Physical activity in people with osteoarthritis and comorbidity: a multi-method study.

Sarah McKevitt

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Declaration

This PhD project was advertised as an 'ACORN studentship' funded by Keele University. The funding for the studentship was obtained by Dr Emma Healey. The initial PhD idea and research questions formed part of the studentship project and are credited to Dr Emma Healey, Professor Clare Jinks and Dr Jonathan Quicke.

Throughout the PhD, I developed the research questions and thesis content with ongoing guidance and support from my supervisory team as above. I received additional systematic review support from Jo Jordan and Dr Opeyemi Babatunde who provided data synthesis advice. The Patient and Public Involvement and Engagement (PPIE) group meeting was completed with organisational help from Laura Campbell, a member of the Keele PPIE team. I received additional statistical assistance from Trishna Rathod-Mistry and Professor Kelvin Jordan regarding model building and checking statistical methods and outputs. For study two I conducted secondary data analysis on two trial datasets (from BEEP and MOSAICS) collected by others before my time on the PhD. Professor Nadine Foster and Professor Krysia Dziedzic were the principal investigators for the BEEP and MOSAICS trials, respectively. Prof Kelvin Jordan and Dr Alyn Martyn Lewis were the responsible data custodians for these projects and cleaned the data prior to its use in this PhD.

As the doctoral researcher, I created and drafted all study documents with feedback from the supervisory team (JQ, CJ, EH). This included all stages of the systematic review, quantitative model building and interpretation, qualitative recruitment and interviews. I also led the applications for approval from the Keele University research ethics committee and data requests. One of my supervisors attended the larger participant recruitment meetings (to assist in conversing with potential participants, answering queries and providing the relevant documentation). The interviews were carried out in a one-on-one setting, between myself and the interviewee. I conducted analysis of each thesis study followed by discussions and feedback from my supervisory team.

Abstract

Osteoarthritis (OA) is common and associated with one of the highest comorbidity rates. OA clinical guidelines recommend physical activity (PA) as core treatment, irrespective of comorbidity. However, no current synthesis of the effectiveness of PA for people with OA and comorbidity exists. The impact of comorbidity on the uptake and experience of PA in this population is unknown and how to successfully implement PA interventions within primary care for people with OA and comorbidity remains unclear. This thesis addressed these three research gaps.

A systematic review examining the effectiveness of PA interventions in people with OA and comorbidity found the evidence to be limited and heterogeneous (n=14 studies, of which 10 were OA and obesity studies). Trends suggest PA interventions may improve clinical outcomes of pain and function, although uncertainty remains.

Secondary data analysis of two large randomised controlled trials for older adults with knee (n=514) and joint (knee, hip, hand and foot) OA (n=525) found an association between comorbidity presence and lower PA levels. A potential dose-response relationship exists between comorbidity frequency and lower PA levels, and the presence of specific comorbidity types (e.g. cardiovascular disease) were associated with decreased PA levels.

Qualitative semi-structured interviews in 17 older adults with OA and comorbidity found barriers to PA were multiple and dynamic. OA was often prioritised as more important over other health conditions based on the disruption it caused to QOL. Participants reported; a lack of knowledge about how best to manage their conditions, and the role of PA; negative perceptions regarding the role of PA in managing their conditions, which appeared to impact self-efficacy for self-management of conditions and PA. Healthcare professionals and social support were found to facilitate PA.

This multi-method thesis has contributed to a better understanding of PA in the context of OA and comorbidity.

Acknowledgements

I began my PhD in September 2016 which was made possible by a Keele University ACORN studentship.

I would like to acknowledge my supervisory team; Dr Jonathan Quicke, Dr Emma Healey and Professor Clare Jinks. As a team, they have had an invaluable part in crafting this thesis and developing me as a researcher. Further, they have been a huge support for me personally. All three are inspiring academics, supervisors and individuals, with the perfect balance of wisdom and kindness, which has made a lasting impression on me. I can't thank you enough.

I would also like to acknowledge the wider team that had an input in the thesis, from advice and support on the systematic review, through to support with the statistical methods and interpretation. I would like to thank those involved in the BEEP and MOSAICS studies and those participants who volunteered their time to participate in my study.

I have made some great friends at Keele who not only provided great encouragement but also the finest distraction from work, as necessary (I'm sure the latter is reciprocal). Finally, I will remember this thesis as a great accomplishment in my professional and my personal life as this chapter in my life has not been without hurdles. My parents' constant support and compassion to succeed in my PhD and life, my mum's non-stop words of wisdom and my father's irrefutable humour and reality checks have carried me through many challenging days. Also, Jackie and Dave Thorne have fuelled me through a balance of kindness and absurdity. Finally, Bill, who has listened every day, I thank you for getting me through each chapter and giving me so many reasons to look forward to the next.

My research experience

My background is in PA and health. I have always had an interest in the wider health benefits of leading a physically active lifestyle and a fascination with the different ways that PA can influence people and their health and well-being. I undertook a BSc in Sport and Health Science, graduating in 2012. From here I moved on to complete an MSc in PA and Health, graduating in 2016. I developed a strong knowledge base on PA and its use in a health context and was keen to contribute to the development of its clinical use. Throughout my undergraduate and postgraduate research, I used and experimented with different research methods, methodologies and tools to gather, analyse and interpret data and information. On undertaking the PhD at Keele University, I was excited by an opportunity to further expand on my research method interest and combine this with my passion for health and physical activity.

This PhD research was undertaken full time. The initial title and project outline of the PhD was defined prior to my involvement but were developed throughout the PhD duration.

Research output and funding

Throughout the PhD duration, outputs from the research have been disseminated, including a publication and presentations at conferences. Further dissemination is planned.

Peer-reviewed publication

Mckevitt, S., Healey, E., Jinks, C., Rathod-Mistry, T. & Quicke, J. (2020). The association between comorbidity and physical activity levels in people with osteoarthritis: Secondary analysis from two randomised controlled trials. *Osteoarthritis and Cartilage Open*, 2020 Jun;2(2):100057. Doi:10.1016/j.ocarto.2020.100057

Systematic review registration

The effect of physical activity based interventions on physical functioning, pain, quality of life and global health for individuals with osteoarthritis and co-morbidity: a systematic review. PROSPERO 2017 CRD42017055582. Available from: https://www.crd.york.ac.uk/prospero/displayrecord.php?ID=CRD42017055582

Conference presentations

2016 PAN wales – poster & 90-second pitch Swansea University	The effectiveness of exercise interventions in adults with osteoarthritis and comorbidity: Methods for a systematic review.
2017 Keele Institute of Liberal Arts and Sciences – poster Keele University	The effectiveness of exercise interventions in adults with osteoarthritis and comorbidity: Methods for a systematic review.
2017 Postgraduate symposium – poster Keele University	The effectiveness of exercise interventions in adults with osteoarthritis and comorbidity: Methods for a systematic review.
2018 European League Against Rheumatism – abstract published Amsterdam (Did not attend)	McKevitt S, Jinks C, Healey E, et al. AB0972. The effectiveness of physical activity interventions for people with osteoarthritis and obesity: a meta-analysis. *Annals of the Rheumatic Diseases* 2018; 77**:** 1609.

2018 Keele Institute of Liberal Arts and Sciences – 3MT competition Keele University	Physical activity (PA) in people with osteoarthritis (OA) and comorbidity: A multi-method study.
2018 Postgraduate symposium – 10-minute oral presentation Keele University	The effectiveness of physical activity based interventions for people with osteoarthritis and comorbidity: A systematic review.
2018 Three Minute Thesis competition (Bob Beattie award) Keele University	Physical activity (PA) in people with osteoarthritis (OA) and comorbidity: A multi-method study.
2018 Society for Academic Primary Care – poster & 3-minute pitch London	The effectiveness of physical activity based interventions in adults with osteoarthritis and comorbidity: A systematic review. https://sapc.ac.uk/conference/2018/abstract/pitch-systematic-review-investigate-effectiveness-of-physical-activity
2018 Society for Social Medicine – 5-minute rapid-fire presentation Glasgow, Scotland	Mckevitt, S., Jinks, C., Healey, E.L., & Quicke, J. (2018). RF26 The effectiveness of physical activity interventions for people with osteoarthritis and comorbidity: a meta-analysis of obesity. *Journal of Epidemiology & Community Health, 72*, A55.
2019 Osteoarthritis Research Society International - Poster with poster tour (2 days) (7-minute oral presentation) Toronto, Canada	McKevitt, S., Healey, E.L., Jinks, C., Rathod-Mistry, T. and Quicke, J.G., 2019. The association between comorbidity and physical activity levels in people with osteoarthritis: secondary analysis from two randomised controlled trials. *Osteoarthritis and Cartilage*, 27, S494.
2019 Multimorbidity conference – poster displayed Keele University	The association between comorbidity and physical activity levels in people with osteoarthritis: secondary analysis from two randomised controlled trials.
2019 Postgraduate symposium – poster Keele University	The association between comorbidity and physical activity levels in people with osteoarthritis: secondary analysis from two randomised controlled trials.

Awards

Keele Institute of Liberal Arts and Sciences conference – 3-minute thesis competition – winner and 'people's choice' award

Society of Social Medicine – Conference attendance and accommodation grant awarded

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List of abbreviations

ACR - American College of Rheumatology

ACSM - American College of Sports Medicine

ARUK - Arthritis Research United Kingdom

BEEP - Benefits of Effective Exercise for knee Pain

BMI - Body Mass Index

BP - Blood Pressure

CI - Confidence Interval

CJ - Clare Jinks

CMO - Chief Medical Officer

COPD - Chronic Obstructive Pulmonary Disease

CVD - Cardiovascular Disease

DALY - Disability Adjusted Life Years

DOH - Department of Health

EH - Emma Healey

ELSA - English Longitudinal Study of Ageing

EQ-5D - EuroQol 5 Dimensions

EULAR - European League Against Rheumatism

FAST - Fitness Arthritis and Seniors Trial

FITT - Frequency Intensity Time Type

GAD 7 - General Anxiety Disorder 7

GP - General Practitioner

GPE - Global Perceived Effect

GUG - Get Up and Go

HCP - Healthcare Professional

HIV - Human Immunodeficiency Viruses

HOC - House Of Care

HOOS - Hip injury and Osteoarthritis Outcome Score

HR - Heart Rate

HRR - Heart Rate Ratio

IBM - International Business Machines corporation

IBS - Irritable Bowel Syndrome

ICC - Interclass Correlation Coefficient

ID - Identification

IPAQ - International Physical Activity Questionnaire

IRMD - Inflammatory Rheumatic and Musculoskeletal Disease

ITE - Individually Tailored Exercise

JJ - Jo Jordan

JQ - Jonathan Quicke

KLS - Kellgren and Lawrence score

LTC - long-term condition

KOOS - Knee injury and Osteoarthritis Outcome Score

MCS - Mental Component Scale

MESH - Medical Subject Headings

MET - Metabolic equivalent score

MHR - Maximum Heart Rate

MI - Myocardial Infarction

MOSAICS - Management of OSteoarthritis In Consultations Study

MRR - Medical Record Review

MSK - Musculoskeletal

N - Number

NHS - National Health Service

NICE - National Institute for Health and Care Excellence

NSAID - Non-Steroidal Anti Inflammatory Drug

OA - Osteoarthritis

OARSI - Osteoarthritis Research Society International

OCD - Obsessive-Compulsive Disorder

OMERACT-OARSI - Outcome Measures in Rheumatology Clinical Trials- Osteoarthritis Research Society International

OP - Osteoporosis

PA - Physical Activity

PASE - Physical Activity Scale for the Elderly

PCS - Physical component Scale

PF - Physical Function

PhD - Doctor of Philosophy

PHQ8 - Patient Health Questionnaire 8

PICO - Participants Intervention Control Outcome

PPIE - Patient and Public Involvement and Engagement

PROSPERO - International prospective register of systematic reviews

PT - Physiotherapist

QOL - Quality Of Life

RA - Rheumatoid Arthritis

RCT - Randomised Controlled trial

REF - Reference category

ROB - Risk Of Bias

ROM - Range Of Movement

SD - Standard Deviation

SE - Standard Error

SEM - Standard Error of Measurement

SF12 - Short Form 12 Health Survey

SF36 - Short Form 36 Health Survey

SF8 - Short Form 8 Health Survey

SM - Sarah McKevitt

SMD - Standardised Mean Difference

SPSS - Statistical Package for Social Sciences

T2DM - Type two Diabetes Mellitus

TEA - Targeted Exercise Adherence

UC - Usual Care

UK - United Kingdom

US - United States

VAS - Visual Analogue Scale

VIF - Variance Inflation Factor

WHO - World Health Organisation

WOMAC - Western Ontario and McMaster Universities Osteoarthritis Index

β - Beta Coefficient

Language and definitions used in this thesis

This section outlines key terminology used in the thesis as there are different ways in which language can be used in research. For the purpose of this thesis, the following terms and definitions are used:

Multi-method

Multi-method research integrates compatible aspects of different research approaches (Bazeley, 2018). *'Multi-method research is when different approaches or methods are used in parallel or sequence but are not integrated until inferences are being made'* (Johnson et al., 2007). Compared with mono-methodology, a multi-method approach can integrate compatible aspects of different research methods (Johnson and Onwuegbuzie, 2004), to seek a deeper understanding (Maxwell, 2011). Multi-method designs also exist where both quantitative and qualitative approaches are used, but they remain separate and independent until the final stage of the research process. In such a type of research, the goal is to create a dialogue between diverse perspectives, to deepen, rather than triangulate knowledge. (Maxwell, 2011).

In contrast to the chosen multi-method approach, there is an alternative, mixed methods approach to research, not used in the current thesis. Mixed methods research also involves the use of more than one distinct qualitative or quantitative method throughout the research process. Bazeley described mixed methods in comparison to multi-methods;

'Mixed methods research involves the use of more than one approach to method of design, data collection or data analysis within a single program of study, with integration of the different approaches or methods occurring during the program of study, and not just at its concluding point' (Johnson et al., 2007).

Osteoarthritis

Osteoarthritis (OA) is a whole-joint disease of synovial joints which occurs when damage of the cartilage triggers repair processes leading to structural changes. OA is the most common form of arthritis, which affects multiple structures, including; progressive loss of the protective cartilage on joints and joint space narrowing, bone remodelling and osteophytes and synovitis (NICE, 2014). This process can result in swelling, pain, stiffness, muscle wasting and weakness, and functional limitations (NICE, 2014; ARUK, 2015). OA can exist in any joint but is most common in the knee, followed by the hip, hands and feet (ARUK, 2015). OA can be diagnosed radiologically or clinically (Litwic et al., 2013). Whether or not individuals are diagnosed with OA influences the treatments that they may seek and receive (Healey et al., 2018); therefore, diagnosis is a pivotal point in patient care (Bedson and Croft, 2008). Radiologically, OA is most widely assessed using the Kellgren and Lawrence score (KLS), which grades the severity related to the appearance of osteophytes, joint space loss, sclerosis and cysts (Litwic et al., 2013). However, radiological definitions of OA are often considered to be arbitrary (Nüesch et al., 2011) as discordance exists between radiographic findings and symptoms (Bedson and Croft, 2008; Dhalwani et al., 2016). Furthermore, the use of radiological diagnosis in isolation disregards what symptoms of OA are important at the patient level, such as pain or disability (Bedson and Croft, 2008). The National Institute of Health and Care Excellence (NICE) recommend a diagnosis of OA if the person is; '*aged 45 or over with activity-related joint pain and either no morning joint-related stiffness or morning stiffness that lasts no longer than 30 minutes'* (NICE, 2014).

Comorbidity

It is important to acknowledge that the meaning of comorbidity in this thesis is different from other related concepts, described below. Several terms exist to conceptualise the presence of more than one health condition co-existing or define combinations of conditions co-occurring, including comorbidity, complexity and multimorbidity (Smith et al., 2016; Sharfstein and Chrvala, 1999; Webster et al., 2019; Valderas et al., 2009).

Multimorbidity, for example, is a general term used for patients with multiple long-term conditions (LTCs) (Ford and Ford, 2018; Watt, 2017). However, there are several problems with the concept of multimorbidity for both healthcare services and individuals (Ford and Ford, 2018). For example, as the prevalence of multiple LTCs is so vast and varied (Kingston et al*.,* 2018), the patients that have 'multimorbidity' are heterogeneous. Without further explanation of the health conditions included within the term multimorbidity, the practicality of what healthcare professionals (HCPs) can do with multimorbidity as a patient diagnosis, is limited (Watt, 2017; Ford and Ford, 2018). For example, on its own it offers limited disease-specific focus and tailored management strategies (Smith et al., 2016). Within the House of Care model (HOC) (discussed further in section 2.7), the overarching theme of integrated care centred around the individual and their needs is lost in the concept multimorbidity, because it lacks detail of what the LTCs mean to the individual, or how they impact on their lives (Webster et al., 2019; Ford and Ford, 2018; Coulter et al*.,* 2013).

Patient complexity promotes a broader viewpoint of the whole patient by expanding beyond the biological and clinical presentation, to incorporate the personal, social and environmental aspects that complicate patient care (Shippee et al., 2012; Manning and Gagnon, 2017; Loeb et al., 2015). The concept of patient complexity acknowledges that LTC burden is influenced by several dynamic interacting characteristics, such as increased age, education level and treatment characteristics (Nardi and Scanelli, 2007; Valderas et al*.,* 2009). Patient complexity as a concept considers the individual with LTCs and patient-specific concerns, including their health priorities, symptoms and well-being. However, as a stand-alone term, it remains a little vague in its practical usefulness and ability to inform patient management (Valderas et al., 2009).

Comorbidity is the co-existence or combination of conditions occurring simultaneously with a defined index condition (OA) and the presence of '*distinct additional clinical entity'* (comorbidity) (Feinstein, 1970). Comorbidity orientates toward emphasising one disease, which may be better suited than other terms to inform patient management and care (Valderas et al., 2009). Kerr et al*.* (2007) have described

comorbidities to either exist as; *concordant,* those which share conventional treatment approaches, or in contrast, *discordant,* with unrelated pathophysiology and those that do not share treatment approaches. Discordant comorbidity requires separate management of the distinct conditions, avoiding conflicting strategies, polypharmacy, interactions and side-effects (Kerr et al*.,* 2007). However, the concordant comorbidities of interest to this thesis all share physical activity as a management option. Furthermore, comorbidity is the language used in the National Institute for Health and Care Excellence (NICE) guidelines for OA, alongside the need for a holistic assessment (NICE, 2014; P12). Therefore, although many definitions are acknowledged that describe co-existing LTCs, for this thesis, having a defined index condition (OA) with any additional condition(s) co-existing (e.g. T2DM or depression) is defined as having comorbidity.

