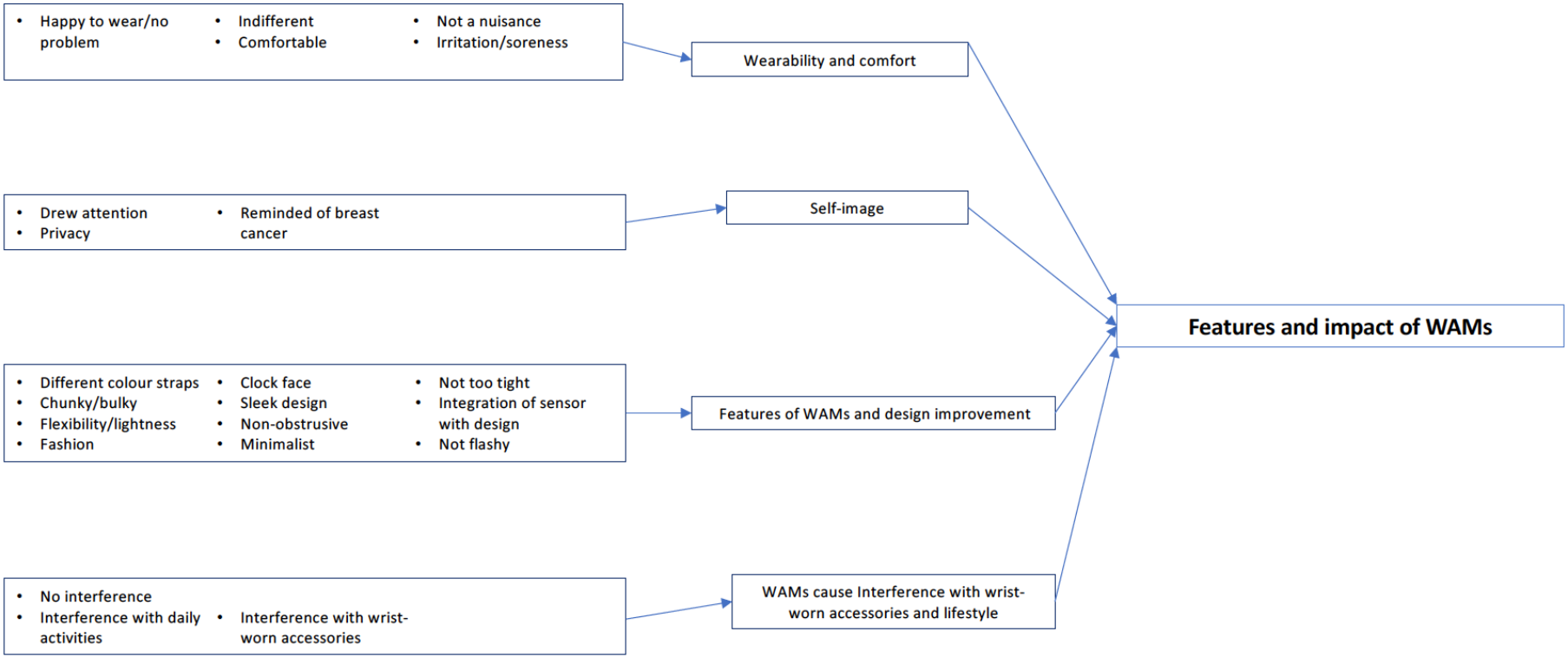
Prompts: In your opinion, what are the ways that we can use to encourage/give feedback to the patients about their level of activities? Should we send nudges e.g vibration or light system? Should we send simple messages e.g encourage patients to make a cup of tea, walk around their house, do simple arm exercise