Physical activity

Physical activity (PA) has been defined by the World Health Organisation (WHO) as "*any bodily movement produced by skeletal muscles that require energy expenditure, including activities undertaken while working, playing, carrying out household chores, travelling, and engaging in recreational pursuits*" (WHO, 2015). PA also encompasses exercise (planned and structured PA) and therapeutic exercise (health specific, preventative and rehabilitative) (DOH, 2009; WHO, 2015; Fransen and McConnell, 2015). Other forms of PA exist such as occupational activity and sport which can vary in mode and intensity, from walking to extreme sports, consisting of any energy expenditure above resting levels (CMO, 2019; Caspersen et al., 1985; Osthoff et al., 2018). For the purpose of this thesis, 'physical activity' has been adopted in accordance with the language used in the NICE guidelines (NICE, 2013; Public health guideline [PH44]).

Patient and Public Involvement and Engagement

Patient and Public Involvement and Engagement (PPIE) is described as an active partnership between the researcher and the patients and public in the research process (INVOLVE, 2018). PPIE in research focuses on the role of the patient and public being involved with assisting research design and in

carrying out research, rather than being the subject of a study (INVOLVE, 2018). In the current thesis, PPIE played an important role in the design of the interview research process and forming of public-facing documents.

Healthcare professional

Primary care in the NHS, often the first-line care point, includes a range of community clinics and health centres. Healthcare professionals including GPs, nurses, pharmacists, and other allied health professionals such as physiotherapists (NICE, 2012) commonly deliver care for people with OA in these settings. However, people with OA and comorbidities also often access alternative, independent and community-based providers of exercise and PA (Walsh et al., 2016). Patients and the participants in the qualitative study (see chapter 6), referred to healthcare professionals broadly as someone that engages with them, acknowledges their individuality, and lived experience of OA and comorbidity and supports their condition self-management. This includes both more traditional NHS primary care health professionals and extends to alternative health professions such as community and independent health workers (e.g. exercise professionals and mind-body practitioners). Therefore, in this thesis, the term 'healthcare professional' is used to refer to both traditional healthcare professionals employed by the NHS and other people in the community who support healthcare and advise on PA supporting OA self-management.

This inclusive term corroborates well with the House Of Care model (detailed in Chapter 2), as a whole-system approach, with the fundamental multidisciplinary, collaborative, and informed healthcare professionals and carers working together, to bring the optimal treatment to support self-management and PA for people with OA and comorbidity (Coulter et al., 2016).

Chapter 1

Thesis introduction and overview

Chapter 1. Thesis introduction and overview

1.1 Introduction

This chapter introduces the thesis research context with a rationale for, and a brief summary of, the topic under study. Following this, gaps in current research are highlighted which inform the overall thesis aim and research questions. Finally, an overview of the thesis structure is presented.

1.2 Thesis rationale

Osteoarthritis (OA) is the most common form of arthritis and a Long Term Condition (LTC). It is a whole-joint condition that causes progressive loss of joint cartilage and joint space narrowing (NICE, 2014; ARUK, 2015). In the United Kingdom (UK), 8.75 million people have sought treatment for OA, which can exist in any joint but is most common in the knee, hip, hands and feet (ARUK, 2015). In adults aged 45 and over, it is estimated that one in five have knee OA and one in nine have hip OA, and this prevalence is likely to increase because of the ageing population and rising obesity levels (ARUK, 2017). People with OA experience symptoms such as pain and stiffness which lead to functional limitations (NICE, 2014; ARUK, 2015). However, OA also affects many aspects of a person's psychosocial life, including mental health, work and social relationships (Hurley et al., 2018; ARUK, 2013).

Since there is no known cure for OA, primary care management of this condition aims to control pain and improve function and quality of life (QOL) (Felson et al., 2000). The National Institute for Health and Care Excellence (NICE) guidelines for OA (Clinical guideline CG177; 2014) have recommended physical activity (PA) as a core treatment for all, inclusive of those with comorbidity, and as part of supported self-management for OA in primary care (NICE, 2014). PA is any bodily movement, that results in energy expenditure above resting levels (WHO, 2015; CMO, 2019), ranging from recreational pursuits to therapeutic exercise. Common guideline-recommended types of PA for OA include muscle strengthening and aerobic activity (NICE, 2014). However, despite PA recommendations (NICE, 2014), PA is underused as a treatment approach for patients with OA (Healey et al., 2018) and under half

(48.7%) of General Practitioners (GPs) prescribe PA to this population (Denoeud et al*.,* 2005). Further, 40% of people with OA scheduled for total knee arthroplasty reported not having been recommended non-surgical treatments including PA (King et al., 2019). Levels of PA in the OA population are lower than those in the general population (Wallis et al., 2013; Herbolsheimer et al., 2016; Holden et al., 2014). Barriers to PA exist at individual, social, healthcare and environmental levels (Marks, 2012; Dobson et al*.,* 2016; Holden et al*.,* 2012; de Rooij et al*.,* 2014; Haseler et al*.,* 2019), and key barriers include a lack of PA endorsement, low levels of self-motivation for PA, lack of social support and problems with access to PA opportunities (Kanavaki et al., 2017; Manaf et al*.,* 2013).

A key potential barrier to PA in people with OA, and the focus of this thesis, is comorbidity. Comorbidity is the co-existence of an additional condition alongside a defined index condition (Kadam et al*.,* 2004). OA often exists alongside other LTCs such as obesity, type two diabetes mellitus (T2DM), cardiovascular disease (CVD), respiratory conditions and depression (Smith et al*.,* 2016; ARUK, 2015; Wshah et al., 2018; Gleicher et al., 2011; Louati et al., 2015; Wang et al., 2016; NJR, 2018). Over the previous decade in England, the number of people living with more than one LTC increased momentously (Dhalwani et al*.,* 2016) and in 2018 it was reported that 54% of people aged 65 and above have two or more LTCs (Kingston et al*.,* 2018). Furthermore, around a third of the population over 45 have sought treatment for OA (ARUK, 2015; NICE, 2014), of which the proportion of people with OA that also have comorbidity is reported to be up to 80% (ARUK, 2017; Zambon et al., 2016).

Comorbidities can have a significant impact on LTC management (Theis et al., 2016) and the presence comorbidity alongside OA is suggested to be associated with more limitations to PA participation compared to those without comorbidity (Ernstgård et al., 2017; Van Dijk et al., 2008; Reeuwijk et al., 2010), for example, comorbidity could aggravate OA symptoms (Campbell et al., 2001) or cause fatigue (Simonik et al., 2016). However, the relationship between comorbidity and PA in people with OA has not been thoroughly investigated. For example, comorbidity has appeared as an emergent theme, in broader PA qualitative studies and has not been thoroughly investigated (Campbell et al., 2001; Wilcox

et al., 2006; Marks, 2012) or as a covariate within multivariable models of PA in people with OA (Quicke et al., 2017).

Undertaking PA may be more complicated for people with OA and comorbidity than for those with OA alone. This is relevant to UK healthcare policy as the need for a holistic assessment of patients with OA that takes account of comorbidity is recognised in OA specific NICE guidelines (NICE, 2014 P12). Furthermore, supporting people with LTCs to be physically active and able to self-manage their LTCs is a key part of the House Of Care (HOC) framework proposed by National Health Service (NHS) England (NHS, 2019; Coulter et al., 2016). The framework highlights how people with LTCs play a key role in managing their own health, but how effective this is, in part, depends on their level of confidence and skill to manage tasks that are sometimes quite challenging, especially for those with comorbidities (Coulter et al., 2016). The HOC model was designed to address the challenges of LTC care and fit integrated care around people with LTCs (NHS, 2019). Using the HOC model as a policy backdrop, this thesis seeks to better understand how comorbidity impacts on PA in people with LTCs, using OA as an exemplar index condition.

1.3 Physical activity in people with osteoarthritis and comorbidity

There is a recognised requirement for research to determine the effects of comorbidity on guidelines for care, treatment plans, clinical practice and outcomes in LTC management (Theis et al., 2016). The prevalence and impact of OA and comorbidity has become a national and international priority (NHS, 2019; MacMahon, 2018) and there are calls for research in the field of OA that establishes the factors associated with PA levels in this patient group (Veenhof et al., 2012). NICE OA guidelines (2014) recommend PA and supported self-management as a core treatment for OA; however, how to implement this successfully within primary care for people with OA and comorbidity remains unclear. Thus, three gaps in the current research have been identified, and will be the focus of this thesis:

1. There is a lack of evidence regarding the effectiveness of PA as a treatment for OA inclusive of comorbidity.

Few studies explicitly focus on individuals with OA and comorbidity and it remains unclear what PA interventions are potentially successful for this patient group. Previous evidence syntheses and systematic reviews have explored PA in people with OA (Fransen et al*.,* 2015), but these often contain Randomised Controlled Trials (RCTs) that exclude comorbid participants, and therefore may have questionable generalisability to real-world comorbid populations.

2. Increasingly, individuals with OA are living with comorbidity; however, the relationship between comorbidity and PA has not been thoroughly investigated.

People with OA have lower levels of PA than those without the condition, which may in part be due to the existence of comorbidities (Kraus et al., 2016; Dunlop et al., 2011; Herbolsheimer et al., 2016; Quicke et al., 2017). Comorbidities that are prevalent in OA may influence PA levels. Furthermore, investigating comorbidity in different ways, such as measuring comorbidity frequency in people with OA and comparing different ways of collecting comorbidity data (e.g. self-report and Medical Record Review (MRR)) are novel approaches and may add to the knowledge of how comorbidity influences PA level.

3. NICE guidelines have recommended PA as a core treatment for OA, however, knowledge of how to implement this successfully within primary care for people with OA and comorbidity remains unclear.

Previous research suggests that the effects of PA may be improved for people with OA and comorbidity when individualised by taking comorbidity into account (Bennell and Hinman, 2013), however, how to do this is not well understood. Previous qualitative studies provided narratives of experiences of PA in those with OA and chronic pain (Kanavaki et al., 2017; Hendry et al., 2006; Hurley et al*.,* 2018), and comorbidity has appeared as a factor affecting OA management and PA participation in a small number

of studies (Campbell et al, 2001; Hendry et al., 2006; Paskins et al., 2014; Hurley et al., 2010; Marks, 2012). However, comorbidity has not been further explored nor been the principal research focus. Therefore, how and why comorbidity may influence PA or compound PA effects and how to overcome comorbidity barriers and increase PA level, is unknown.

In summary, OA is a condition which is associated with one of the highest comorbidity rates and lowest PA levels. Therefore, there is a clear need to synthesise existing knowledge about the effectiveness of PA for people with OA and comorbidity. An increased understanding of PA behaviour in people with OA and comorbidity could inform future treatment strategies within primary care. To inform future OA and comorbidity targeted interventions, there is a need to generate new knowledge about PA behaviour, attitudes towards, and beliefs about, PA in people with OA and comorbidity. This new knowledge could be used to make recommendations aiming to increase PA levels and improve clinical outcomes. The Venn diagram below summarises the gaps in the current research concerning OA, comorbidity and PA (Figure 1.1).

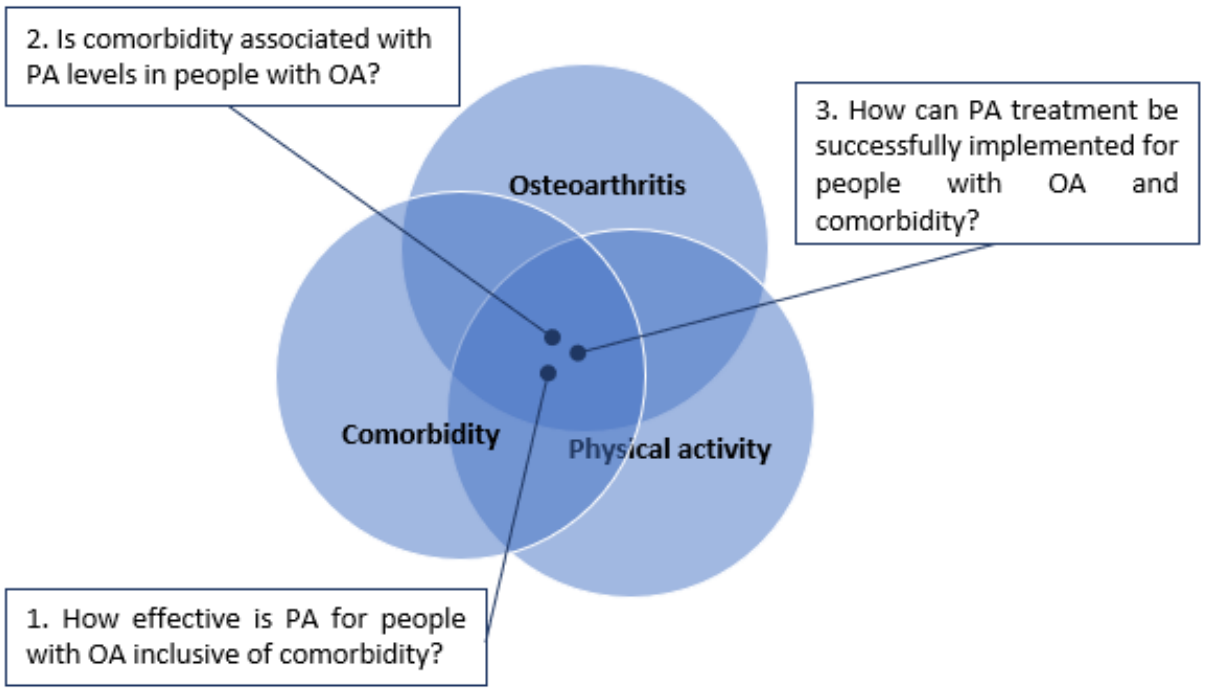


Figure 1.1 The gaps in current research this thesis seeks to fill

1.4 Thesis aim and research questions

1.4.1 Aim

The overall aim of this thesis is to investigate the impact of comorbidity on PA and clinical outcomes in those with OA in primary care. To fulfil the research aim, there are three specific research questions.

1.4.2 Research questions

1. What is the effectiveness of PA interventions for people with OA and comorbidity?
2. Is comorbidity associated with PA levels in people with OA?
3. How do people with OA experience PA in the context of comorbidity?

By addressing these research questions, this thesis will contribute to a new understanding of how people with OA and comorbidity can be better supported to self-manage and increase PA levels in primary care. The use of a multi-method approach is a novel contribution to provide a more in-depth understanding of PA in people with OA and comorbidity.

1.5 Structure of the thesis

To address the thesis research questions, three individual studies were conducted using multi-methods. The three studies are displayed below (Figure 1.2), and the chapter structure is then provided. Further detail of the thesis structure is presented as a conceptual map in Appendix 1.

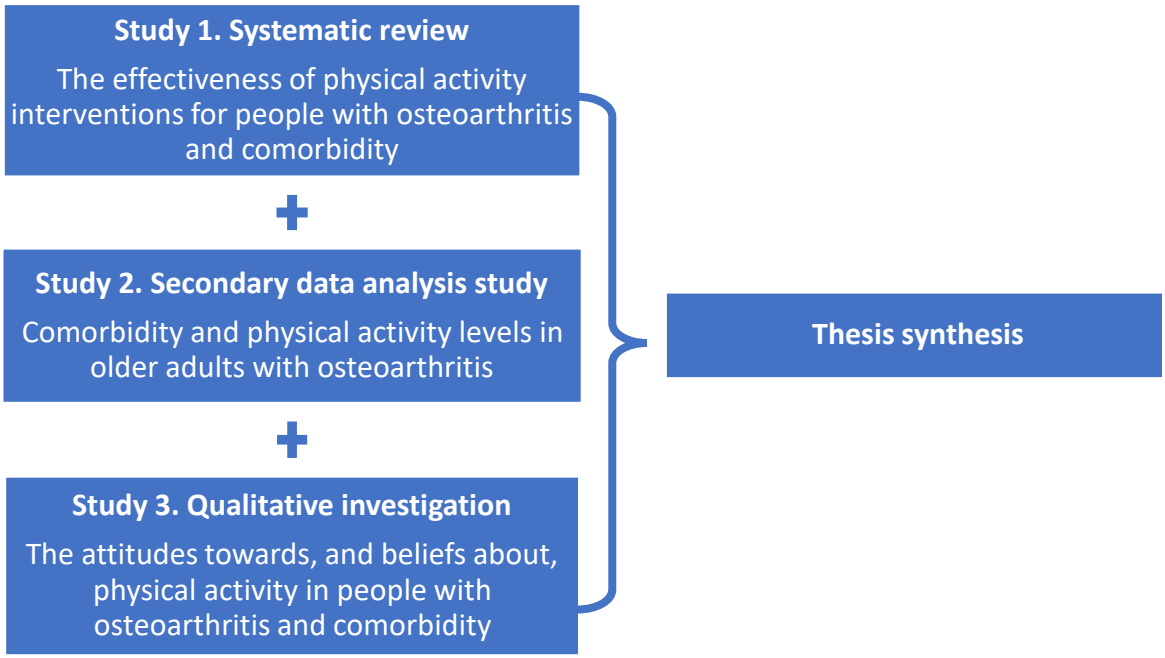


Figure 1.2 The three studies conducted to address the research questions within this thesis

Chapter 1. Thesis introduction and overview

This chapter introduces and provides a rationale for the thesis. It then goes on to highlight gaps in current research and presents the overarching aim, research questions, and thesis structure.

Chapter 2. Background

This chapter provides a background thesis work-up discussing literature regarding OA, comorbidity and PA. It describes the individual, healthcare and global burden that OA presents and introduces the HOC as a high quality framework for delivering person-centred coordinated care. Clinical guidelines recommending PA as a core treatment for OA and general health are provided. Following this, the current PA levels in the OA population are explored and known barriers to PA outlined. The relevance of comorbidity to patients with OA is introduced and discussed as a potential barrier to PA.

Chapter 3. Methodology

This chapter outlines the multi-method approach adopted within this thesis. It includes a brief overview of research paradigms and the rationale for selecting the pragmatic paradigm. It outlines how this approach is used, the methods, and order of the research conducted, to answer the thesis research questions.

Chapter 4. The effectiveness of physical activity interventions for people with osteoarthritis and comorbidity

Chapter 4 addresses the first research question, using a quantitative paradigm. It describes a systematic review synthesising existing research of previous RCTs investigating the effectiveness of PA interventions on clinical outcomes of; pain, function and QOL, in adults with OA and comorbidity.

Chapter 5. Comorbidity and physical activity levels in older adults with osteoarthritis

Chapter 5 addresses the second research question using quantitative methods in the form of secondary data analyses. It examines the PA levels of those with OA with and without comorbidity. The chapter introduces and justifies the datasets and choice of variables used, followed by the regression analyses methods to investigate the association between comorbidity and PA levels in people with OA.

Chapter 6. The attitudes towards, and beliefs about, physical activity in people with osteoarthritis and comorbidity

Chapter 6 addresses the third research question using a qualitative paradigm to gain an in-depth insight into the attitudes towards, and beliefs about, PA in people with OA and comorbidity. Face-to-face semi-structured interviews with individuals with OA and comorbidity are used to investigate how people with OA experience PA in the context of comorbidity and how people with OA and comorbidity can be better supported to be physically active.