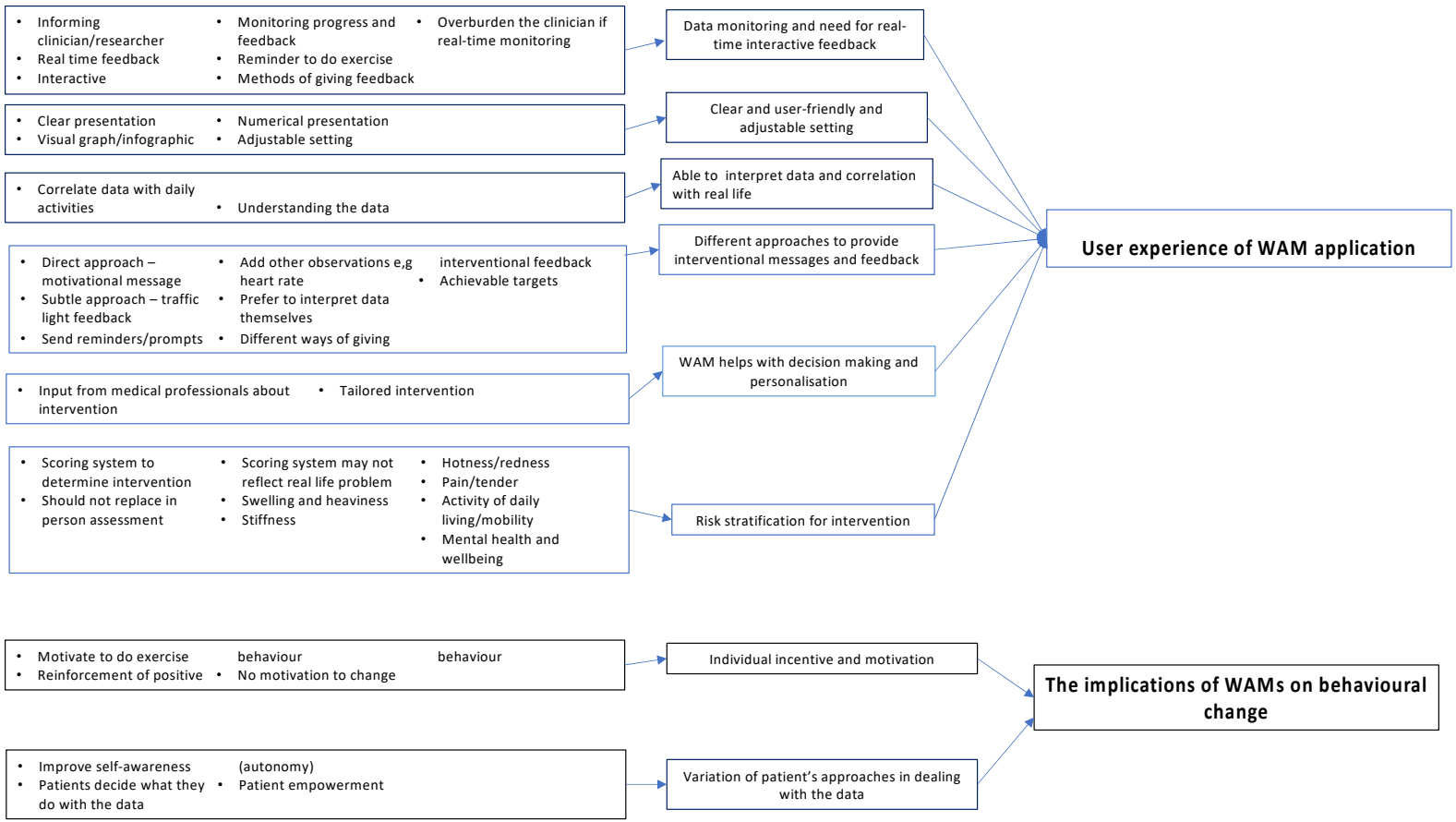
Appendix 23. Demographics of the Patient and Public Involvement and Engagement (PPIE) group

Age range	**Gender**	**Ethnicity**	**Comorbidities**
55-65	Female	Black African	Breast cancer survivor
75-85	Female	White British	Breast cancer survivor
45-55	Female	White British	Breast cancer Survivor
55-65	Female	White British	Breast cancer survivor
65-75	Female	British Chinese	Breast cancer survivor
55-65	Female	Indian Asian	N/A
25-35	Female	White British	Breast cancer survivor

Appendix 24. Coding hierarchy and thematic table analysis




Happy to wear/no problem
Indifferent
Comfortable
Not a nuisance
Irritation/soreness
Wearability and comfort
Drew attention
Privacy
Reminded of breast cancer
Self-image
Features and impact of WAMs
Different colour straps
Chunky/bulky
Flexibility/lightness
Fashion
Clock face
Sleek design
Non-obstrusive
Minimalist
Not too tight
Integration of sensor with design
Not flashy
Features of WAMs and design improvement
No interference
Interference with daily activities
Interference with wrist-worn accessories
WAMs cause Interference with wrist-worn accessories and lifestyle


Informing clinician/researcher
Real time feedback
Interactive
Monitoring progress and feedback
Reminder to do exercise
Methods of giving feedback
Overburden the clinician if real-time monitoring
Data monitoring and need for real-time interactive feedback
Clear presentation
Visual graph/infographic
Numerical presentation
Adjustable setting
Clear and user-friendly and adjustable setting
Correlate data with daily activities
Understanding the data
Able to interpret data and correlation with real life
Direct approach – motivational message
Subtle approach – traffic light feedback
Send reminders/prompts
Add other observations e,g heart rate
Prefer to interpret data themselves
Different ways of giving interventional feedback
Achievable targets
Different approaches to provide interventional messages and feedback
User experience of WAM application
Input from medical professionals about intervention
Tailored intervention
WAM helps with decision making and personalisation
Scoring system to determine intervention
Should not replace in person assessment
Scoring system may not reflect real life problem
Swelling and heaviness
Stiffness
Hotness/redness
Pain/tender
Activity of daily living/mobility
Mental health and wellbeing
Risk stratification for intervention
Motivate to do exercise
Reinforcement of positive behaviour
No motivation to change
Individual incentive and motivation
The implications of WAMs on behavioural change
Improve self-awareness
Patients decide what they do with the data
(autonomy)
Patient empowerment
Variation of patient's approaches in dealing with the data

Theme	Subtheme	Category	Code	Example quotes
Breast cancer survivorship	Concerns related to breast cancer treatment	No impairment		*"I had no problems after the surgery. I came out of hospital feeling the same way that I went in, and I came out the same day as well"(P4)*
				"No, I bowl a good ball at cricket as well. I can throw a ball overarm, underarm! No, it doesn't impair me at all"(P1)
		Physical/arm impairment	Pain	*"...I literally could not shift it; and obviously, if I tried to, it was painful..." (P6)*
				"...I can carry on my right hand but I feel like after that, it hurt me a lot..." (P7) *"... it was so painful when I was moving" (P7)*
			Movement restriction	*"...I couldn't lift it beyond a certain – shoulder height..." (P6)* *"...It did restrict me for a while..."(P6)*
				"I couldn't move my arm, I couldn't lift it up at all..."(P7)
				"...I couldn't move my right arm at all, above my head. I was like that for quite a few months" (P8)

				"...I don't have full mobility. I do struggle. For example, I can't reach my back, or the back of my hair…" (P3)
			Heavy	*"..I did notice that my right arm, it always felt a little bit heavy…" (P2)*
			Swelling	*"..there was always a slight size difference in my arm after the surgery"(P2)*
			Stiffness	*"I was very stiff…"(P8)*
			"Burning" feeling	*"...the only thing I feel now is I get a burning around where the lymph nodes were removed…" (P1)*
			Scar	*"...the scar wasn't too bad…." (P1)*
			Tired	*"... I was just too tired…"(P3)*
				"For at least three months I was lethargic, tired…"(P9)
			Affecting hobby/daily activities	*"... I have an allotment, so digging is quite a physical thing – certainly after my operation, I couldn't do any serious digging for a while, because, initially, I couldn't hold a big fork…" (P6)*
				"...I couldn't cut anything, food or vegetables. Well, I could eat, I could move it, feel myself, but not too much, and I could not sleep on the right side…" (P7)

				"...I had the drain in as well...I used to carry things, do shopping, and now I can't. When I come home with the shopping, I can only buy few things, and only I can carry on my left hand..." (P7)
				"...I can't do, like bra straps and stuff is so awkward. I just can't reach back, so if I've got back buttons on a dress, or a zip - which most people struggle with anyway, but I can't reach at all" (P3)
				"I can recall that when I got home I could not pick the kettle up with my right arm. The surgery was in my right wrist and under my right arm, and it was possibly several days before I could pick the kettle up..."(P9)
				"I didn't do any hoovering, I didn't really wash the dishes, unload, not even laundry, just putting things away a little bit, folding laundry..."(P3)
			Late diagnosis	*"...maybe if they had been picked up, you know, I wouldn't be wearing the compression garment now" (P3)*
		Mental health	Emotional	*"I still feel a bit emotional sometimes, when you think, gosh, look at these last three months" (P1)*
			Feeling lonely/isolated	*"Sometimes I regret that, because I didn't really get to talk to people about what they were going through, because obviously, privately, you just went*

				into a room and obviously you got treated and then you were sent home. So you never really got to speak to other patients about how they felt or how I felt…" (P2)
			No bond	*"...never really got to bond with - you know, sometimes you bond with people at hospital because you talk to them, and you're going through the same thing, and I didn't have that…" (P2)*
	Support network is important		Husband/partner's help	*"...for quite a number of weeks, my husband had to wash my hair, and things like that, or comb my hair, because I couldn't do things like that"(P3)*
				"because I was living with my partner, so he could help with things like getting stuff off shelves and carrying anything. Even now, he'll still take my bag if it's heavy…" (P10)
			Daughter's help	*"...daughter was looking after me and she was helping with yes, getting dressed and all that…" (P8)*
			Friend's/neighbour's help	*"I was lucky to have a friend who came and picked me up from the hospital and drove me home; and one of my neighbours looked after me - I was able*

			to stay with her for the first night and she kept an eye... I got her keeping an eye out for me, to make sure I wasn't keeling over or anything ..” (P6)
		Caregiver	*“I've got an elderly aunt, so I look after her, I do her shopping, run around, you know, pay her bills and things.” (P3)*
	Impact on employment	Job loss	*“Yes, I lost my job” (P7)*
			“It was brilliant until I got ill, and once I got the breast cancer, I was very ill and had all the treatment so in the end I did try go and go back. My manager furloughed me for a short time to see if I could go back, but it came to the point I was never going to go back. I wasn't able to carry out the duties that I did. So it wouldn't haven't been safe, so I packed up” (P8)
		Supportive employer	*“...my work and my manager were very, very supportive. I had chemotherapy first, and I was on 12 weekly sessions. At the beginning, I took two-and-a-half to three days off while I had the chemo, and then I worked for two days, and then the weekend...I think November time, I just decided to give up work for a bit. They were fine about it. Then I went back*