Chapter 7. Thesis synthesis

Chapter 7 brings together the findings from the three studies. The findings are summarised, integrated, and synthesised. This chapter evaluates the strengths and limitations of the thesis and, based on the synthesis of the three studies, makes clinical and research recommendations for future work in the field of PA in people with OA and comorbidity.

Chapter 8. Thesis conclusion

The thesis concludes with a synopsis of the thesis and concluding remarks.

1.6 Chapter summary

This chapter introduced the thesis and provided a concise rationale. The gaps in current research which informed the thesis aim and research questions were stated. The thesis structure and outline of the chapters were then provided.

Chapter 2

Background

Chapter 2. Background

2.1 Introduction

This chapter provides the background of key topics relevant to this thesis. First, the UK healthcare and policy context of the management of LTCs is outlined, as this provides a policy backdrop for the thesis and is relevant to the management of OA in primary care. Second, OA as a LTC is described in order to outline the global burden, symptoms and impact of this condition. Third, PA as part of supported self-management and a core treatment in the management of OA is introduced. Previous research investigating barriers to PA are outlined. Finally, comorbidity is discussed as an important consideration for people with OA due to the common co-occurrence of OA and other LTCs and the implications that this may have on recommendations for care and supporting self-management through PA.

2.2 Management of long-term health conditions in the UK

In England, about 26 million people have at least one LTC (NHS, 2019) and one in four adults are living with two or more health conditions (Stafford et al*.,* 2018). By age 65, it has been estimated that 54% of the population over 65 in England have two or more co-existing LTCs (Kingston et al., 2018; DOH, 2012) and these numbers are projected to rise significantly with the ageing population (Stafford et al*.,* 2018). A large cross-sectional study analysed 1,751,841 registered primary care patients from 314 general medical practices in Scotland found that 42.2% of patients had at least two LTCs and of those, 54.9% had three or more (Barnett et al*.,* 2012). Further, by age 50, half the population had at least one LTC and by 65, most people had comorbidity (Barnett et al*.,* 2012). Therefore, the prevalence of LTCs is not just a problem in England, but a UK-wide issue.

In primary care, people with multiple LTCs are routine service users; six out of 10 (58%) patients have multimorbidity (2+ co-existing conditions) but account for eight out of 10 (78%) GP consultations (Salisbury et al*.,* 2011). Recent figures show LTCs account for 50% of all GP appointments and 70% of

health and care expenditure in the UK (NHS, 2019). LTCs often require ongoing attention and adjustments to life and interaction with the healthcare system (Goodwin et al*.,* 2010).

The NHS Five Year Forward View (2014) and following this, the NHS Long Term Plan (2019), were published to set out a new vision for the future of the NHS and practical plans for implementing improvements to care (NHS, 2019). These policy documents both highlighted how LTCs are increasing in prevalence and that providing care for LTCs is a central task of the NHS (NHS, 2014; 2019). The scale of LTCs means that clinical practice needs to shift from a disease-focused, reactive and fragmented model, toward a holistic, proactive and collaborative model which would place the person with LTCs at the centre of their care (Coulter et al*.,* 2016). The NHS vision emphasises supporting individuals with multiple health conditions, by listening to, and involving patients, in patient-centred care (NHS, 2014; 2019). Personalised care was one of the major practical changes in the NHS long-term plan, which promotes a new relationship and a positive shift in power to enable the patients to have a voice in determining their own care and support needs (NHS, 2015). The HOC model is a whole-system approach, developed to address the barriers to effective care for people with LTCs which include (Figure 2.1);

1. Single condition services
2. Lack of care coordination
3. Emotional and psychological support
4. Fragmented care
5. Lack of informational continuity (coherent shared information between the HCP and patient)
6. Reactive, not predictive services
7. Lack of care planning consultation

The HOC model aims to build care around the patient, not make the patient fit the care. This approach is designed to optimise healthcare through co-creation of a care plan which activates and supports patients (Coulter et al*.,* 2016). The HOC model is presented as building blocks of

highly person-centred and coordinated care and typically relies on four components; 1) commissioning, training and development (floor), 2) engaged and informed individuals (and carers) (wall 1), 3) HCPs working in partnership (wall 2) and 4) the organisational systems and clinical processes (structured around the needs of the individuals and HCPs, to improve identification, appointment linking, consultations, recording systems and monitoring care plans and outcomes) (the roof).

Figure 2.1 The House of Care model (NHS, 2019)

2.3 Osteoarthritis: a long-term condition

The HOC provides the policy backdrop to this thesis. OA is one of the most prevalent LTCs (Theis et al., 2016; Simões et al., 2017), and places a huge demand on both the healthcare system and individuals. OA as a LTC requires ongoing care and management and situates well within the HOC model (Smith et al., 2012). OA is predominantly managed in primary care by GPs and practice nurses (Foster et al., 2014; Healey et al., 2015). Other practitioners such as physiotherapists and pharmacists may also be involved in decision making and treatment within primary care (Healey et al., 2015).

2.3.1 The global burden of osteoarthritis

In the UK, 8.75 million or approximately a third of all adults aged 45 and over have sought treatment for OA (ARUK, 2015; NICE, 2014). One in nine people have hip OA (ARUK, 2015) and over one in five adults have knee OA (4.11 million people) which amounts to 18.2% of the population in England (ARUK, 2019; Kraus et al*.,* 2016; Litwic et al*.,* 2013). OA is often also multisite; a cross-sectional study of 15,083 adults aged 45 and over, found 11,928 reported peripheral joint pain (hands, hips, knees and feet), of which, 68% reported multisite joint pain (pain in two or more of the sites) (Finney et al*.,* 2017). OA is associated with reduced physical and mental health (Kraus et al., 2016) which is compounded by each additional site of joint pain in those with multisite pain (Finney et al*.,* 2017). The prevalence of knee OA has doubled in women and tripled in men over the last 20 years (Tsai et al*.,* 2013) and this prevalence is projected to increase aligned with the number of people living longer (Vogels et al*.,* 2001; Wilkie et al., 2019). These factors make OA especially important, as it not only has a considerable impact on the population but also creates a high economic burden and puts greater demands on healthcare (Chen et al., 2012; OARSI, 2016; Wilkie et al., 2019).

2.3.2 The symptoms and impact of osteoarthritis

OA impairs a person's ability to perform basic daily activities and live independently (Zambon et al*.,* 2016). OA symptoms are associated with functional impairment and reduced general health and QOL (Kraus et al., 2016). OA is the second largest musculoskeletal (MSK) contributor to disability-adjusted life years (DALYs) across the world (Simões et al., 2017) and arthritis-attributable life limitations (limitations in any usual activities because of arthritis symptoms) are projected to increase (Hootman et al*.,* 2016). Immobility resulting from OA can add to a reduced lifespan by increasing risk factors for other condition mortality (e.g. CVD) (Wilkie et al., 2019; Nüesch et al*.*, 2011). The existence of arthritis alongside other LTCs is associated with significant and progressively worse clinical outcomes (Qin et al*.,* 2015). For example, in a study of adults with multiple LTCs in the United States (US) (n= 34,506), people with arthritis were shown to experience higher prevalence of adverse outcomes in physiological, psychological and social domains, when compared with those living with multiple

conditions but excluding arthritis (Qin et al*.,* 2015), highlighting the importance of OA for population health.

The symptoms experienced by people with OA can impact the individual beyond their physical health. Limitations in mobility attributable to knee OA alone is greater than any other health condition in people age 65 and over (Guccione et al*.,* 1994), which impacts several areas of living, such as independence, personal care, household management, social relations and work (Zambon et al., 2016, DOH, 2012). The natural course of pain and function in OA patients is highly variable and individual (Nicholls et al*.,* 2014; de Rooij et al., 2016), but the experience and impact of OA pain can dominate and affect many areas of life in multiple ways (e.g. physical dysfunction or psychosocial distress) (Hurley et al*.,* 2018).

The impaired psychosocial functioning from OA can have a hugely detrimental impact on people's sense of self and personal narrative (Bury, 1982). The loss of control, freedom and independence can accumulate to biographical disruption in a person's QOL (Bury, 1982). Knee pain is strongly associated with depression and anxiety (Hawker, 2008), which can, in turn, significantly influence participation restriction and physical limitation (Sharma et al., 2016). Furthermore, psychological distress and depression have been found to worsen pain in a vicious cycle (Barnett et al*.,* 2012). The psychological burden of symptoms is significantly higher in individuals with multisite pain (Hoogeboom et al., 2012; Finney et al*.,* 2017). Taken together, a person with OA can experience life-altering physical symptoms, impairments to psychosocial functioning, and losses in social belonging and relationships, all of which can subsequently reduce QOL (Vitaloni et al*.,* 2019).

2.3.3 Osteoarthritis risk factors

OA is considered a complex interplay or reciprocity of several risk factors (Silverwood et al*.,* 2015; ARUK, 2017; Palazzo et al*.,* 2016). These risk factors can be split into person-level factors and joint-level factors (Palazzo et al*.,* 2016). The most common person-level risk factors for developing OA include; increased age, female gender, higher BMI and genetic factors (Silverwood et al*.,* 2015; ARUK,

2017; Kraus et al., 2016; Suri et al., 2012). At a joint-level, patient history such as trauma or injury to the OA joint site, joint abnormalities, surgery, occupation or lifestyle that places abnormal loading on the joint and malalignment or repetitive movements, can all contribute to OA incidence (Suri et al., 2012, Palazzo et al., 2016).

Obesity is one of the most important risk factors to OA development (ARUK, 2017; Palazzo et al., 2016), initially attributed to the excessive load placed on the weight-bearing joints (hip and knee). However, recent studies have suggested that obesity plays a further role than biomechanical mechanisms. Increased load, inflammation, low muscle mass to body mass ratio, and aberrant biomechanics from obesity, can contribute to increased OA risk (Holden et al., 2019). Also, other conditions that affect blood flow or inflammation (e.g. diabetes, gout, underactive thyroid) can affect the risk of OA development (ARUK, 2017). Hand OA pathogenesis is different from the weight-bearing joints (Qin et al., 2017). Altered metabolic regulation and increased levels of inflammation associated with obesity are suggested to contribute to the development of hand OA (Qin et al., 2017). Importantly, several of the risk factors in OA and many other LTCs, are modifiable and can be altered by lifestyle behaviours such as diet and PA (Qin et al., 2015).

2.4 Osteoarthritis care and treatment

In the absence of a current cure for OA, the goal of OA management is targeted toward reducing pain and improving function (Felson et al., 2000; Bennell et al., 2016), reduce the overall disability from OA and maximise QOL (Ernstgård et al., 2017; Loza et al., 2009; Kraus et al., 2016; Tsai et al., 2013; Rejeski et al., 2002).

Core treatment of OA includes the provision of good quality written and verbal information, education about the condition and how to manage it, and advice and interventions including PA programmes and weight loss (NICE, 2014). Education and self-management are central to the recommendations to enhance patient understanding of OA and its management, change misconceptions and foster positive behaviour change (NICE, 2014). Non-pharmacological management (e.g. PA and weight loss) are

recommended before pharmacological treatment, such as; oral analgesics and non-steroidal anti-inflammatory drugs (NICE, 2014) because of their comparable effectiveness for pain relief and favourable safety profile (Quicke et al., 2015; Kraus et al., 2016; Henriksen et al., 2016). Some pharmacological therapies have significant toxicity risk (e.g. nonsteroidal anti-inflammatory drugs (NSAID)), which limit their continual use in the long-term (Kraus et al., 2016) and fewer than 40% of patients with chronic pain report satisfactory relief from them (Tsai et al., 2013). Joint surgery is only recommended after the patient has been offered the core non-surgical treatment options and experiences prolonged and established functional limitation and severe pain, prior to referral (NICE, 2014).

2.4.1 Physical activity in osteoarthritis

PA has been deemed an effective intervention for OA in primary and secondary care, and also as a preventative method for OA and various LTCs (DOH, 2019; WHO, 2015; Felson et al., 2000; Kyu et al., 2016) with effective activities varying from; aerobic exercise, walking, aqua-based activity, strength training, neuromuscular education and tai chi (Kraus et al., 2016). Strengthening activities can also include; stair climbing, using a wheelchair, carrying and lifting shopping and children (DOH, 2019). Felson et al. (2000) suggest PA for OA can be subcategorised into; range of motion and flexibility enhancing, muscle strengthening and conditioning, and aerobic cardiovascular exercise. However, the optimal type of PA for treatment of this population remains under debate (Uthman et al., 2013). Activities such as dance and tai chi are examples of PA options that encompass strengthening, balance and flexibility (DOH, 2019).

PA, when adopted and maintained, has the potential to provide numerous health benefits, including improved physical and psychological health and an overall enhanced QOL (Dallosso et al., 2018; Uthman et al., 2013; Felson et al., 2000; Geneen et al., 2017; ACSM, 2009). PA is a strategy to maintain general health, but also reduces mortality and the likelihood of increasing morbidity (DOH, 2011; Slater et al., 2011), by both preventing the onset of over 25 LTCs and improving the general health of

individuals living with such conditions (Keats et al*.,* 2017). For example, PA has been proven an effective treatment for LTCs such as OA, cancer, CVD, T2DM and respiratory diseases (DOH, 2019; Dekker et al*.,* 2019). Furthermore, research has indicated that merely walking and 'getting out and about' more, could be protective against excessive mortality in people with OA (Wilkie et al., 2019).

Regular participation in PA is reported to reduce hip and knee OA pain by 6% (Hurley et al*.,* 2018) and can improve the physical status of the OA population without exacerbating further joint damage (Quicke et al., 2015; Bricca et al., 2019; Foster et al., 2014). PA also contributes to enhanced joint motion and elasticity of periarticular tissues and strengthens muscles which are necessary for the normal functioning, stability and support of joint structures (Felson et al., 2000). People with OA also benefit from the wider health benefits of PA, such as improved self-esteem, balance, sleeping, stress management, fall prevention and social opportunity (DOH, 2019; Hurley et al*.,* 2018).

2.4.2 Physical activity guidelines for osteoarthritis

It is recommended that people with OA should aim for the current adult PA recommendations of at least 150 minutes of moderate-intensity or 75 minutes of vigorous-intensity PA throughout the week alongside muscle-strengthening activities, activities to improve flexibility and balance, and to break up long periods of sedentary time (DOH, 2019; WHO, 2015; McAlindon et al., 2013). The WHO (2015) suggests that this level of PA is necessary to gain health benefits. Most recent evidence suggests that the 150 minutes PA per week can be achieved in bouts of any length, such as 10 minutes, and this could be an effective behavioural goal for people with low PA levels and may help break up long periods of sedentary time (DOH, 2019).

International guidelines, expert committees and health institutions have all recommended PA as part of a regimen for the treatment and management of OA (Kraus et al., 2016). Key guidelines that include PA or exercise recommendations for people with OA and one guideline for OA and comorbidity are outlined in Table 2.1. The OA NICE (2014) guideline recommends three core treatments for people with OA; education and information to enhance understanding of OA and its management, advice on

muscle strengthening and aerobic exercise, and advice on weight loss for those who are overweight or obese (NICE, 2014). PA is recommended by NICE as a core treatment, *irrespective of age, comorbidity, pain severity or disability* and should include local muscle strengthening and general aerobic fitness training (NICE, 2014). OA Research Society International (OARSI) produced guidelines for the non-pharmacological management of all individuals with OA, which includes PA (OARSI, 2014). The guideline suggested that land-based exercise and weight management are the most appropriate forms of non-pharmacological treatment for those with OA, *regardless of comorbidity status* (OARSI, 2014).

Other guidelines exist including those from the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR). These guidelines focus on lifestyle changes through interventions such as education, support meetings, coping strategy training, self-management programmes and psychosocial interventions, in which PA, exercise and weight reduction are subcomponents (EULAR, 2013; ACR, 2012). These guidelines emphasise a more holistic approach inclusive of patient preference, mixed PA programs and linking PA into daily activities to integrate them into a lifestyle change, which could be essential for PA uptake and maintenance. The guidelines also step away from traditional aerobic and strengthening PA and suggest alternative modes of activity, such as tai chi programmes (EULAR, 2013; ACR, 2012), but do not provide guidance for comorbidity.

Table 2.1 Guidelines for PA in patients with OA

	ACR OA, 2012	**EULAR OA, 2013**	**NICE OA, 2014**	**OARSI OA and comorbidities, 2014**
PA specific	• Aerobic • Resistance • Land-based • Aquatic • Manual-therapy • Tai chi	• Mixed exercise • Strength • Aerobic • Water-based • Strengthening • ROM / stretching	• Local muscle strengthening • Aerobic fitness	• Land-based • Strengthening • Water-based
Non PA	• Weight management • Psychosocial interventions • Self-management	• Long-term lifestyle • Education • Self-management • Weight loss	• Self-management programmes	• Weight management

OA=Osteoarthritis; PA=Physical Activity; ACR=American College of Rheumatology; EULAR=European League Against Rheumatism; OARSI=Osteoarthritis Research Society International; NICE=National Institute for health and Care Excellence; ROM=Range Of Motion

2.4.3 Supported self-management

Supported self-management is an integral aspect of disease management and has been recommended in several OA guidelines above-mentioned (Table 2.1). Effective supported self-management can influence the effectiveness of treatments, such as PA (Valderas et al*.,* 2009). Effective supported self-management empowers patients and facilitates participation in their care plan and maintenance (Dallosso et al*.,* 2018). Patients with LTCs and HCPs have identified three key factors which affect engagement in self-management: capacity to manage (time, knowledge, access and energy), responsibility (ownership over areas of disease management) and motivation (readiness to self-manage) (Coventry et al*.,* 2014). Subsequently, the effect of treatment is greatly enhanced when patients are supported and taught how to independently self-manage treatment recommendations (Coulter et al., 2016; Rejeski et al*.,* 2002).

To achieve patient-centred care, people with LTCs need to build knowledge, skills and confidence to self-manage and live well with their conditions (Coulter et al., 2016). For successful self-management, patients need education, which can come in several forms, such as information on the safety and benefits of PA. This can be supported through teaching and encouragement, collaborative HCP and patient communication and mutual goals and treatment plans (Gay et al*.,* 2016). Conversations between the HCP and patient are essential if the patients are to succeed in managing their health, but also in integrating health and well-being plans within the context of their whole personal circumstance (including, for example, environment and family demands) (Hurley et al., 2018; Hammer et al., 2016).