				in February for a month, so they slightly changed my job to fit in…I had my surgery on the 16th, literally just before lockdown…I think I had radiotherapy, and then I went back to work on phase return…" (P3)
			Working remotely	*"...it was fine, actually. I actually had the operation around Christmas, and the organisations that I work with, they kind of wind down from about the second week of December, so it was very quiet anyway, and I've been working remotely since 2016, so it wasn't like I was supposed to be anywhere. I could literally just pick my computer up and stay in bed if I wanted to, so actually, I was very fortunate in that way" (P5)*
	Postoperative exercise helps in recovery process	Exercise advice and leaflet		*"I had a little chat and was given a leaflet with a load of things on: with simple things to start off with; and then, as it got into things, a bit more complex, or a bit more strenuous, as I went through"(P6)*
				"...I think I was quickly shown how to do the exercises…" (P10)
				"...I did, I had an exercise sheet that I followed…"(P8)
				"...I think they gave me a little booklet…" (P9)

			"...they gave me a leaflet on stretches, particularly on stretches, what to do..."(P3)
			"My consultant actually, after the surgery, she gave me a list of exercises to do. That was like trying to walk up - you know, things like - I can remember things like putting your hands against the wall and trying to walk up the wall as far as you can stretch your arms up"(P2)
			"The breast care nurse came on to the ward. I can't remember which day. I was in for five days, and she came on to the ward and explained all the exercises and gave us all a pamphlet..." (P5)
			"The surgeon was very clear with me about what I should do and how I could gradually increase the exercises and so on and I accelerated that because I felt that I was able to. For instance, at that stage I was still rowing, I used to row, and I row in the Venetian style, so I row standing up and that puts no load on one's shoulders or back as English rowing does. So it was a very suitable sort of exercise to do after surgery for on my breasts and under my arm" (P9)

		Physiotherapy support	*"they refer me to do physiotherapy. I did physiotherapy in St Mary's every three weeks" (P7)*
			"A physio person did come when I was in the hospital…"(P10)
		Useful exercise	*"Oh, very good, yes, it helped me because I was so stiff. My back was - I had so much pain on my neck and on my back, on my lower back and she... I still do some exercise still. She video me on my phone and she told me to do - she gave me leaflet with some of them, and then she video. I did some in St Mary's and when I was doing it she video me, and then when I came home I had to do every day for ten minutes, those exercise. Watch it on my phone and do the exercise, and they were very good, very useful exercise"(P7)*
			"They were useful and I did read them all and they were useful" (P9)
			"Yes, they were okay, they did help a lot. Your mind and your body doesn't work to be able to just do a walk or something, but you know you have to do those exercises two times a day, so it was good to focus on those and

			just do them. So you could do them if you're sitting down or lying down" (P3)
			"Yes, I think they definitely helped, obviously, with the scar tissue and just keeping my arm mobile"(P10)
			"I did those and I found them very good" (P6)
	Early detection of complications	WAM can identify issues	*"... if you're able to get some sort of feedback from a clinician or regularly maybe earlier, or from the actual device itself telling you. Maybe you could plug it into your computer or something, and check your graph on pathway. They definitely do have a place in there" (P1)*
			"I can see that feeding back that data to somebody might be helpful in whether they think I'm improving at a normal level or a slower level or faster level; that kind of thing" (P6)
		Early detection of complications	*"... other people that may have the earlier signs of this condition, maybe getting help earlier" (P2)* *"...if you were giving it to somebody, you know, in the early days, that maybe the condition is recognised…" (P2)*

		Clinicians ask questions at follow up clinic	*"If people have regular follow-ups after surgery, then that's the point at which they get prompted to - you get asked quite general, how are you feeling, is there anything wrong, but you don't really - nobody says, 'How is your arm?" (P5)*
		Remote follow up	*"Maybe some telephone follow-up, maybe early on to ask how people are doing… or even maybe a Zoom call for a physio or something. I think you do need to do some exercise in the area regardless of whatever surgery you've had" (P1)*
			"They gave me a couple of calls to say: 'How's it going?' By and large, I was able to say: 'It's going fine, and thank you for checking up on me.' I felt comfortable that somebody was bothering to follow up and deliberately gave me a call or email to say: Is it all right? - because then I knew I had a pathway, that if anything went wrong," (P6)
		Physical examination	*"It was obviously quite early on when after the op, obviously, my right arm always looked a lot more swollen than my left arm. I wished maybe that, you know, the consultant or whoever may have measured that arm against my left arm and measured my right arm" (P2)*

		Combine WAM measurement and clinical examination	*"Probably measuring it before and after, so I don't know, maybe that would be a tracker like a Fitbit and seeing a physiotherapist before and after. I don't remember seeing a physiotherapist before and after the… I guess it's hard to know, if you haven't seen the patient beforehand, how good their mobility was before, and also how - if they are recovering along a normal timescale" (P7)*
		Better communication	*"Well, better communication must be better for the patient because the patient will know that the consultant, whoever, they're wanting to help, they're wanting to reduce the possibility of them having lymphoedema or other issues. So I think that would be a very - I think anybody that's been through that type of surgery would only accept that as a really positive thing" (P2)*
			"…it would definitely increase communication. I just feel that the nurses are very busy, but they are so knowledgeable and so experienced, and they are compassionate. The doctors are great as well, but they just don't have the time" (P3)

		Challenges during COVID-19	*"...because of lockdown in the early days of the COVID when I had the surgery, I wasn't getting that from the physio. Therefore, I wasn't doing enough, and then the consequences were, if it was a bit painful" (P2)*
	Importance of patient education and awareness	Education and awareness	*"Coming from the patient end, you could possibly be - raise people's awareness of what those complications look like more, and then make it clear to them that if they see X, Y, Z, they identify whatever red flags, how they then contact or what they do about that" (P5)*
			"By talking to your patient. Generally I feel that I wasn't aware of a lot of things. Don't take this the wrong way, but I feel that the medical staff don't tell you what to expect. They just said, 'Oh, yes, everything's going to be fine,' but it's not fine" (P3) *"...I don't know what to be aware of, so just make your patients more aware of things, those signs" (P3)*
			"Well, you don't want to go out too much and keep getting examinations. No, maybe not. Just to be aware, maybe. Maybe a call with a physio before you leave the hospital or something and say, 'If you need anything,' or 'Do you know what you're doing?" (P1)

				"...if I had been more aware of the implications of my surgery, and I'd had people talking to me regularly about the possibility" (P2)
				"...if the patient has the information and the education, I suppose, to interpret it, the patient would be the first person to recognise that. (P9)
Features and impact of WAMs	Wearability and comfort	Happy to wear		*"Perfectly happy to wear it. After the first day I really didn't notice it... "(P9)*
				"Yes, it's a good way forward, isn't it? (P1)
				"Yes, they were fine, yes"(P1)
		No problem wearing WAMs		*"I didn't have any problem with them, I put them on..." (P8)*
				"Well, it was a bit boring, having them on my wrist; but, other than that, it was fine..." (P6)
		Indifferent about wearing WAMs	Like wearing a watch/bracelet	*"Wearing it? It was no different to wearing a watch or a bracelet, was it?" (P4)*
				"I don't think it was good or bad, it was just indifferent. It was a bit weird at first, I had them on. It's like when you suddenly start wearing a Fitbit or something. Then I just didn't think about it. They were just there"(P3)

				"I didn't really have any negative or positive experiences. It was just like wearing two Fitbits" (P10)
		Comfortable		*"I think the stuff they were made of was comfortable and I didn't have a problem with them"(P5)*
		Not a nuisance/bother		*"It happened to fit me very easily and comfortably, so it didn't feel trivial, but it also didn't feel as if it was a nuisance"(P9)*
				"...I got used to them so I felt like, not to give them back! Yes, it was comfortable afterwards, didn't bother me" (P7)
		Irritation and soreness		*"I think it had made my - I think it was right or it could have been my left, wrist, a little bit sore" (P2)*
	Self-image	Drew attention		*"Wearing two I think draws attention - it was summer - draws a bit of attention to yourself. I didn't want to go telling everybody wherever I went that I was waiting to have cancer surgery, etc. People would often say… With one, people think it's a Fitbit, an exercise, but when you've got two, people tend to say, 'Oh, why are you wearing two?' If I was going anywhere where I was going to meet quite a few people, I tended to take one off, on about two occasions. I went to a garden party thing, I thought I*
		Privacy		

				really don't want people to come and say, 'What you doing? What you up to?' Just taken part in surgery. I like to keep it all a bit private" (P1)
		Reminded of breast cancer		*"I guess it also made me conscious of the fact that I was undergoing treatment and post treatment and all of that" (P6)*
	Features of WAMs and design improvement	Negative aspect of the design	Different colour straps	*"I had a black one and a blue one, which made it a bit strange! If you're wearing two, wear the same colour or something…" (P1)*
			Chunky/bulky	*"I mean, they're a bit big. They're a bit chunky, you know…I wouldn't say they were the most comfortable things to wear, due to the size of them…" (P2)*
				"…I've got really thin wrists, so they're a little bit bulky as well, but it's a medical device…" (P3)
		Positive aspect of the design	Flexibility and lightness	*"I liked its flexibility, I liked its lightness"(P8)*
			"Cute" strap colour	*" they were cute somehow"(P7)*
		Indifferent about the design	Indifferent about the strap colours	*"Oh, I don't care about that"(P5)*
				"It didn't matter what colour, white, black" (P8)

		Improvement	Fashion	*"I've just changed the strap to - I bought some on Amazon, so different colours, just to sometimes match my outfit. I like bright colours, so I've got a nice bright one.."(P3)*
				it's possible maybe, if they were more - not so in your face, the product, if it was made with a see-through strap" (P1)
			Clock face	*if you were able ever to improve and put the time or something on them, that would be great, because then obviously, you know, you can see what the time is and you don't have to look at your phone or anything…" (P2)*
			Sleek design	*"I think, relatively sleek, so nothing too bulky. I've seen people with quite thin ones, which look quite nice. I'd say that I wouldn't want them to be noticeable, especially if you're going out, for example. Especially if you're going out somewhere nice for dinner and you want to wear a wearable, you don't want to have a big watch or whatever that kind of ruins the outfit, so I think they should be quite sleek and unnoticeable"(P10)*
				There should be sizes, or something. Other than that, if I had to wear them longer-term, ideally I would have liked them a bit not so cumbersome, not so bulky" (P3)