Previous PA programmes for people with OA have also found that the opportunity to be in a group, meet new people, share stories and gain peer support were beneficial to PA adoption and maintenance (Hendry et al*.,* 2006). Having meaningful relationships, such as friends, can contribute to a support network that can assist both practically and emotionally in PA (Taskforce, 2018). Qualitative analysis of patients with OA has revealed that support from family, friends, peer groups and group classes, provided a sense of camaraderie and community (Hurley et al*.,* 2018). Furthermore, peer support can

foster shared and enjoyable experiences, instead of negative feelings that PA is an additional burden (Moody et al., 2012). Thus, to change PA behaviour in people with OA, it is important to not only consider how to introduce PA but also how to successfully implement and maintain change in the long-term.

2.4.4 Self-management and physical activity behaviour change

It is widely recognised that a complex range of factors can influence a person's engagement, participation and maintenance of PA (Bennell and Hinman, 2011). Multiple previous studies have reported the psychological, social and environmental factors including illness beliefs, PA beliefs, knowledge and attitudes about PA that may influence the decision to engage in PA (Hurley et al., 2018; Kanavaki et al., 2017; Bennell and Hinman, 2011). A plethora of behaviour change techniques can be applied and may be necessary to successfully guide patients to learn to self-manage and establish new behaviours, such as PA (Willett et al., 2019). Social cognition theories examine factors that predict behaviour intentions and behaviour such as PA (Becker and Maiman, 1975; Hurley, 2018; Bandura, 1977). For example, the Health Belief Model (HBM) (Hochbaum et al*.,* 1950's; Becker and Maiman, 1975; Janz and Becker, 1984) suggests that for people to adopt and change their health behaviour, the perceived threat of barriers must be outweighed by the perceived benefits. By targeting interventions to build patient confidence, form positive PA health beliefs, outcome expectancies for PA and encourage self-management, patients may be more likely to engage in their treatment actively and sustain behaviour change, such as PA.

The COM-B model (Michie et al., 2011) is a widely used model of behaviour in health research. The COM-B model proposes that there are three essential conditions to any behaviour change: capability (psychological and physiological capability, e.g. strength, knowledge, skills), opportunity (external factors, both physical, e.g. time, location, and social, e.g. cultural norms, social cues) and motivation (internal processes of decision making, both reflective, e.g. plans, evaluation, and automatic motivations, e.g. desires, impulses and inhibitions) (Michie et al., 2011). Furthermore, COM-B is an

interactional model, which suggests that by changing behaviour, there is also an impact on the determinants of behaviour, which fosters long-term behaviour change (Michie et al., 2011), especially important for sustained PA behaviour change.

The goal of PA behaviour change can be met through several characteristics of LTC management including the provision and development of knowledge, skills, roles, beliefs, reinforcement, communication and environment (Willet et al., 2019). Previous research has highlighted how people with OA need additional help not just to adopt, but also to maintain PA as part of their daily lives (Garber et al*.,* 2011). For example, motivation to do PA is best defined by the self-determination theory (Deci and Ryan, 1985) which describes how intrinsic motivation (i.e. enjoyment) and extrinsic motivation (weight loss) are enhanced by autonomy (control), relatedness (connection) and competency (mastery). Therefore, people with OA may engage in PA if it has value to them, if they perceive it to be important, and if they gain enjoyment from participation (Taskforce, 2018; Hurley et al*.,* 2018).

Furthermore, a person's attitudes and beliefs about PA, such as having higher confidence in their ability to successfully carry out PA, have been associated with higher levels of PA (Berry et al., 2020; Quicke et al., 2015). Self-efficacy is best described as a person's belief in their ability to successfully undertake or manage a task (Bandura, 1977). Therefore, PA self-efficacy in this thesis refers to the belief and capacity of people to undertake PA (Bandura, 1997). Self-efficacy might be enhanced by teaching the value of PA in the management of conditions (verbal persuasion) and through the positive experience of completing PA with the appropriate guidance (mastery) (Bandura, 1977). For example, to facilitate PA, it may help if the advice is delivered and guided by an informed HCP, who could alleviate any concerns regarding the safety of PA, provide awareness about the benefits and importance and correct and realign the interpretation of PA experiences (such as muscle soreness and fatigue) (Hurley et al*.,* 2018; ACSM, 2018).

Self-efficacy spans further than PA, with lower condition self-efficacy a risk factor for functional declines in arthritis and OA (Baruth et al., 2013; Dekker et al., 2009; Marcum et al., 2014). OA and comorbidity self-efficacy (condition self-efficacy) in this thesis refers to the capacity of people to cope with and self-manage their conditions. Developing patient beliefs in their ability to manage their symptoms and function normally is an essential consideration in OA self-management, as these beliefs about their capabilities also influence their subsequent engagement in treatment, such as PA (Bandura, 1977).

2.5 Barriers to physical activity in people with osteoarthritis

Despite the numerous benefits of PA, the activity levels of the general population are low (NHS, 2016). The latest self-report data from the Health Survey for England revealed that less than half (44%) of the population aged over 65 are meeting the target PA recommendations (NHS, 2016), and this reduces further in people with OA (De Groot et al 2008; Blair, 2009; Fishman et al., 2016; Holden et al., 2014). Physical inactivity is common in people with OA despite its documented benefits on pain, function, general health and QOL (Fenerandes et al*.,* 2013; Ernstgård et al., 2017; Veenhof et al., 2012).

Patients with OA experience several barriers associated with PA which are recognised as important influences on whether people adopt, participate and maintain the behaviour (Campbell et al*.,* 2001; Petursdottir et al*.,* 2010; Manaf et al*.,* 2013). The most recognizable barriers to PA in people with OA are the dominating pain, stiffness and functional impairment which increase disability which can make PA more challenging (Hawker et al., 2008; Kraus et al*.,* 2016; Simões et al*.,* 2017; Kanavaki et al., 2017).

Barriers to PA can exist beyond the immediate physical symptoms, extending to psychological, motivational and behavioural too. For example, people with OA may have negative health beliefs, such as the perception that their age and accompanied body deterioration and 'wear and tear' is inevitable, untreatable and worsening with time (Hurley et al*.,* 2010; 2018; Wilcox et al*.,* 2006) and thus, they feel they may not benefit from being more physically active (Campbell et al., 2001). Furthermore, fear of harm, worsening disease and symptoms and even fear of discrimination relating to age or disability

(Fries, 1996; Hurley et al., 2018; Paskins et al., 2014; Hendry et al., 2006; Haseler et al., 2019), mean that people with OA not only have doubts about the benefits they might obtain from PA participation but also can believe it would worsen their health state (Petursdottir et al., 2010). To achieve a change in PA behaviours, patients must also believe that the behaviour is safe and achievable (Hurley et al., 2010; Janz and Becker, 1984).

Despite PA being one of the key recommendations for the management of OA (NICE, 2012; de Rooij et al., 2014) and acknowledged as a safe and effective treatment for people with OA (Quicke et al*.,* 2015), under half (48.7%) of GPs prescribe PA, compared to 95.8% prescribing paracetamol (Denoeud et al., 2005). As a result, some people with OA have been recommended PA, whilst others have been discouraged (Hendry et al., 2006). HCPs have a lack of awareness and uncertainty about safety, the benefits and what PA options are available or suitable for people with OA (Hurley et al., 2018; Haseler et al*.,* 2019). A lack of knowledge, time, and specific guidance on the mode, frequency and intensity, create an obstacle for HCPs to confidently provide and endorse PA as a treatment for OA (De Souto Barreto, 2017; Dekker et al*.,* 2019; Wilcox et al*.,* 2006). Mixed messages and a negative attitude toward PA from HCPs can create patient doubts and reduce PA levels (Hendry et al*.,* 2006; Campbell et al*.,* 2001; Petursdottir et al*.,* 2010; Cuperus et al*.*, 2013). Further, a lack of support and perceived dismissive attitude about OA prognosis from HCPs can further exacerbate the dominating experience of pain, coping with pain, disability and activity restriction from OA (Wallis et al., 2019) which may reduce PA levels further.

Individuals may experience multiple other barriers to PA participation, such as previous negative PA experiences (Petursdottir et al*.,* 2010) and not experiencing the desired outcomes from PA (Campbell et al*.,* 2001; Hendry et al*.,* 2006). In a person with OA, the participant's intention to participate in PA and PA behaviour could be determined an interplay of barriers across biopsychosocial domains (Ajzen et al., 1985). Several models exist that can be used to conceptualise the multiple

barriers and facilitators in behaviour change (Michie et al., 2005; Petursdottir et al., 2010; Kanavaki et al., 2017; Marks, 2012).

For example, the Theoretical Domains Framework (TDF) was developed to integrate behaviour change theories to inform the development of interventions (Michie et al., 2005). The TDF provides a platform comprising of 14 distinct domains that are considered to influence behaviour change, such as knowledge, goals and social influence, acting as barriers or facilitators (Michie et al., 2005), which has informed several models of PA behaviour change. Key factors determining PA have been found in the Attitude, Social influence and self-Efficacy (ASE) model (De Vries et al., 1988), including various domains which can determine behaviour. Previous research has also found that readiness to do PA is constantly fluctuating based on the complex nature of the conditions (physical impairments, mental health challenges, uncertainty), interacting with other domains (social, perceptions, experience and accessibility) (Simonik et al., 2016).

Kanavaki et al. (2017) describe how there is a complex interplay among dynamic physical, intrapersonal, psychological and socio-environmental barriers and facilitators of PA, of which can be applied to several LTCs, but some are specific to OA. In OA, facilitators and barriers are primarily conceptualised as internal or external (Kanavaki et al., 2017; Marks, 2012; Petursdottir et al., 2010), including; individual attributes and personal experience with PA, and social and physical environments (Petursdottir et al., 2010) which can all exist in one person and interact and influence PA (Marks, 2012).

2.6 The challenge of osteoarthritis and comorbidity

The above sections have introduced OA and how it is managed, with a focus on supported self-management and PA, before briefly introducing evidence about levels of PA in people with OA and then common barriers to PA in this population. This section now switches attention to describe the challenge of OA and comorbidity. Comorbidity as a concept corroborates with the HOC model, as it considers the multimorbid and complex patient, but focuses on the patient perspective of how LTCs affect their health, well-being and thus, promotes patient-centred and integrated care (Valderas et al.,

2009). By defining a specific index disease, the perceived most important condition to the patient and HCP can be preserved, followed by the consideration of comorbidities (Dekker et al., 2016). Buffel du Vaure et al. (2016) summarised this well;

"*We need a paradigm shift in planning research and elaborating clinical practice guidelines. We should move from the current 'single-condition' approach to developing clinical practice guidelines toward a patient-centred approach*" (Buffel du Vaure et al., 2016).

MSK conditions are ubiquitous in comorbidity because of their high prevalence, shared risk factors and links with other LTC pathogenic processes (DOH, 2012). The proportion of people with OA reporting comorbidity ranges from 68 to 85% (depending on the definition and type of comorbidity) (Zambon et al., 2016). Over half of all adults with OA have at least one other LTC including CVD, obesity, depression and T2DM (Barbour et al., 2017; Hawker et al., 2011; Vos et al., 2012; Kriegsman et al., 2004; Theis et al., 2016; Hall et al., 2016) with most recent evidence reporting that 66% of people with OA have at least one other LTC (Swain et al., 2019).

There are possible explanations for the strong correlation of OA and comorbidities, including shared disease aetiology and physiopathology, and the association between age-related biological decline and the risk of LTCs (Leite et al., 2011; Slater et al., 2011). In a large population-based cohort study by Nüesch et al. (2011), radiographical diagnosis of OA of the hip or knee was found to have excess all-cause mortality compared with the general population, and prominent predictors of excess mortality were T2DM, CVD and cancer (reported at baseline) (Nüesch et al., 2011). This burden of comorbidity is higher in people with OA, whereby they are more likely to develop 21 different comorbidities than non-OA controls (Swain et al., 2020).

Some LTCs can develop and exist independent from each other, such as OA and asthma (ARUK, 2015). However, some LTCs have shared causal factors (obesity contributing to OA and T2DM), or sometimes one condition exacerbates symptoms of another (OA and depression) (ARUK, 2015; Slater et al., 2011).

It is also possible that OA and associated symptoms may contribute to lower levels of PA, increased sedentary time and thus increase the risk of other LTCs (Leite et al., 2011; Kadam et al*.,* 2004; Parkinson et al*.,* 2017; Slater et al*.,* 2011). Prolonged inactivity due to OA can also result in lowered aerobic capacity and increase the risk factors for other conditions such as CVD and obesity (Felson et al*.,* 2000).

2.6.1 Bringing together osteoarthritis, physical activity and comorbidity

NICE OA guidelines (2014) acknowledge that due to the ageing of the population, there is a high incidence of comorbidities in people with OA which may influence the appropriateness of management options. However, how to address comorbidity, when recommending PA to people with OA, is not outlined. It has been recognised that prescription and advice regarding PA should consider the impact of comorbidities such as cardiometabolic, respiratory and psychological conditions (Simões et al*.,* 2017). However, currently, the common use of a 'one size fits all' approach to PA prescription for OA does not account well for tailoring treatment to the clinical presentation including comorbidity (Bennell et al., 2015).

Historically, the guidance for patients with more than one LTC involves combining the separate guidance for each condition with no true coordination of management or treatment recommendations (Dekker et al., 2016). This is problematic as one treatment might interact negatively with another treatment or affect the natural trajectory of co-existing disease (de Rooij et al., 2014). Alternatively, one condition may impede the applicability of treatment for another condition.

A necessary consideration when recommending PA is that comorbidity in the person is individual and not merely the sum of conditions (Schoenberg et al., 2009). The NICE OA guidelines (2014) recommend that comorbidities that may compound the effects of OA are taken into consideration to ensure that self-management approaches for OA such as PA are acceptable in their nature and setting (NICE, 2014; P14). In 2016, NICE published their multimorbidity guidelines (Clinical guideline NG56; 2016). This guideline acknowledged that health conditions interact, and that patient care should account for

individual needs, preferences, priorities, lifestyle and goals to improve QOL (NICE, 2016). The guideline suggested that an improvement in the coordination of care could reduce treatment burden, adverse events and unplanned care and improve QOL in people with multiple LTCs (NICE, 2016). However, the guideline does not tackle PA treatment recommendations, only suggesting PA as an alternative to some medicines and in discussing treatment burden in day-to-day life, with no further guidance (NICE, 2016). Furthermore, despite the publication of NICE multimorbidity guidelines, many services for those with OA and other LTCs remain single disease focused (Dhalwani et al*.,* 2016; Reuben and Tinetti, 2012) and other existing guidelines do not provide recommendations for OA, exercise and PA when the person also has comorbidity.

It has been acknowledged that co-existing health conditions alongside OA may bring additional impairments which require adaptation of PA protocols (Reeuwijk et al., 2010). When OA is defined as the index disease, it is necessary to understand which co-existing disorders are further disabling, associated with further activity limitations and increased symptom burden (Reeuwijk et al., 2010). Some conditions such as unstable angina may make PA unsuitable (Dekker et al., 2016), however, many conditions such as T2DM, would necessitate adaptations to the PA treatment (Reeuwijk et al., 2010).

Recent research in secondary care settings in the Netherlands has investigated the application of specific comorbidity adapted exercise interventions in people with OA and comorbidity and have shown promising results, proving PA to be both safe and effective in these populations (de Rooij et al., 2017). Further, a recent narrative review by Dekker et al. (2019) provided a four-part framework for successful development for PA guidance for people with comorbidity or multimorbidity. However, these PA treatment strategies tested to date are far removed from the UK setting, with diverse PA intervention recommendations which are mostly non-generalisable to the UK or primary care population (de Rooij et al*.,* 2017).

2.6.2 Comorbidity is an important consideration of physical activity in people with osteoarthritis

As seen in section 2.5, people with OA have lower levels of PA than those who do not, therefore, it is important to consider why this is the case. Stubbs et al. (2015) suggested that in OA populations, comorbidity along with increased age, female gender and higher BMI, were correlated with lower PA levels. Similarly, other research from the US has reported in people with knee OA (n=2678), that amongst other variables, older age, female gender and more comorbidities were associated with reduced PA level (Dunlop et al., 2011). These findings concur with The English Longitudinal Study of Ageing (ELSA), a national representative cohort of the English population aged 50 years and over, which found an inverse dose-response association between comorbidity and PA levels in the general population (Dhalwani et al., 2016). Therefore, comorbidity has been identified as a potential barrier to PA in OA and it is important to consider the reasons for this.

At the individual patient level, OA and comorbidity can create additional physical, psychological and socio-environmental barriers to PA (Haseler et al., 2019; Manaf et al., 2013). First, disability from LTCs results in an impaired ability to perform daily activities, such as PA (Zambon et al., 2016; Haseler et al., 2019) and a higher number of LTCs is consistently associated with a higher prevalence of functional limitations and disability (Pisters et al., 2012; Kriegsman et al., 2004; Van Dijk et al., 2008). The presence of comorbidity alongside OA is associated with more limitations to PA participation (e.g. pain) than in those without comorbidity (Juhakoski et al., 2013; Reeuwijk et al., 2010; Van Dijk et al., 2008; Caporali et al., 2005).

A study by Ettinger et al. (1994) found that knee OA was associated with lower physical function, but when comorbid heart disease, pulmonary disease and obesity existed, the disability from knee OA increased. Having combinations of physical barriers and limitations from OA and additional comorbidities, such as pain, breathlessness and fatigue may lead to an inverse relationship with PA participation (Zullig et al., 2015; Campbell et al., 2001; Hammer et al., 2016; Hendry et al., 2006). A study by Zullig et al. (2015) found that comorbidities influenced function, fatigue and depression levels,

in people with knee and hip OA. This created an inverse relationship between increased comorbidity existence and decreased PA participation (Zullig et al., 2015).

The presence of comorbidity can also further reduce QOL in people with OA (Caporali et al., 2005; Loza et al*.,* 2009; Juhakoski et al*.,* 2013; Reeuwijk et al*.,* 2010) by affecting psychosocial domains, including mental health, work and social relationships (Hurley et al*.,* 2018; ARUK, 2013). The results from 906,578 responders in the English General Practice Patient Survey (2012) found that patients who had increased LTC prevalence, had a poorer QOL (Paddison et al., 2015). Furthermore, an ethnographic study of people with two or more LTCs in England found that people mostly described their experience of living with multiple LTCs as a loss of mobility, normal social functioning and social connectedness (Taskforce, 2018). Psychosocial barriers resulting in limitations and restrictions in daily life could lead to negative feelings such as mental stress and unhappiness, and thus a complex reciprocal relationship exists between condition symptoms and disability with psychosocial functioning (Hammer et al*.,* 2016; Petursdottir et al*.,* 2010; Campbell et al*.,* 2001).