			Not flashy	*"...something that's not flashy…" (P9)*
			Non-obtrusive	*"Something that is nonobtrusive…" (P9)* *"...something that fits my body well and moves as I have to move, something that does not inhibit my movement in any way whatsoever…" (P9)*
			Not too tight	*"....I can't bear things tight, so it can't be too tight and that had a little buckle so the buckle could be adjusted if I chose to…." (P9)*
			Minimalist	*"...Discretion, appearance in it should be minimalist, for me anyway…"(P9)*
			Integration of sensor with design	*"...The integration of the sensor within the design of the bracelet so it wasn't something that stuck out the side or out the top" (P9)*
	WAMs cause Interference with wrist-worn accessories and	No interference		*"They didn't impede anything you did. You could shower with them on, and you just carried on as normal with them, actually"(P1)*
				"I've got a thing on my wrist... If I'm washing and stuff, it's just like, 'Oh, I've got this thing on my wrist.' But they didn't impact in other ways, really" (P6)

	impact on lifestyle		*"I wear a religious bangle on my right arm, but I just wear that anyway, so I wouldn't take that off. You get used to it, it's not a big deal" (P3)*
		Interference with daily activities	*"I just thought it was a bit of an annoyance, occasionally - particularly getting in the way with things like washing and all that kind of stuff"(P5)*
		Interference with watch	*"I could still wear my watch; but yes, I just like to wear it slightly differently - sometimes I just put it in my pocket instead of wearing it on my wrist"(P6)*
			"I couldn't wear my watch. Obviously, I'm quite used to wearing my watch, but again, it was only for a short period of time, and I had my phone, so if I needed to see the time, I just used my phone" (P2)
User experience of WAM application	Data monitoring and need for real-time interactive feedback	Informing clinician/researcher	*"... if it gave someone else information, like you, as part of the study" (P9)*
		Real-time feedback	*"...I suppose if the data was concurrently available to an individual and they could see that the data was showing that things weren't going well and they felt things weren't going well, then they could seek help" (P9)*
		Interactive	*"...would be wonderful if it was interactive and you could log on and look and see, or maybe get something with your wristband. I don't know if it's possible..."(P1)*

		Monitoring progress and feedback	*"if you were giving it to somebody, you know, in the early days, that maybe the condition is recognised, and you were showing them the graphs and you were explaining the graphs, I definitely think that would be very positive for anybody…I looked at the graph, and honestly, I could see, you know, it was going up and it was going down, but it might be helpful if there was a way of showing - I don't know, if I'd had this information earlier, I might have been able to have a look at it and go, 'Oh actually, yes, I know, what was I doing on that day?"(P2)*
			"You see, I'd expect to be talking to the doctor about what was happening to me… The graph is an indication to me about what my conversation is. So I suppose it depends on the emphasis that one puts on the graph. The graph is only to show me my progress, it's only my progress that I care about, the graph is simply an indication of that or whatever one wants" (P9)
		Reminder to do exercise	*"Yes, it felt you were being watched, and that if I didn't do the exercises, then you would be able to tell from tracking it… It's reassuring, because as you say, it does manage to track that you're doing exercises and everything*

			and using it. It did remind me to do them, in a way. I thought this is being tracked, people are following me up" (P1)
		Methods of giving feedback	*"...if there's a central system, then via email is fine, or a text..."*
			"... just a text message maybe.."(P1)
		Overburden the clinician if real-time monitoring	*"I suppose the issue is the relation of the data to the time at which it's occurring, because presumably a difficulty that arises, it's better if it's picked up sooner rather than later. Now, I would suggest that there is no way in the world in which any person, other than the individual wearing it, could possibly monitor hundreds of people all with medical devices..." (P9)*
	Clear and user-friendly and adjustable setting	Clear presentation	*"...it's quite good. It's quite clear. I can see from the right arm to the left, the difference"(P8*
		Visual graph/infographic	*"...visual graphs, like the ones I've got... I probably can understand them a little bit better, just because I've dealt with these quite a lot in my career" (P3)*
			"I suppose it would be nice to have more of an infographic. I think the way the Fitbit does their interface is quite useful because they've got little

			graphs and... I'll just have a look, actually, and see if I can - yes, having little graphs and quite simple charts to show progress. I think the Google Fit on my phone does it as well, but it's got a little circle and, basically, when you hit 10,000 steps, it fills the circle in. Then you've got, for example, other little circles, like how much distance you've walked or ran, and calories burned, and then the circle goes round, and it fills up the more you do, until you meet your daily target" (P10)
		Numerical presentation	*"...'Oh, your minute mobility today has been ten per cent lower than yesterday,' something like that. Anything, really, anything that's easy in modern life" (P3)*
			"...the steps, if you've not done enough, then I know I've got to go up and down the stairs or keep on. If they feel perhaps they're not doing enough - because you don't know what is the right amount to do, of arm exercises, at a push" (P1)
		Adjustable setting	*"...There are all sorts of settings..." (P3)*
	Able to interpret data and	Correlate data with daily activities	*"You can see the days that I was in hospital, and I think it's - I haven't actually got it in front of me now, but day four, you can see that they were*

	correlation with real life		*getting me up and making me walk. So I think that bit is accurate, and I think, at the end of the two weeks, it tails off a bit, and that, for me, is probably when my iron levels dropped and I was starting to flake out a bit because I wasn't eating" (P5)*
			"On the day ten and also the right hand, I remember one day I did cleaning in my house..." (P7)
			"First days, you're just a bit lazy, effects of all drugs and stuff, and then you start moving around a little bit, and doing a bit more movement, so I think that is a reflection" (P3)
		Understanding the data	*"I looked at my left and I looked at the right, and I could see that I'm still more active with my right arm…." (P2)*
			"Let me see the graph. So it shows on the day ten, I move my left hand the most…" (P7))
			"I think I was probably more surprised by my left arm because I think that looks like it dropped quite a bit. I wasn't expecting that. The right arm didn't surprise me…" (P10)

			"Both my movements before and after surgery? It was the same as normal, like they always were. Having this operation didn't affect my movement at all…" (P4)
			"Seeing the two sides, it didn't seem to me that there was a huge difference. Obviously, a slight difference but not huge…" (P6)
	Different approaches to provide interventional messages and feedback	Direct approach - motivational message	*" I would prefer to be told that I'm not doing enough… 'You haven't done enough exercise,' right, and that's what you need to do. That's just me. I am that type of person, that when I get into something, then I really get into it" (P2)*
			"Sometimes, I sit here, and I'm watching TV, and I think, oh, I should get up, but I can't be bothered, but if there's a physical thing saying, 'Get up, get up,' then I will, because I think...it's a game in your mind, it just pushes you… Not to say, 'Exercise, exercise, just do the exercise.' Just say, 'If you can only manage three minutes, then three minutes walking on the spot is better than nothing…" (P3)

			"...it would probably amuse me and delight me to have a little sentence that tells me as well, because it does make it concrete, it does tell me what I should actually do about it" (P9)
		Subtle approach - traffic light feedback	*"I think the traffic light thing would work" (P5)*
		Send reminders/prompts	*"It's a good reminder that I need to get up, and make sure I make time to go out for a walk or do some exercise. I think, especially people working from home, it's just so easy to spend the day inside, working. Whereas before, even though I don't like commuting, it is useful that you'd have that - you'd walk to the station, or in your lunchtime, you'd make the effort to get out of the office and go for a walk, so I think those reminders are quite helpful" (P10)*
		Add other observation such as heart rate	*"I just like that you can track exercise, tracking steps, and even things like heart rate" (P4)*

		Prefer to interpret data themselves	*"I'd regard it as too bossy, but I wouldn't mind reading it at the end of the day. In other words, intervention throughout the day, I personally would… [Laughs] My attitude would be, mind your own business, I'm doing something. I do think that sort of feedback, if I could read it off at the end of each day, I would find that helpful, yes, but the constant interference is not the way I live" (P9)*
			" I can tell if I'm doing all right…" (P6) *That would have caused me to get rid of them (to prompt to move around); I would have ripped them off!" (P6)*
		Different ways of giving interventional feedback	*"...design one that is a bit more subtle and the other one that prompts people to do certain activities..." (P2)*
		Achievable targets	*"If you can only manage three minutes, then three minutes walking on the spot is better than nothing" (P3)*
	WAM helps with decision	Input from medical professionals about intervention	*"if patients who are wearing them are monitored, and especially if they're very high risk to lymphoedema, and then somebody who's medically trained can say...Look, we don't think you're moving enough. Maybe try*

	making and personalisation		*this. If you can't do this, then try this….Give them good education on - or a physio and say…This is exactly what you need to do"(P3)*
			The interpretation has to be with the knowledgeable person, which is the medic. Without the patient being able to recognise it and presumably the patient can make the first judgements. For instance, as I said, I was terribly aware that I was protecting the areas where there was surgery, but it has to be an informed person who's likely to make the best judgement… So that every decision is an informed decision" (P9)
			"but if you had say a one-week follow-up and then a three-week follow-up or whatever, and you were looking at the data, I guess a healthcare professional could go, 'Ooh, it looks like you've not been moving too much, is everything okay? What's going on?' So I think, yes, that definitely could be useful at that point for the healthcare professional to prompt questions about mobility" (P5)
		Tailored intervention	*"Something, somewhere, can work, but it's just trying to find the right steps" (P3)*