Furthermore, the presence of comorbidity may contribute to low condition self-efficacy, depressed mood and subsequent activity limitations (Beckwee et al*.,* 2015; Holla et al*.,* 2013). The process of giving up activities, inability to meet life roles, adjustment to life and associated feelings of embarrassment, unhappiness and weakness are described by Bury (1982) as biographical disruption, which could be a component of the OA and comorbidity experience. In OA and comorbidity, the complexity and uncertainty (Simonik et al., 2016; Wilcox et al*.,* 2006; Shippee et al., 2012), can create social restriction, psychological distress and daily life limitations (Bury et al., 1982), which are often coupled with socio-environmental barriers, such as a lack of support and encouragement from peers and family (Petursdottir et al*.,* 2010). Also, fear-avoidance of PA could be exaggerated in OA and comorbidity with additional vulnerabilities, fears and perceptions of PA flaring symptoms, causing harm and further damage (Vlaeyen et al*.,* 2000).

People with comorbidities experience poorer health outcomes and as a result use healthcare more frequently (Barnett et al*.,* 2012), which can lead to multiple appointments, with different HCPs and being prescribed numerous treatments (Schoenberg et al., 2009; Barnett et al., 2012). The episodic nature of diseases and fluctuating levels of well-being and health crisis can then correspond with the ability and motivation to do PA (Simonik et al., 2016). In addition, with work and other commitments, PA is often not prioritised and regarded as a burden (Hurley et al*.,* 2018; Taskforce, 2018; Paskins et al, 2014). A plethora of other environmental barriers including the cost of participation, accessibility and transport are all common barriers to PA participation (Petursdottir et al*.,* 2010) but also, waiting lists to receiving care are often experienced by people with any single LTC (Barnett et al*.,* 2012), let alone comorbidity.

In addition to the individual-level barriers to PA, there are also healthcare-level barriers. How healthcare services are organised and delivered may be a barrier to how PA is promoted as a treatment for people with OA and comorbidity who are inherently complex with multiple health needs. Despite the increasing numbers of people with multiple LTCs, condition guidelines and the delivery of primary care is often built around managing single diseases (Smith et al., 2012; Prior et al., 2012; Barnett et al., 2012; Salisbury, 2011).

Holistic condition assessment considering comorbidity has been identified as a quality indicator of care for people with OA (Edwards et al., 2015), however, this is challenging in current clinical practice which is restrained by time and system pressures. Without clear guidance on comorbidity, even when people with OA and comorbid disease are referred to physiotherapists, the intensity of PA may be reduced to an ineffective level (Dekker et al., 2016). Furthermore, people with OA and comorbidity may be at higher risk of adverse events such as injury whilst participating in PA, in part due to inadequate PA dosing and specification (Tamari, 2010).

Current clinical OA guidance does not account for both the physical and subjective experience of OA and comorbidity, which makes recommending PA for this group challenging (Kittelson et al., 2014).

Limited guidance on how best to tailor PA to patients with OA and comorbidity could mean HCPs, as a result, underuse PA interventions in people with OA (Healey et al., 2018; Porcheret et al., 2007). Further, comorbid patients are often excluded from relevant clinical trials and few studies have specifically examined the effectiveness of PA in OA and comorbid populations (de Rooij et al., 2017; Jadad et al., 2011; Valderas et al., 2011), but even when not excluded, it is difficult to know whether the results can be extrapolated for people with comorbidities. Thus, many questions remain concerning the type and format of PA that should be prescribed and the predictors of response and adherence in people with OA and comorbidity (Holden et al., 2017; Legha et al., 2020).

A lack of communication between the patient and the HCP also contributes to patient hesitancy and amplifying comorbidity as a barrier (Paskins et al, 2014). Evidence from interviews with physiotherapists in the Netherlands suggests that there is suboptimal HCP collaboration and a lack of referral of patients with OA and comorbidity due to a lack of belief and knowledge about PA effectiveness (de Rooij et al., 2020). The attitude and endorsement of PA from HCPs often creates patient doubts as a barrier to being physically active (Cuperus et al., 2013), which opposes the movement toward a self-management perspective (Paskins et al., 2014). Theoretically, there is a cycle; unclear guidance for PA treatment, uninformed HCPs not confidently endorsing PA treatment, and a subsequent lack of comparable information about the relative PA effectiveness to support people with OA and comorbidity (Ong et al., 2019; Duguay et al., 2014; Dobson et al., 2016; Holden et al., 2012; de Rooij et al., 2014). These barriers at healthcare level feed into the barriers at individual patient-level, which combined, make it more likely that people with OA and comorbidity experience a block in terms of endorsement, information or support, that they need to successfully self-manage and change their respective PA levels (Ong et al., 2019).

Comorbidity has only been identified as a barrier to PA, as a factor impacting PA participation, and as an emergent theme in qualitative studies, as a complication for management of conditions and reason for patient hesitancy to take part in PA (Campbell et al., 2001; Wilcox et al., 2006; Marks, 2012;

Petursdottir et al., 2010; Paskins et al., 2014; Hurley et al., 2010), but not explored further. In the recent systematic review by Kanavaki et al. (2017), the findings revealed several qualitative studies investigating the barriers to PA in people with OA, identified comorbidity generally as a barrier to the uptake and maintenance of PA amongst people with OA. However, how comorbidity acts as a barrier and how best to support people with OA and comorbidity to be more active, remains uncertain.

2.7 Applying the background and methodology to the House of Care context

This section brings together the background and the policy context of LTC management in UK healthcare settings. The HOC framework has been used to provide a framework within which investigating PA in people with OA and comorbidity can be understood.

Drawing on the HOC model, this thesis places the person with OA and comorbidity at the centre of the model (see section 2.2, Figure 2.1). The roof represents the overarching NHS guidelines and organizational systems in place for structuring and guiding the healthcare process for people with OA and those for comorbidity or multimorbidity. The first pillar represents the patient with OA and comorbidity (and carers) who take an active role in the conversation of their healthcare plans, to understand their conditions and be empowered and supported to actively self-manage their conditions and PA. The second pillar represents the well-structured, guided, informed and collaborative HCPs and multidisciplinary teams working together to bring about the optimal services and treatments to support self-management, in terms of PA for those with OA and comorbidity. The centre of the model highlights the specific patient to this model; a person with OA and comorbidity. This is the crucial feature of the model, bringing together the perspectives and expertise of the individual and the HCP to tailor PA treatment with the support and competence for self-management (Coulter et al., 2016).

2.8 Chapter summary

OA is a LTC with huge global, healthcare and patient-level burden. OA is primarily managed in primary care and guidelines recommend that core treatment should include supported self-management and PA. However, in people with OA, PA treatment is underused, and PA levels in this population remain

low. Furthermore, OA rarely exists in isolation and evidence suggests comorbidity may be a barrier to PA level. The HOC model emphasises a patient-centred approach which takes a holistic view of the whole patient and their needs, in collaboration with HCP knowledge and expertise, however current care in OA and comorbidity management is often suboptimal.

To increase PA levels in people with OA, the impact of comorbidity needs further investigation to guide future treatment and models of care. Although PA has been well documented to improve OA symptoms as well as various LTCs in isolation, a dearth of evidence remains in people with OA and comorbidity. The effectiveness of PA for people with OA and comorbidity is unclear. The relationship between comorbidity frequency and specific types of comorbidity is also not well understood. There is a need for further insight into how comorbidity acts as a barrier to PA level in people with OA and what can be done to increase PA levels from the perspective of the patient with OA and comorbidity. This information could be combined to make recommendations about how best to tailor PA for people with OA and comorbidity which may, in turn, inform clinical guidance.

To maximise the opportunity to understand PA in OA and comorbidity, it is necessary to consider diverse research methodologies and methods. The following chapter (Chapter 3) outlines the different methodologies chosen to answer the research questions for this thesis.

Chapter 3

Methodology

Chapter 3. Methodology

3.1 Introduction

This chapter outlines the methodological approach to address the research questions in this thesis. It provides an overview of the methodology, followed by an explanation of the pragmatic paradigm selected for the research, before describing how the chosen multi-method approach was used. Throughout the chapter, alternative approaches and methods that were not chosen are acknowledged and briefly described.

3.2 Methodology overview

Research can be conducted by using many different procedures and methods (Walsh and Koelsch, 2012), but it is important, throughout the research process, from methods through to write up, to appreciate the communities, languages and traditions used (Walsh and Koelsch, 2012). Therefore, situating in a paradigm provides a platform to guide the choices, without questioning the philosophical commitments, in order to perform research (Sparkes, 1992). Understanding the philosophical stance and how it impacts every feature of the research process is invaluable to provide consistently and systematised knowledge and thus, successfully answer the research questions.

For this thesis, the term methodology refers to the overarching philosophical principles that underpin the research design, process and interpretation. The methods refer to the tools and techniques used to gather and analyse the data (Creswell, 2009; Bandura, 2006). The chosen methodology is exploratory and informed by both quantitative and qualitative inquiry. Thus, a multi-method approach has been incorporated to maximise the potential for an in-depth and rich exploration of PA in people with OA and comorbidity.

3.3 Pragmatic paradigm

To fulfil the aim and research questions of this thesis, a pragmatic stance has been adopted. Pragmatism was initially suggested by Pierce in 1905 and has been developed as an established

philosophical approach for mixing research methods (Johnson and Onwuegbuzie, 2004). Embracing both the positivist paradigm (namely quantitative and objective) and the constructivist paradigm (qualitative and subjective), pragmatism provides a middle position for using both, to answer research questions (Johnson and Onweugbuzie, 2004). Therefore, pragmatism does not necessarily situate within an individual philosophical view or reality but is more concerned with the research aim and questions and the outcomes of research (Creswell, 2009). Pragmatists believe that philosophical facets, such as meaning and belief are all better viewed in terms of their practical application (Anguera et al., 2018).

A pragmatic stance to methodology allows for the mixing and matching of design components that congregate to offer optimal opportunity to answer complex research questions (O'Cathain et al*.,* 2007; Mason, 2006; Johnson and Onwuegbuzie, 2004). Ritchie and Lewis (2003) describe the principles of pragmatism as a stance where the elements of both qualitative and quantitative research form part of the researcher's 'toolkit'. Therefore, the pragmatism approach encompasses the ability to break down paradigms into separate tools, which can be used independently from their independent paradigmatic framework (Maxwell, 2011). Through my pragmatic stance, my focus is on judiciously selecting the best methods and practicalities for addressing the thesis research questions, without being limited by philosophical tensions between methods (Ritchie and Lewis, 2003).

'if the only tool researchers have is a hammer, they tend to see every problem as a nail' (Stange and Zyzanski, 1989).

As a pragmatist, I believe that both objective analysis and measuring of numbers, as well as personal interaction with participants, is necessary to answer the research questions set out in this thesis.

3.3.1 How pragmatism fits in healthcare research

It is essential to consider all possible ways for advancing knowledge about aspects of social life, such as healthcare. Healthcare is complex and needs a range of methodologies to understand and evaluate

it effectively (O'Cathain et al*.,* 2007). An interdisciplinary and dynamic process is, therefore required to approach and answer complex healthcare research. An appreciation of both quantitative and qualitative methods as complementary approaches can enhance the opportunity to answer these complexities (Borkan, 2004; Ritchie and Lewis, 2003). Methodological diversity is a concept that fits the heterogeneous everyday life and practices involving healthcare research to create an engaging and coherent story of multiple views (Schwandt, 2012).

Healthcare has been globally improved by the systematic collation, synthesis and application of research evidence (Greenhalgh et al., 2014). In the last two decades, the research, teaching and practice of medicine and health disciplines have taken a paradigm shift from a 'one size fits all' toward combining evidence from high quality RCTs and observational studies; with both clinical and patient perspectives and needs (Greenhalgh et al*.,* 2014). Philosophical stances act as lenses through which to understand research questions, but the complex nature of the research questions within this thesis requires rich and in-depth knowledge of the phenomena under study and therefore needs a pragmatic stance with multiple lenses (Maxwell, 2011).

3.3.2 Alternative paradigms

Various alternative paradigms exist to fulfil both quantitative and qualitative research designs independently (Creswell, 2009), which were not selected for this thesis. In contrast to the selected pragmatic paradigm, other purist views advocate the incompatibility of paradigm combinations for research (Johnson and Onwuegbuzie, 2004; Tariq and Woodman, 2013; Hall, 2012). This argument distinctly separates qualitative and quantitative research paradigms and associated research methods (Johnson and Onwuegbuzie, 2004).

For example, positivism is by nature a quantitative, and reductionist approach, which aims to confirm the knowledge and facts of a subject (Bryman, 2006); or social constructivism, a qualitative exploration, which emphasises the subjective, meanings and interactions (Creswell, 2009). Interpretivism is commonly used in qualitative research focused on the participant experience, meaning of actions,

perceptions and truths (Bryman, 2006) and rejects the objectivist view that '*meaning resides within the world independently of consciousness'* (Collins, 2010). Instead, interpretivism allows the researcher to appreciate the differences between people to reflect different aspects of the research (Creswell, 2009). However, purist paradigms, which keep the social and scientific worlds separate, do not always provide the optimal platform for answering complex research questions (Guba and Lincoln, 1994).

3.4 Multi-method research

Multi-method research is suited to situations where one independent data source is insufficient to fulfil the aims of the research (Creswell, 2009). To gain the most from having a multi-method approach, research design tends to be complex in nature, multifaceted and require the depth of both quantitative and qualitative exploration (Tariq and Woodman, 2013). For example, results from the quantitative analysis may need more qualitative explanation, or further exploration and expansion could better generalise results (Creswell, 2009). While quantitative methods may be useful for seeing relationships amongst variables, qualitative methods can help the understanding of what the relationships mean or why they occur (Creswell, 2009).

Table 3.1. displays some of the advantages and disadvantages of using a multi-method approach to research compared to a mono-method approach. The choice of using multiple sources of data, obtained from multiple methods, has been selected within this thesis to strengthen the research and provide greater insight and understanding regarding PA behaviour in people with OA and comorbidity.

Table 3.1 Potential advantages and disadvantages of a multi-method approach

Advantages	Disadvantages
It can add more meaning to results	The approach is time-consuming
Provides an 'intuitive argument' to better reflect real life	There is a requirement of more skill and perhaps multiple researchers due to the complex nature
Provides an opportunity to generate and test a theory	Contradictions exist within the individual underpinning research paradigms Methodological purists contend that work should be contained within one paradigm
Allows a broader and more complete range of research questions to be answered	The synthesis of results is complex
Offers a flexible approach	There is potential for inequality between the use of research methods
Ability to use the strengths of one method to overcome weaknesses in another	A lack of understanding exists as to how to mix paradigms or interpret conflicting results
Provides stronger evidence for conclusions through corroboration of findings	
It can add insights and understanding that might otherwise be missed	
Provides more context to research	

(Gathered information from; Creswell, 2009; Tariq and Woodman, 2013; Maxwell, 2011)

3.5 The multi-method approach used in this thesis

The multi-method approach to this thesis involves three independent studies, with separate research questions, using separate samples, designed not to be reliant on each other, with findings synthesised after analysis of each data set.

The design of the research methods in this thesis is based on the optimal way to achieve the overall aim of investigating the impact of comorbidity on PA and clinical outcomes in those with OA in primary care and answer the three research questions; what is the *effectiveness of PA* interventions for people with OA and comorbidity? *Is comorbidity associated with PA* level in people with OA? How do people with OA *experience PA* in the context of comorbidity?

A multi-method approach was selected over a mixed methods approach because the goal was to create a dialogue between diverse perspectives, to deepen, rather than triangulate knowledge (Maxwell, 2011), in order to develop a comprehensive and holistic understanding of PA in OA and comorbidity.

All methods were given equal weighting with sufficient detail to stand alone and remain independent until interpretation (chapter 7), to cover a bigger picture, combining the use of both quantitative and qualitative research methods, using both measuring of numbers and personal narrative from participants. As outlined in the 'language and definitions' section of the thesis (see page xxii), multi-methods differs from mixed methods research, which integrates the different approaches or methods during the program of study, and not just at the concluding point (Johnson et al., 2007). Employing a pragmatic multi-method stance, focus is placed on the best way to address the research questions and improve healthcare, concerning less with ontological and epistemological issues. The goal of applying the multi-method approach was not to disregard or compromise on the traditional paradigms, but to maximise the strengths and minimise the weaknesses combined in one single research practice (Johnson and Onwuegbuzie, 2004).

3.5.1 Phases of the multi-method approach

In *multi-method* research, "multiphase combination timing" is appropriate, characterised by multiple phases of individual studies completed over the project period (Johnson and Onwuegbuzie, 2004). Multiphase timing best suits this thesis to enable each research question to be answered individually, prior to their interpretation and integration together as a broad picture of OA, comorbidity and PA (Figure 3.1).

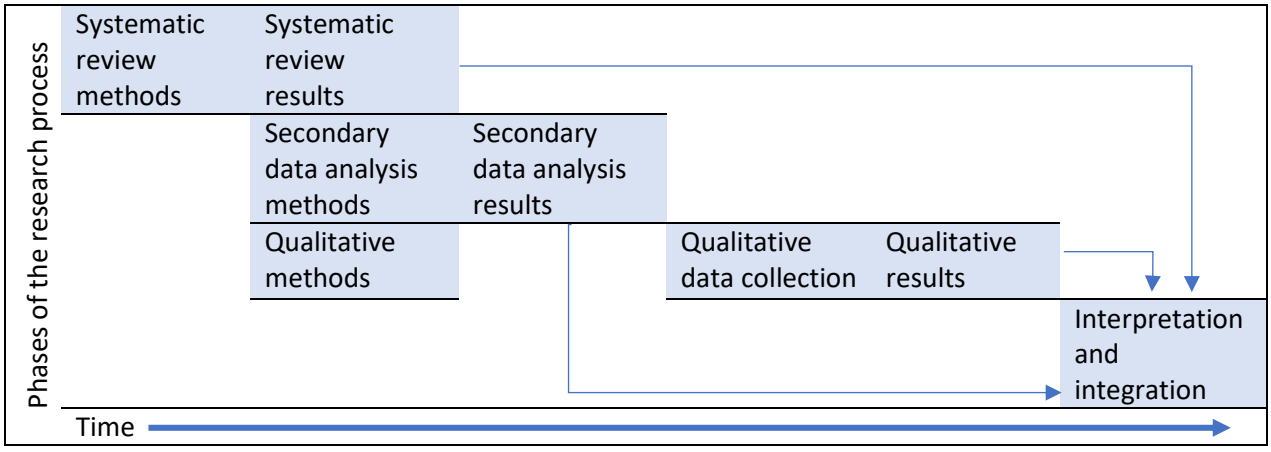


Figure 3.1 The multi-method approach used for this project

3.5.2 Quantitative methods in this thesis

Quantitative research is praised for understanding relationships between variables and determining the best conditions for desired outcomes (Creswell, 2009). A quantitative approach was first employed to systematically identify and review existing evidence regarding the effectiveness of PA interventions for people with OA and comorbidity. Quantitative methods were then used to investigate whether comorbidity presence, frequency or type are associated with PA level in people with OA. Within the investigation of the association between comorbidity and PA in people with OA, secondary analysis of two previous RCTs was chosen as the method to obtain the quantitative data. These datasets provided a large sample of adults with OA, or joint pain attributable to OA, including information on comorbidity health status, clinical and socio-demographic characteristics and PA. Using existing cross-sectional data was a low cost and timely solution to accessing data to answer the research question of interest.