	Risk stratification for intervention	Scoring system to determine intervention	*"Just for example, one-to-ten, and somebody falls into seven-to-ten, so that's the red area, then yes, give them education on what you need to do, and exactly what you need to do. Even leaflets, and a small - just a… I don't know, a small parcel, or you know Maggie's charity? They do a lot. Even if they have just a nurse going in and saying that this is what you can or can't do, or they used to do even chair yoga, things like that, to encourage people to move" (P3)*
			"...because the higher the score, you understand the patient need more assistance" (P7)
		Scoring system should not replace in-person assessment	*"I'm always a bit wary of scoring systems. You can have people who are classified as low risk for cancer, for example, based on a scoring system. That doesn't tell the whole story. I think technology is great, I think it's a good guideline as well, but then what about if someone - someone could fall through the crack. So I think it's a good idea, but I still think that shouldn't replace patients being able to see a doctor in person as well" (P9)*

		Scoring system/numbers may not reflect real-life problem	*"It is all too easy for numbers to become goals on their own. I prefer a graph that shows progress, and so a scoring system that says you've got to four out of five, unless I know what five is, I have no idea what four is. That's one of the really serious problems with marking anything or converting anything at all to some sort of numeral" (P10)*
		Swelling and heaviness	*"I mean obviously, the swelling. (P2)*
			"...my breast was so swollen, it'd feel so heavy and horrible. Yes, those kind of things..." (P3)
			"...swelling..." (P10)
		Stiffness	*"...and stiffness..." (P10)*
		Redness/hotness	*"the redness, the hotness, so that could be a - you know, if somebody has a couple of episodes with soreness, with redness, that could be a sign as well" (P2)*
			"If your skin is slightly hot to touch..." (P3)
		Pain/tender	*"Pain, tender. I'd been up in the morning," (P3)*
			"Yes, I think, pain...(P10)

				"First, the pain…" (P7)
		Activity of daily living and mobility		*"…if we're looking at things such as mobility… For example, if they have trouble doing things day-to-day, whether that's dressing or washing themselves, or carrying things or doing more strenuous activities or exercise" (P10)*
				"I think, definitely, mobility and activity" (P5)
The implications of behavioural change on WAMs	Individual incentive and motivation and impact on WAMs	Positive change of behaviour based on data	Motivate to do exercise	*"…when you see something like that, it makes you more conscious about making sure you make the - you know, doing the exercises, and you can actually see on the graph the results. So I think that actually might even be a way of motivating and helping people with this kind of condition, to do the exercises" (P2)*
				"You're more motivated if you can see you've not been as active as you usually would be…" (P10)
				"…certainly I feel that it encourages you wearing it, it encourages you to know that you can be tracked, and to - particularly with the exercise regimes and things, and the movement" (P1)

				"Yes, it's a game in your mind, it just pushes you" (P3)
				"Maybe if I'd seen the - maybe I would have tried to be more active or something, or tried to improve it...I think it's just a good day-to-day reminder of things, like just making sure you're active, and also just tracking your general activity and overall health" (P10)
				"...if I saw on those watches something like, well, it's painful but you can do a little bit more and you can do a bit more exercise today, I could manage to get over the pain quick, or maybe not end up in physiotherapy, or maybe today I'm not, I'm still in pain because the nurse told me you didn't do enough exercise" (P7)
			Reinforcement of positive behaviour	*"I base what I do on evidence and I have all my life. So if I had evidence that something was improving I would have repeated it" (P9)*
		No change of behaviour based on data	"Do it on my own time"	*"No, I would do it in my own time, I think. - didn't find the feedback useful and will not change behaviour" (P4)*
			Know their own body	*"Not to me, because I obviously can tell, whether I can lift my arm or not... I was aware of when it started improving and getting better. As I say, I was*

				doing the exercise I was given, and I could tell when I could do things" (P6)
				"If it's only a couple of weeks post-op, you're really doing what you feel like doing, rather than - for me, I don't think I'd look at data and think, ooh, I haven't been doing very much today, I'd better do more. You're just too concerned with how you feel, I think...when you've had a big operation like that, I think your priority is maybe not what you should be doing and shouldn't be doing. It's more, I feel rubbish, so I'm going to lie down" (P5)
			No motivation to change behaviour	*"I think it's interesting, definitely. It's interesting to see, but in terms of would it change my behaviour if I had the data, probably not at that point...." (P5)*
				'I'd behave in the same way, I probably would, yes. - didn't think data was useful..."(P4)
	Variation of patient's approaches in	Improve self-awareness		*"...it gives you more awareness of yourself..." (P3)*
				"...when you see something like that, it makes you more conscious about making sure you make the - you know, doing the exercises.." (P2)

	dealing with the data	Patients decide what they do with the data (autonomy)	*"It's up to people then, isn't it? You know, at the end of the day, if you're saying to somebody, 'You haven't had a lot of exercise, go for a walk,' and they decide to ignore you, well, that's fine" (P2)*
		Patient empowerment	*"I suppose I take the view that from the age of 12 it's the duty of every individual to manage their own health…" (P9)*

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