By using quantitative methods, statistical patterns can determine whether comorbidity is significantly associated with PA in people with OA. A benefit of the quantitative methods is that they do not involve the participation of the researcher or participants as subjective influencers on the results. However, quantitative research can be strengthened when partnered with qualitative methods, described below.

3.5.3 Qualitative methods in this thesis

The use of qualitative research in healthcare brings a patient-centred approach to the study (O'Cathain et al*.,* 2007). Qualitative research is beneficial as it aims to explore a problem, honouring the perspectives of participants to explain a circumstance (Creswell, 2009). Qualitative methods were used to understand *how* comorbidity may act as a barrier to PA, and *how* to increase PA levels this population, from the patient perspective.

For the qualitative investigation of the attitudes and beliefs of people with OA and comorbidity regarding PA, semi-structured one-to-one interviews were used. Qualitative interviews are considered the most direct interaction between the researcher and the participant (O'Cathain et al*.,* 2007).

Interviews gain the other person's perspective and develop an in-depth description of the social world (Kvale, 1983). The interviews aimed to elicit people's understanding and meaning of their own experiences of having OA and comorbidity and how this influenced their PA participation.

3.5.4 Integrating findings

The thesis methods were given equal weighing, meeting appropriate rigour to stand alone (Morse, 1991), but together capture a more comprehensive holistic portrayal of PA in OA and comorbidity (Heale and Forbes, 2013). To evidence conclusions from the whole thesis in a valid, credible and transparent way (Younas et al., 2020; Cohen et al., 2013), a process was used to integrate the findings, where possible, through a joint display and accompanying narrative.

The use of a joint display offers the structure to integrate the findings from each of the studies, providing insight beyond the independent study results (Younas et al., 2020; Creswell and Clark, 2017). The joint display offers a visual which compares and contrasts the thesis study results side-by-side (systematic review, secondary data analysis, qualitative interviews), with both qualitative themes and example excerpts, and explicit quantitative statements and statistics (Fetters et al., 2013). The demonstration of integration is through inferences presented in a separate column to describe the findings as; 'convergent' (lead to the same conclusion), 'divergent' (different and at times contradictory findings) and 'expanded' (extends findings through additional insight), in relation to comorbidity, PA and clinical outcomes in those with OA (Fetters et al., 2013; Östlund et al., 2011; Creswell and Clark, 2017).

3.6 Chapter summary

This chapter first introduced methodology as a concept. It outlined why a pragmatic stance was selected as the most appropriate approach and how it fits within the overarching healthcare context. The multi-method approach was defined, compared to other approaches, and its practical use in this thesis was described. The following chapters will now use this approach to address the thesis research questions.

Chapter 4

Systematic review

Chapter 4. The effectiveness of physical activity interventions for people with osteoarthritis and comorbidity: a systematic review

4.0 Introduction

This chapter describes the systematic review that forms study one of the thesis. The chapter begins with the research question, overarching aim and objectives of the review. Following this, a rationale for the chosen review methods and a description of these methods is provided. The following parts of the chapter then present and discuss the systematic review results.

Systematic reviews efficiently integrate multiple study results by collating available evidence fitting pre-specified eligibility criteria to answer a specific research question (Higgins and Green, 2011; Mulrow, 1994). They provide a comprehensive, transparent and reproducible evidence synthesis and help to establish whether previous research findings are consistent and generalizable (Mulrow, 1994). However, the strength of conclusions and the impact of the review relies heavily on the methods used and the identification of high-quality studies (Higgins and Green, 2011).

4.0.1 Research question

What is the effectiveness of PA interventions for people with OA and comorbidity?

4.0.2 Aim and objectives

This systematic review aimed to investigate the clinical effectiveness of PA interventions in people with OA and comorbidity. More specifically, the individual objectives were to;

1. Identify existing RCTs investigating the clinical effectiveness of PA interventions for adults with OA and comorbidity.
2. Critically appraise the methodological quality of the identified RCTs.
3. Examine the effectiveness of PA interventions on the primary outcomes of pain, physical function, QOL and global health.

4. Examine the impact of PA interventions on additional secondary outcomes; long-term follow-up (of the primary outcomes) and adverse events in people with OA and comorbidity.

4.1 Methods

4.1.1 Study selection

The following section describes the eligibility criteria set out for this systematic review. Table 4.1.1. summarises these criteria in an expanded PICO format (Participants, Intervention, Control and Outcome, setting and publication type).

Table 4.1.1 Summary eligibility criteria for studies to be included in the review

	Inclusion criteria	**Exclusion criteria**
Design	Randomised Control Trials (RCTs)	Study designs other than RCTs
Participants	Adults with a mean age ≥45 years old with clinical or radiographic OA OA at any site and at least one (or more) of the comorbidities of interest (COPD, depression, CVD, hypertension, obesity*, T2DM)	Studies including mixed samples of participants with OA and other index conditions (such as rheumatoid arthritis) without separate results explicitly for those with OA
Intervention	Any PA intervention alone or in combination with other interventions	
Control	Usual care, placebo, other interventions, and waiting list control	
Outcomes	Primary outcomes; pain, function, QOL and global health impact (immediately post intervention) Secondary outcomes; adverse events and long-term follow-up (≥6 months)	
Setting	All settings and countries	
Publication type	All languages Grey literature	Abstract only, non-peer-reviewed

*OA=Osteoarthritis; COPD=Chronic Obstructive Pulmonary Disease; PA=Physical Activity; RCT=Randomised Control Trial; T2DM=Type Two Diabetes Mellitus; QOL=Quality Of Life; *One study (Lim et al., 2010) was based on the Korean cut-off point for obesity (≥25 BMI).*

4.1.1.1 Types of participants

Studies were eligible for inclusion in this review if they included adults with a mean age of 45 years old and over with clinical or radiographic OA at any site. The ACR and NICE have two different but commonly used definitions of clinical OA. The ACR define clinical OA through a combination of physical

examination and patient history (Litwic et al*.,* 2013; Altman et al*.,* 1991). NICE (2014) recommend a diagnosis of OA if a person is 45 years and over, has activity-related joint pain and has either no morning joint-related stiffness or stiffness that lasts less than 30 minutes. Radiographically, OA is commonly assessed using the Kellgren and Lawrence score which grades OA structural severity related to the appearance of osteophytes, joint space loss, sclerosis and bone cysts (Litwic et al*.,* 2013).

To maintain a review of clinical importance and generalisability, the comorbidities focused on in this systematic review were selected based on their perceived clinical importance in relation to OA. Key elements considered when selecting comorbidities to include were; the global burden of disease (most deaths, premature deaths and disability), prevalence and co-existence with OA, and patient impact. For a comorbidity to be selected, it was also deemed important that PA was recommended in NICE clinical guidelines as part of that condition's management and for the conditions to be routinely managed in primary care (NICE Clinical Guidance: CG28; CG90; CG115; CG136; CG181; CG189). Appendix 2 provides decision-making rationale informing the selection of comorbidities which, in brief, was gathered from global burden of disease metrics (Institution for Health metrics and Health Evaluation profile for the Global Burden of Disease, 2015), health research centres (Mayo Clinic, 2015), disease foundations (Arthritis Foundation) and the Quality of Outcomes Framework (NICE guidelines 2016). Final selection of comorbidities was agreed by myself and the supervisory team. Participants needed to have at least one (or more) of the comorbidities of interest alongside OA to be included. The comorbidities included in this review were; COPD, depression, T2DM, CVD, hypertension and obesity.

4.1.1.2 Types of intervention

All types of PA interventions (for example; aerobic PA, strengthening exercises, stretching or range of movement exercises, functional exercises) alone or in combination with other interventions (e.g. education, weight loss) were included in the review. Studies that did not test the effectiveness of PA interventions were excluded.

4.1.1.3 Type of control

Eligible study control groups included; non-PA interventions, usual care, placebo, and waiting list controls. Also, comparisons of one PA intervention to other PA interventions were included.

4.1.1.4 Types of outcome measures

Included studies were required to contain outcome measures from at least one of the following primary outcome domains; pain, function, QOL and global health impact (for example; The SF-36 physical functioning component and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), the Hip / Knee Injury and Osteoarthritis Outcome Score (HOOS / KOOS)). Other outcomes of interest included adverse events and long-term follow-up data of the primary outcomes (first measure at a time-point at least six months after intervention cessation (Fransen et al*.,* 2015)).

4.1.1.5 Settings

Studies from all healthcare settings (e.g. primary or secondary health care settings) were included in the review. Studies from any country published in any language were also included. This reduced the likelihood of publication bias in the form of excluding a study from the review solely due to the country of origin and language of publication, which would potentially influence the conclusions of the review (Higgins and Green, 2011).

4.1.1.6 Types of studies

Only RCTs were included in the review as they offer strong comparative and causal inferences of treatment effectiveness in controlled experimental conditions, whilst minimising bias (e.g. allocation and selection bias) and confounding factors (e.g. unequal distribution of prognostic factors) (Higgins and Green 2011). Non-randomised trials, quasi-randomised studies and observational studies were excluded from the review due to their potentially higher risk of bias (ROB) (Higgins and Green, 2011).

4.1.2 Stages of the systematic review

The following section describes the four stages of the systematic review; the search strategy, data extraction, ROB and data synthesis (summarised in Figure 4.1.1).

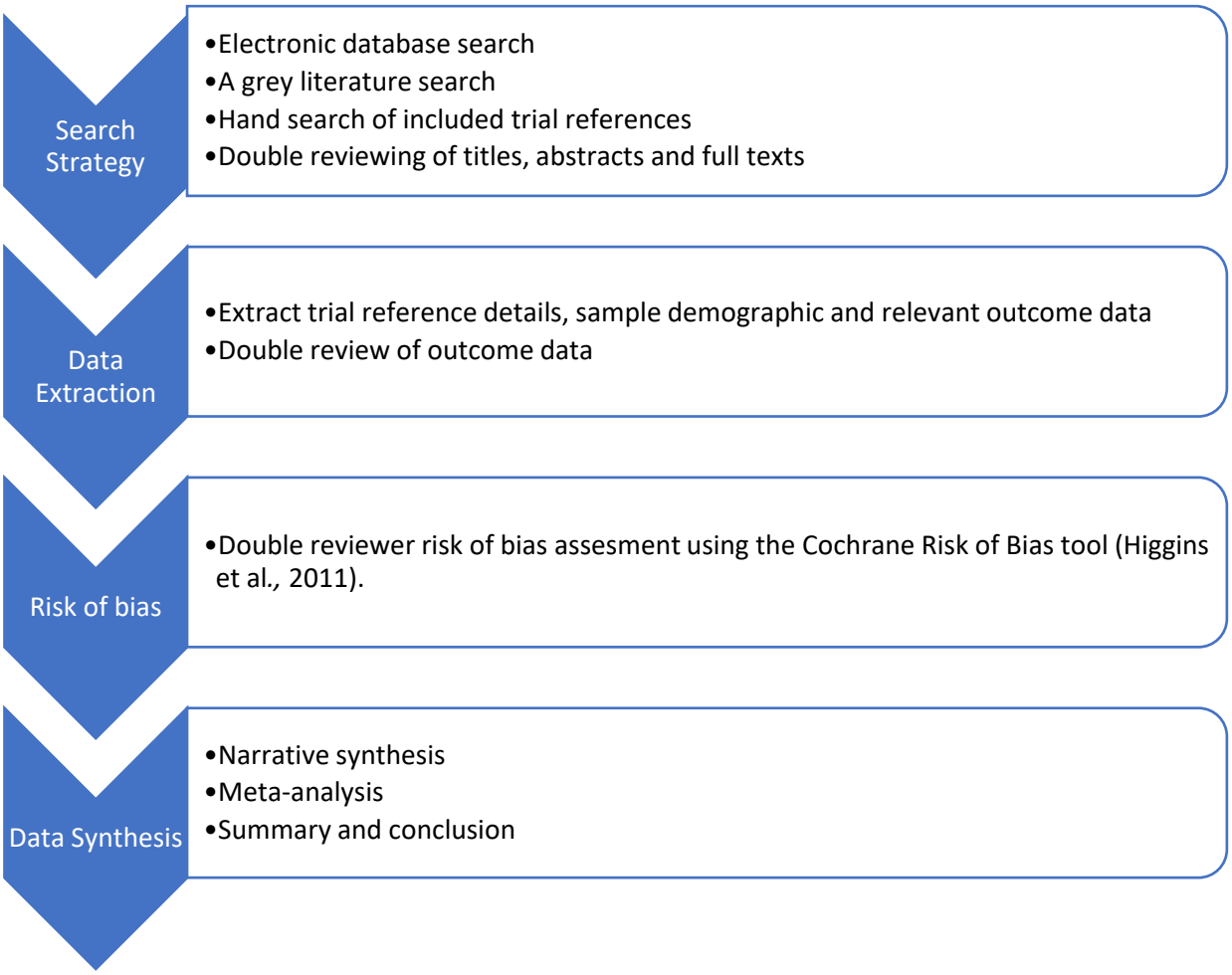


Figure 4.1.1 Stages of the systematic review

4.1.3 Search strategy

Systematic review study identification strategies typically have three sets of search terms or filters (Higgins and Green, 2011). These terms include those to search for the health condition of interest (OA and comorbidity), those to search for the intervention evaluated (PA) and those to identify the study design to be included (RCT). The filters were created by combining and adapting current Cochrane systematic review filters, OA, PA and comorbidity filters (Fransen and McConnell, 2015; Higgins et al., 2019) and an OA update search strategy (developed at Versus Arthritis Primary Care Centre, Keele

University). In addition, a novel comorbidity filter was designed and integrated as described below. The search filter comprised of four main subtopics; OA, PA, comorbidity and specific diseases (Figure 4.1.2).

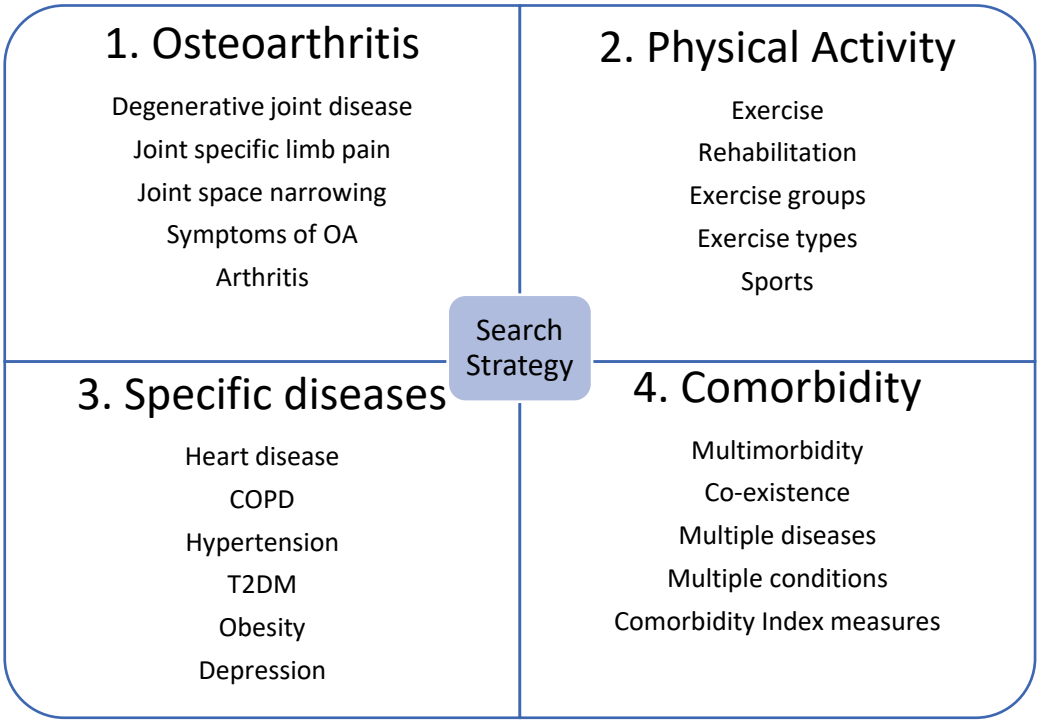


Figure 4.1.2 Search strategy sub-topics

OA=Osteoarthritis; COPD=Chronic Obstructive Pulmonary Disease; T2DM=Type Two Diabetes Mellitus

4.1.3.1 Electronic databases

The search was run in six electronic databases; MEDLINE, EMBASE, AMED, CINAHL, SportDiscus and CENTRAL, from their inception until March 2017 (29.03.17). The searches were carried out through the OVID, NHS and EBSCO interfaces. MEDLINE and EMBASE are the two largest electronic medical databases which contain many exclusive journal records allowing for the search of medical, clinical and treatment studies. AMED (The Allied and Complementary Medical Database Database) allowed for the potential inclusion of additional physiotherapy and rehabilitation studies since many of the journals included in AMED are not indexed by other biomedical sources. SportDiscus and CINAHL (The Cumulative Index to Nursing and Allied Health) were searched to potentially identify any additional exclusive relevant journals in the context of allied health literature and sports medicine. Finally, the

Cochrane Library (CENTRAL) database was searched to access the Cochrane register of controlled clinical trials which also contains unique content and records.

4.1.3.2 Search filter

The term "comorbidity" has low sensitivity to capture the full range of research relating to this area. Sensitivity in the current context is the number of relevant studies identified by the search strategy, divided by the total number of relevant studies in existence (Higgins and Green, 2011). For example, studies may define comorbidity differently, such as 'multimorbidity' or 'co-existence' or use specific disease terms (e.g. obesity). To tailor the search strategy to capture comorbidities, which may not be identified with the generic search terms, the use of multiple specific disease search terms and synonyms were used, which can be seen in Figure 4.1.2.

The initial search strategy (section 4.1.3.3) was developed for use in MEDLINE and adapted appropriately for each of the other databases (section 4.1.3.1). The search strategy developed for MEDLINE was peer-reviewed (Jo Jordan (JJ): a member of the systematic review team within the Versus Arthritis Primary Care Centre, Keele University and member of the Cochrane Collaboration) prior to being finalised and translated into other databases. Adapting the search strategy involved searching for the MEDLINE Subject Headings (MeSH terms) and matching them to appropriately similar database topic-specific search terms in the other databases (Appendix 3). To increase the sensitivity of the search, both MeSH terms and free text searching of titles and abstracts were utilised. In addition, sensitivity was increased by adding synonyms, substitutes, plurals and different spellings to increase the chance of capturing relevant research.

4.1.3.3 Medline search strategy

1. exp Osteoarthritis/
2. exp Exercise/
3. exp Comorbidity/
4. exp Rehabilitation/
5. exp Myocardial Ischemia/
6. exp Pulmonary Disease, Chronic Obstructive/
7. exp Hypertension/

8. exp Diabetes Mellitus/

9. exp Obesity/

10. exp Depressive Disorder/

11. exp Depression/

12. osteoarthri*.ti,ab.

13. osteo-arthriti*.ti,ab.

14. osteoarthros*.ti,ab.

15. osteoarthrotic.ti,ab.

16. "degenerative joint".ti,ab.

17. "joint pain".ti,ab.

18. "hand pain".ti,ab.

19. "hip pain".ti,ab.

20. arthrosis.ti,ab.

21. "degenerative joint disease".ti,ab.

22. "joint space narrowing".ti,ab.

23. Osteophyte.ti,ab.

24. "knee pain".ti,ab.

25. "knee osteoarthritis".ti,ab.

26. "musculoskeletal pain".ti,ab.

27. arthritis.ti,ab.

28. coxarthrosis.ti,ab.

29. osteoarthr*.ti,ab.

30. Exercise.ti,ab.

31. aerobic*.ti,ab.

32. Hydrotherap*.ti,ab.

33. sports.ti,ab.

34. movement.ti,ab.

35. yoga.ti,ab.

36. walk*.ti,ab.

37. cycling.ti,ab.

38. treadmill.ti,ab.

39. aquatherap*.ti,ab.

40. swim*.ti,ab.

41. "tai chi".ti,ab.

42. "muscle strength*".ti,ab.

43. "range of motion exercise".ti,ab.

44. "aerobic exercise prog*".ti,ab.

45. ("aerobic" adj3 "train*").ti,ab.

46. "Strength train*".ti,ab.

47. "exercise train*".ti,ab.

48. "exercise movement techniques".ti,ab.

49. "Physical activity".ti,ab.

50. "Physical fitness".ti,ab.

51. "Physical therapy".ti,ab.

52. "exercise therapy".ti,ab.

53. "Circuit-Based Exercise".ti,ab.

54. "High-Intensity Interval Training".ti,ab

55. "Plyometric Exercise".ti,ab.

56. "recreat* activit*".ti,ab.

57. physiotherap*.ti,ab.

58. rehab*.ti,ab.

59. "resistance train*".ti,ab.

60. Comorbid*.ti,ab.

61. Co-morbid*.ti,ab.

62. multimorbid*.ti,ab.

63. multi-morbid*.ti,ab.

64. "coexist* diseas*".ti,ab.

65. "co-exist* diseas*".ti,ab.

66. "co-occur* diseas*".ti,ab.

67. "multiple diseas*".ti,ab.

68. "concurrent dis*".ti,ab.

69. "multiple condition*".ti,ab.

70. "charlson comorbidity index".ti,ab.

71. "heart diseas*".ti,ab.

72. "inflammatory heart disease".ti,ab.

73. "Cardiac failure".ti,ab.

74. "congestive heart failure".ti,ab.

75. "coronary heart disease".ti,ab.

76. "ischemic heart disease".ti,ab.

77. angina.ti,ab.

78. coronary.ti,ab.

79. "cardiac disease".ti,ab.

80. "pulmonary disease, chronic obstructive".ti,ab.

81. COPD.ti,ab.

82. "chronic bronchitis".ti,ab.

83. "pulmonary emphysema".ti,ab.

84. "chronic obstructive airway disease".ti,ab

85. "chronic obstructive lung disease".ti,ab.

86. "chronic airflow obstruction".ti,ab.

87. Hypertens*.ti,ab.

88. "high blood pressure".ti,ab.

89. "high systolic".ti,ab.

90. "high diastolic".ti,ab.

91. diabetes.ti,ab.

92. T2DM.ti,ab.

93. Hyperglycemia.ti,ab.

94. "glucose intolerance".ti,ab.

95. "Diabetes Mellitus, type 2".ti,ab.

96. obesity.ti,ab.

97. overweight.ti,ab.

98. "morbid* obese".ti,ab.

99. depression.ti,ab.

100. depressi*.ti,ab.

101. "depressive neurosis".ti,ab.

102. "depressive syndrome".ti,ab.

103. "mood disorder".ti,ab.

104. "low mood".ti,ab.

105. "dysthymic disorder".ti,ab.

106. 1 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29

107. 2 or 4 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59

108. 3 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 or 101 or 102 or 103 or 104 or 105

109. 106 and 107 and 108

4.1.3.4 Search screening

The total number of reference hits from each individual database was recorded and exported into the reference management program Refworks and subsequently Covidence for screening. Imported references were first screened for exact duplicates which were then removed. I and a second reviewer (JQ) screened the relevant articles in two stages using the study eligibility criteria. Double reviewer screening was used to minimise the chance of human error on study selection and any individual reviewer selection bias. The first stage involved title and abstract screening. Stage two involved the screening of full texts identified from stage one, which matched the study inclusion criteria (Appendix 4). At both stages, where there was disagreement between reviewers regarding the inclusion of articles, a consensus was reached following discussion between reviewers.

4.1.4 Data extraction

I extracted relevant data from each included RCT onto a predesigned data extraction document which was agreed by the review team (SM, JQ, JJ) (Appendix 5). Extracted data included; reference details, sample demographics, intervention details, control details, findings and relevant outcome data.

4.1.4.1 Population

Sample demographics extracted included; total sample size, mean age, OA site, method of OA diagnosis (clinical / radiographic / combined) and comorbidity types.

4.1.4.2 Intervention / control descriptors

Details extracted included; study setting, PA type and intensity, control type, delivery method (e.g. group / individualised, facility / home-based), number of sessions, providers, duration and type of control.

4.1.4.3 Outcomes

Effectiveness results and conclusions associated with the primary outcomes; pain, function, QOL and global health were extracted. Where RCTs provided secondary outcomes (long-term follow-up of

primary outcomes and adverse events), these were also extracted. Baseline and immediate post intervention (dependent on intervention duration) follow-up outcome measures were the key time points extracted. Outcome details extracted included; outcome domain, outcome measure, scale range, values description, follow-up time-point details, adverse events and key findings. Where studies had multiple measures related to one of the primary outcome measures, measures were selected and extracted in priority order according to the predetermined outcome measures list in the systematic review protocol. This order was informed by recommendations from the Cochrane Handbook and OMERACT OARSI recommended OA outcome measures (Smith et al., 2019) (Appendix 6).

4.1.5 Methodological risk of bias

Assessing the ROB of RCTs included in a systematic review is necessary to help to judge whether the findings of individual included studies and subsequent aggregate findings of the review are likely to deviate from the truth as a result of systematic errors within their methods (Popay et al*.,* 2006; Moher et al., 1995). Bias is known as a systematic error in results or inferences, which can lead to under or overestimation of an intervention effect (Higgins and Green, 2011).

A pilot, exploring the strengths and weaknesses of three commonly used ROB tools (Cochrane ROB tool, JADAD scale for reporting randomised controlled trials and the Critical Appraisal Skills Programme (CASP) checklist), was carried out (see Appendix 7 for three ROB tools summary). The decision was made to judge the methodological ROB of the included studies in accordance with the Cochrane ROB tool (Higgins and Green, 2011) due to its empirically informed ROB domain structure with clear instructions informing ROB judgement making. Table 4.1.2 shows the individual domains of assessment for the Cochrane ROB tool for RCTs.

In many situations it is impractical or impossible to blind participants and assessors regarding the intervention received, however, it is important to acknowledge given the well-known placebo effects for self-reported outcomes in knee OA (Zhang, 2010). Evaluating the risk of performance bias due to the ‘blinding of participants and personnel’ to the treatment received in trials of PA interventions has

been handled in different ways in literature (Fransen et al, 2015; Higgins et al., 2017; Quicke et al., 2015). In this review, all RCTs were deemed to be of 'unclear risk of bias', because what happened in the study is known, but the exact risk of bias is unknown (Higgins et al., 2017).

I and two secondary reviewers (JQ, EH) first piloted the ROB assessment in three of the eligible papers as a group. This was to ensure understanding and agreement of the Cochrane ROB tool in practice. Individual ROB of assessment was then carried for the included studies independently with one other reviewer (JQ). Each item was judged as being at high, low or unclear ROB as set out by the criteria defined by Higgins and Green (2011). Justification for the judgement of each ROB item from the included studies was provided using excerpts from the study reports. ROB assessment was not used to exclude any studies from the review. However, it informed the evaluation and discussion of the systematic review conclusions made based on the strengths and weaknesses of each study.

Table 4.1.2 Summary of the Cochrane Risk of Bias tool

Type of bias	**Domain**	**Judgement criteria**
Selection	Random sequence generation	• A method suitable for producing comparable groups • Adequate generation of randomisation sequence
	Allocation concealment	• Adequate concealment of group allocation
Performance	Blinding of patients and personnel	• Methods to blind reported and to what success • Restricted knowledge of intervention prior to engagement
Detection	Blinding of outcome assessment	• Methods used to ensure outcome assessors blinded • No prior knowledge to which intervention was received
Attrition	Incomplete outcome data	• Completeness of outcome data for each outcome • Amount, nature and handling of missing data
Reporting	Selective reporting	• Possibility of selective outcome reporting
Other	Other sources of bias	• Problems or concerns not covered by the other domains • Conflicts of interest and patient generalisability

4.1.6 Data synthesis

Two approaches were used to synthesise the findings of the review: meta-analyses and narrative synthesis. Meta-analysis has the potential to increase the precision around effect estimates for PA, by increasing statistical power through the aggregation of multiple studies. Meta-analysis requires methodological and statistical homogeneity of the included studies to ensure a meaningful quantitative pooling of results from individual studies (Higgins and Green, 2011). Narrative synthesis does not require the same homogeneity of included studies and involves the use of words, visual displays and an exploration of the results to come to meaningful conclusions (Popay et al., 2006).

4.1.7 Registration

This systematic review was registered with the Prospective Registering of Systematic Reviews (PROSPERO Registration: CRD42017055582). Prospective registration aims to reduce research duplication by highlighting ongoing systematic reviews. It also allows a transparent approach to the systematic review methods and assessment of any potential future reporting bias.

4.2 Results

4.2.1 Introduction

This section presents the systematic review results. It describes the number of RCTs identified at each stage of the search and the included study characteristics. The results of a sub-group meta-analysis, a narrative synthesis of the remaining studies and the results of the ROB assessment for all the included studies are also presented.

4.2.2 Identification of studies

Figure 4.2.1. displays the number of studies identified within each stage of the systematic review. There were 11,187 references identified from the electronic databases. This was reduced to 8,171 after removing duplicates. A total of 81 references remained after double reviewer screening of titles and abstracts, 66 studies were then excluded following full text screening and one study was excluded at the data extraction stage. A total of 14 studies were included in the review. Reference list checking did not yield any further studies.

4.2.2.1 Excluded studies

The reasons for excluding studies at full text screening varied and many studies were excluded for more than one reason. Thus, a hierarchy was used to determine which exclusion reason was chosen to be recorded (Figure 4.2.1). Of the 66 studies originally excluded, the main reason for exclusion was the 'wrong publication' type (n=22) (e.g. conference abstract or non-peer-reviewed studies). 15 studies were excluded due to being considered duplications (e.g. same study reported in different journals with a slightly different title or a different format). Other reasons for study exclusion included; wrong population (n=14), wrong outcomes (n=9), wrong study design (n=5) and wrong intervention (n=1). At data extraction, although 15 studies met inclusion criteria, the review team agreed to exclude one study (Zgibor et al., 2017) as it reported insufficient detail across several domains in the methods and results and was deemed unsuitable to add to either meta-analysis or narrative synthesis.

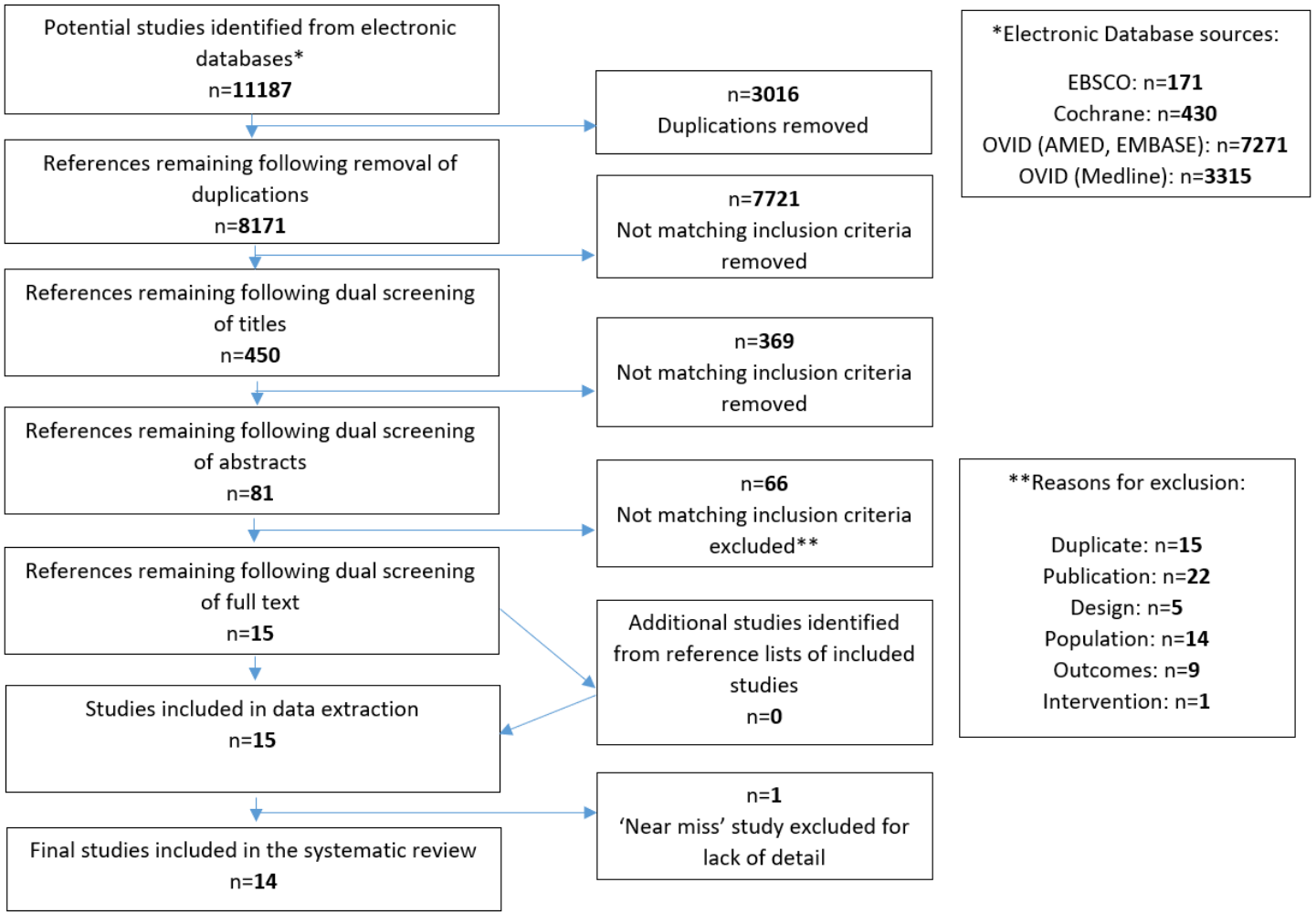


Figure 4.2.1 Study identification and selection

4.2.3 Study characteristics

The studies included in this review were all published in English between 2002 and 2017. Two studies (Messier et al., 2004; Rejeski et al., 2002) were secondary data analysis from the Arthritis, Diet, and Activity Promotion Trial (ADAPT) (Miller et al., 2003). One study (Mangani et al., 2006) was secondary data analysis of the Fitness and Arthritis in Seniors Trial (FAST) (Ettinger et al., 1997).

4.2.3.1 Population and setting

The studies included 4224 participants, with sample sizes ranging from 26 to 2203 participants. Two of the studies were pilot studies with small sample sizes of 40 and 26 (Yeol et al*.,* 2013; Schlenk et al*.,* 2011; respectively) and one other study had a small sample size of 34 (Casilda-Lopez et al., 2017). The study settings were described as outpatient facilities (n=5), community (n=4), primary care (n=3), and unspecified (n=2). The mean age across the included studies was 65 years. Participant mean age within included studies ranged from 58 to 76 years old.

4.2.3.2 Participant osteoarthritis and comorbidity characteristics

All studies were focused on knee OA. OA diagnosis was made based on clinical (n=7), radiographic and clinical (n=5) or radiographic findings (n=2). The total number of possible comorbidities identified in each study ranged from participants having one specific comorbidity to 11 possible comorbidities. Figure 4.2.2 displays the comorbidities identified. 10 studies investigated participants with obesity as the selected sample comorbidity. Of these, one was based on the Korean guidelines for obesity, which included having a BMI >25 kg/m^2 (Lim et al*.,* 2010). The mean BMI of participants in 13 of the included studies (one study did not report BMI) was 33kg/m^2 (ranging from 23 to 37 kg/m^2).

One study sample included participants with T2DM as the comorbidity (Foy et al*.,* 2011) and one study sample included depression as the comorbidity (Yeol et al*.,* 2013). Two studies included more than one comorbidity, from this point onward, referred to as ‘multimorbidity’ group. One of these studies examined four different comorbidities with participants having any one or more of four comorbidities

of interest (Cardiac diseases, T2DM, COPD, obesity; de Rooij et al., 2017) and one study specifically defined comorbidity as having at least two comorbidities alongside OA (Mangani et al., 2006) with participants having a mean of 2.7 comorbidities out of a possible 11 (obesity, hypertension, angina, myocardial infarction, other heart diseases, T2DM, cancer, pulmonary disease, renal disease, vascular disease and stroke).

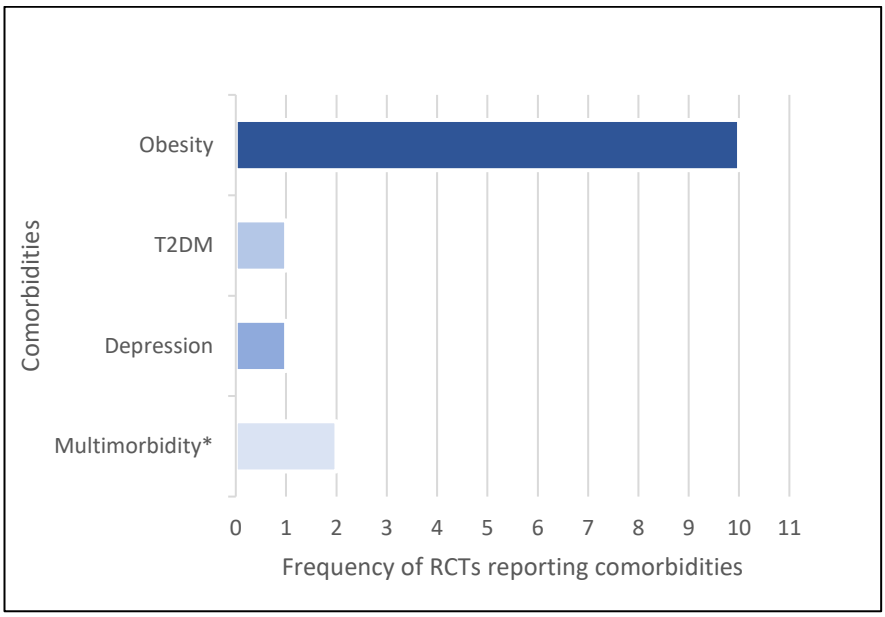


Figure 4.2.2 Chart displaying the participant comorbidities from included studies

**Multimorbidity (OA and: at least 2 additional conditions / one or more of four conditions); T2DM=Type Two Diabetes Mellitus; RCTs= Randomised Controlled Trials.*

4.2.3.3 Physical activity interventions

The characteristics of the PA interventions are summarised in Table 4.2.1. The type of PA intervention varied but most commonly involved land-based mixed aerobic and strengthening components (n=12). The delivery of PA interventions included group sessions (n=5), combined group and individual sessions (n=3) and individual sessions (n=1). The remaining studies described the intervention delivery style as a transition from supervised moving to unsupervised home-based (n=5). The duration of PA interventions ranged from 1 to 24 months. Frequency of contact sessions ranged from one every four months to four sessions per week. The majority involved three sessions per week (n=9). Two studies changed in session frequency throughout the intervention from one session per week and four

sessions per week to one session biweekly (Schlenk et al*.,* 2011; Somers et al*.,* 2012; respectively). Where included studies had both PA as a standalone arm, PA as part of a combined intervention (e.g. PA plus diet, education, behavioural counselling) and a control arm, the PA alone intervention arm was selected for data extraction.

Table 4.2.1 Physical activity intervention details of individual studies

Study	Type	Freq (n/wk)	Session time (mins)	Intensity	Dur (wk)	Delivery detail**	Provider
Casilda-Lopez et al., 2017*	Aquatic dance	3	45	4-6 PE	8	Group (8-10 people) Supervised Facility	Trained PTs
*PA comparison group	Aerobic, ROM, stretching	3	45	4-6 PE	8	Group (8-10 people) Supervised Facility	Trained PTs
Christensen et al., 2015	Circuit training	3	60	Not reported	52	Group facility supervised→ unsupervised home	PTs
de Rooij et al., 2017	Full lifestyle	2	30-60	Comorbidity adapted	20	Individualized Supervised Facility	Trained PTs
Foy et al., 2011	Intensive lifestyle	4	NR	Not reported	52	Group and individual Supervised	Lifestyle counsellor
Jenkinson et al., 2009	Diet and exercise	1 / month	NR	Not reported	104	Individual Unsupervised Home	Dietitian
Lim et al., 2010	Aquatic exercise	3	40	>65% max HR 40-60% 1RM	8	Group Supervised Facility	PTs
Lim et al., 2010	Land exercise	3	40	>65% max HR 40-60% 1RM	8	Group Supervised Facility	PTs
Mangani et al., 2006	Weight training	3	60	Individual tolerance	72	Group Supervised Facility	Nurse
Mangani et al., 2006	Walking	3	60	50-70% MHR	72	Group Supervised Facility	Nurse
Messier et al., 2004	Aerobic and resistance	3	60	50-75% HRR	72	Group Supervised Facility → home	Health educator
Messier et al., 2013	Aerobic and strength	3	60	50-75% HRR	72	Group Supervised Facility → home	Trained PTs
Miller et al., 2006	Aerobic and strength	3	60	50-85% age predicted HRR	26	Group Supervised Facility	Physician

Rejeski et al., 2002	Aerobic and resistance	3	NR	50-75% HRR	72	Group Supervised Facility →home	PTs
Schlenk et al., 2011	Flexibility, strength and functional	6 weeks: 1 / week → 9 weeks: 1 / biweekly	60	Not reported	26	Individual Facility Supervised & telephone counselling	PTs and nurses
Somers et al., 2012	Behavioural weight management	12 weeks: 4 / week → 12 weeks: 1 / biweekly	60	55-70% HRR	26	Group Facility Supervised	Psychologists and exercise physiologists
Yeol et al., 2013	Exercise gaming	3	30	Not reported	4	Facility Supervised	Not reported

*PA=Physical Activity; PT=Physiotherapist; n=Number; mins=minutes; Freq=Frequency; Dur=Duration; max HR=maximum heart rate; 1RM=one Maximal Repetition; HRR=Heart Rate Ratio; PE=Perceived Exertion (Borg scale 6-20, higher scores indicate higher perceived exertion); wk(s)=Week(s); ROM=Range Of Motion; NR=not reported; **where information was available: individual / group, supervised / unsupervised, facility / home-based; → =optional transition to home-based. Lifestyle intervention involved a lifestyle counsellor teaching and encouraging behavioural change strategies regarding nutrition and PA; Exercise gaming involved an Xbox game for 30 minutes.*

4.2.3.4 Control / comparison groups

Control / comparison group types were either usual care (n=5) (routine care for their conditions in the study setting), healthy lifestyle (n=2) or education (n=5) including; leaflets, information, guidance and education sessions, diet (n=1) or other forms of PA (n=1). The majority (n=13) of studies compared a PA intervention to a non-PA control group. Of these studies, two had a control group described as a 'healthy lifestyle group' (Messier et al*.,* 2004; Rejeski et al*.,* 2002). Both of these studies reported outcomes from the ADAPT trial (Miller et al., 2003). The healthy lifestyle control group was described as a method to provide attention, social interaction and health education (Messier et al*.,* 2004; Rejeski et al*.,* 2002). This consisted of a health educator who provided talks on topics concerning OA, obesity (the comorbidity) and PA as well as advice to follow recommendations, such as those from EULAR, regarding treatments for OA. The study that compared one PA intervention to another PA comparison group compared aquatic dance to standard aquatic PA (Casilda-Lopez et al*.,* 2017).

4.2.3.5 Outcome measures

The outcome measure most widely used was the WOMAC (pain and function sub-scales). Other common measures included the six-minute walking test (6MWT), SF-36 and SF-8. Full characteristics of all studies included in the review are described in Table 4.2.2.

Table 4.2.2 Characteristics of the studies included in the review

Author and year	Sample size (n)	OA Diagnosis	Comorbidity type	Age (m)	Intervention	Control / comparison	Follow-up (mnth)
Casilda-Lopez et al., 2017*	34	Clinical	Obesity	66	Aquatic dance	Aquatic physical activity	2, 3
Christensen et al., 2015	128	Clinical & Radiographic	Obesity	62	Circuit training	Usual care	12
de Rooij et al., 2017	126	Clinical	Cardiac Disease, COPD, Obesity, T2DM	63	Aerobic, strength & activity	Current usual care	5, 8
Foy et al., 2011	2203	Clinical	T2DM	59	Lifestyle counselling	Education	12
Jenkinson et al., 2009	267	Clinical	Obesity	61	Flexibility, strengthening, resistance & functional	Information leaflet	6, 12, 24
Lim et al., 2010	75	Radiographic	Obesity	65	Strength, aerobic and general conditioning (1: aqua or 2: land-based)	Physical activity guidance	2
Mangani et al., 2006	197	Radiographic	Angina, Cancer, Diabetes, Heart Disease, Hypertension, MI, Obesity, Pulmonary Disease, Renal Disease, Stroke	68	1: Weight training program or 2: aerobic walking program	Health education program	3, 9, 18
Messier et al., 2004	234	Clinical & Radiographic	Obesity	69	Aerobic & resistance	Healthy lifestyle	6, 18
Messier et al., 2013	454	Clinical & Radiographic	Obesity	66	Aerobic & strength	Intensive diet	6, 18
Miller et al., 2006	87	Clinical	Obesity	69	Aerobic, strength & pedometers	Weight stable control information	6
Rejeski et al., 2002	234	Clinical & Radiographic	Obesity	68	Aerobic & resistance	Healthy lifestyle	Mean of 6 & 18
Schlenk et al., 2011	26	Clinical	Obesity	63	Flexibility, strengthening & videotape, walking encouraged	Usual care	6, 12
Somers et al., 2012	110	Clinical & Radiographic	Obesity	58	Flexibility, strengthening & aerobic	Usual care	6, 12
Yeol et al., 2013	40	NR	Mild Depression	75	Aerobic gaming	Usual care	1

*OA=Osteoarthritis; COPD=Chronic Obstructive Pulmonary Disease; MI=Myocardial Infarction; T2DM=Type Two Diabetes Mellitus; m=mean; n=number; Dur=Duration; mnth=months; NR=Not Reported; *PA vs PA trial*

4.2.4 Risk of bias assessment

The individual ROB domain judgements within the included studies were generally either deemed low risk (n=48, 49% of total judgements) or unclear (n=47, 48%) due to a lack of available information. There were only a small minority of judgements which were considered as having high ROB (n=3, 3%). Table 4.2.3 displays the ROB summary for all included studies and Figure 4.2.3 then displays the pattern of low, unclear and high judgements within each domain.

Table 4.2.3 Risk of bias assessments for each individual study

Author	**Risk of bias domain***						
	1	2	3	4	5	6	7
Casilda-Lopez et al., 2017							
Christensen et al., 2015							
de Rooij et al., 2017							
Foy et al., 2011							
Jenkinson et al., 2009							
Lim et al., 2010							
Mangani et al., 2006							
Messier et al., 2004							
Messier et al., 2013							
Miller et al., 2006							
Rejeski et al., 2002							
Schlenk et al., 2011							
Somers et al., 2012							
Yeol et al., 2013							

Green = Low risk of bias
Orange = Unclear risk of bias
Red = High risk of bias
***1, Random sequence generation; 2, Allocation concealment; 3, Blinding of participants and personnel; 4, Blinding of outcome assessment; 5, Incomplete outcome data; 6, Selective reporting; 7, Other bias (conflicts of interest and patient generalisability)*

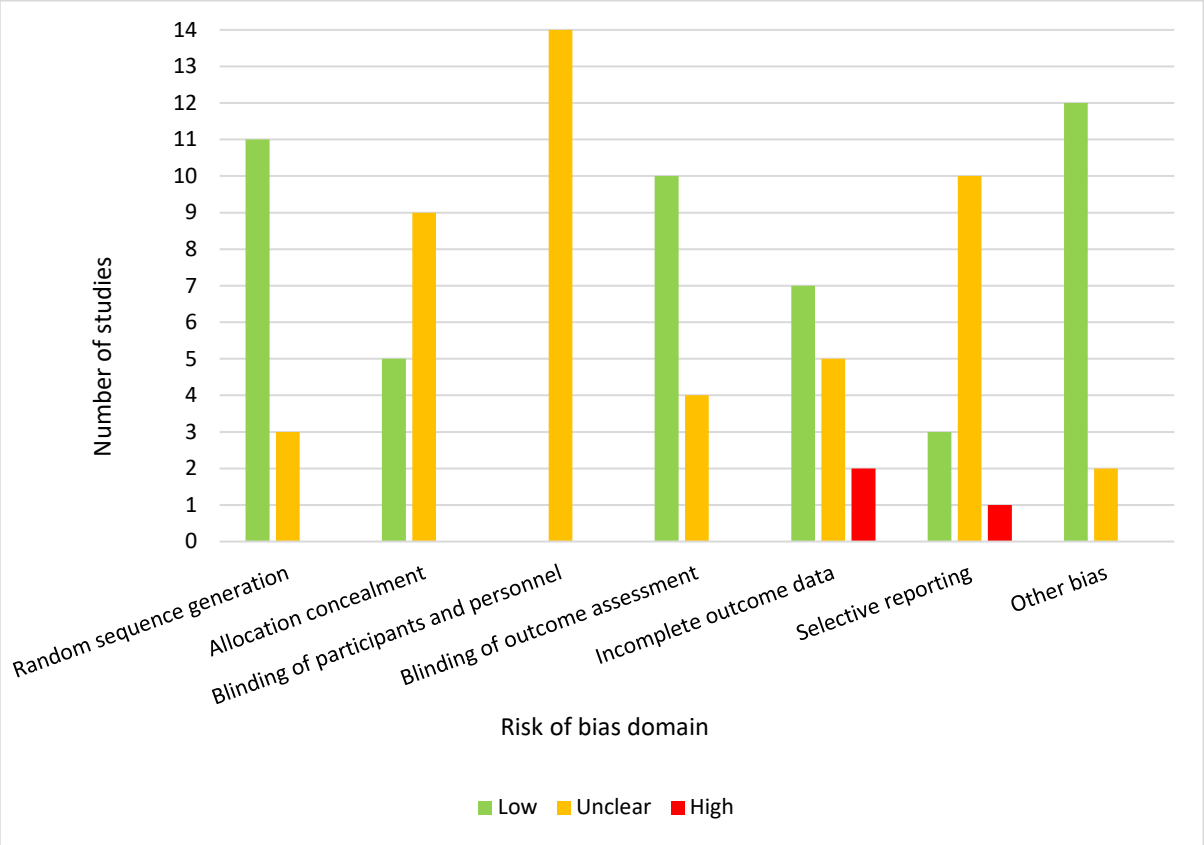


Figure 4.2.3 Summary of risk of bias from the studies included in the review

Risk of selection bias due to random sequence generation was mostly low (n=11, 79%) with the remainder unclear, due to missing information about their methods for randomising participants (n=3, 21%). Selection bias due to allocation concealment was largely unclear (n=9, 64%) as the majority of studies did not explicitly report their methods for allocation concealment. The remaining studies (n=5, 36%) were judged as low in this domain. In contrast to this, the risk of detection bias was more often judged as low (n=11, 79%) as the majority of studies reported that the personnel measuring the outcome assessments were adequately blinded to the intervention group. The remainder were judged unclear (n=3, 21%), due to unclear reporting of blinding methods. Risk of performance bias due to participant and personnel knowledge of intervention was consistently judged as unclear (n=14, 100%).

The risk of attrition bias was commonly deemed to be low (n=7, 50%) as it was clear in these studies how many participants dropped out, when they dropped out, and the reasons for dropout were similar between groups. However, 36% (n=5) were judged to be unclear as it was not possible to either detect explicit numbers of participants who dropped out or reasons for incomplete outcome data were not

reported. Two of the studies (14%) were judged to be at high risk of attrition bias. The study by Lim et al. (2010) had less than 20% dropout, however, the reasons for dropout between the intervention and control groups were different and potentially linked to the intervention received (personal reason n=4, pain n=3, time constraints n=1, heart problems n=1). The study by Somers et al. (2012) was judged at high ROB due to the 30% dropout (n=19 intervention group; 14 control).

To determine the risk of reporting bias due to selective reporting, the a-priori published protocol for each study was examined where available. Although most studies had protocols available, only three (21%) were judged as having low ROB with consistency between the protocol and the published paper. 10 studies were judged as having unclear risk (71%), due to a lack of an a-priori protocol, or insufficient protocol detail to make a judgement. One study was judged to be at high risk of reporting bias (Casilda-Lopez et al., 2017) as the primary and secondary outcomes described in the protocol differed from those reported in the published paper.

The 'other sources of bias' domain assessed components such as conflicts of interest and patient generalisability. This domain was judged to be at low ROB in 12 studies (86%) and unclear in two (14%) as one study did not report conflicts of interest (Rejeski et al., 2002) and one was part-funded by a private dietary produce provider (Slim Fast), who had a potential financial interest in the outcomes of the study (Miller et al., 2006).

4.2.5 Main findings heterogeneity and analysis choice

The participant comorbidities, PA types and outcome measures were very diverse across most studies. An assessment of study heterogeneity determined whether it was possible or appropriate to undertake statistical pooling. Heterogeneity was assessed in terms of clinical heterogeneity (differences in participants and interventions), methodological heterogeneity (differences in study design such as outcome measures) and statistical heterogeneity (differences in outcomes and direction of findings). Studies which were sufficiently homogeneous and thus combined, needed to include the same comorbidity, the same outcome domain and outcome measure. Four of the included studies

were judged to be suitably homogeneous for combining in meta-analysis. A random-effects model was used for the meta-analysis which allowed for differences in the treatment effect from study to study (Higgins and Green, 2011). Further information on the meta-analyses selection process for these studies can be found in Appendix 8.

Where statistical pooling through meta-analysis was not possible due to study heterogeneity, a narrative synthesis of results was conducted by presenting primary outcomes from included studies, organised by comorbidities (Melendez-Torres et al*.,* 2016; Popay et al*.,* 2006). It is important to consider narrative synthesis as a method to develop understandings, not merely to complement meta-analysis (Melendez-Torres et al*.,* 2016). While narrative synthesis can involve the manipulation of statistical data; the defining characteristic is that it adopts a textual approach to the process of synthesis to 'tell the story' of the findings from the included studies (Popay et al*.,* 2006).

The following section first presents the results of all studies split by primary outcome measures; pain (Table 4.2.4), function (Table 4.2.5) and QOL (Table 4.2.6) for each comorbidity. Three meta-analyses of OA and obesity on the outcomes of WOMAC pain (Figure 4.2.4), WOMAC function (Figure 4.2.5) and 6MWT (Figure 4.2.6) are presented. The remaining study results are then presented via a narrative synthesis.

Table 4.2.4 Summary of pain outcome findings

Study	Outcome measure	Post intervention mean ±SD or (SE) or (range)		Post intervention between group mean difference (95% CI), P value	Other outcome reporting style	Notes
		Intervention	Control / comparison			
OA and obesity studies						
Casilda-Lopez et al., 2017	WOMAC P	5.80±4.81	8.02±3.05	NA	NA	PA vs PA
Jenkinson et al., 2009	WOMAC P	5.70±3.96	7.04±4.21	-0.91 (95% CI: -1.66, -0.17) P = 0.016*	NA	NA
Messier et al., 2004	WOMAC P	6.24±0.47	6.02±0.45	+0.48 (0.16, 0.79)	NA	NA
Messier et al., 2013	WOMAC P	4.4	4.8	-0.12 (-0.34, 0.11)	NA	NA
Miller et al., 2006	WOMAC P	4.1(0.4)	6.1(0.5)	-0.67 (-1.10, -0.24)	NA	NA
Somers et al., 2012	WOMAC P	35.5(31.9to39.0)	38.0(34.1to41.8)	NA	NA	NA
OA and T2DM						
Foy et al., 2011	WOMAC P	3.19	3.62	NA	C: -0.28 (3.57) I: -0.51 (3.45)	#
OA and multimorbidity						
de Rooij et al., 2017	WOMAC P	6.9±3.4	8.8±4.2	-1.78 (-2.65, -0.55)*	NA	NA

*OA=Osteoarthritis; PA=Physical Activity; T2DM=Type Two Diabetes Mellitus; WOMAC P=Western Ontario and McMaster Universities Osteoarthritis Index (Pain) (Higher scores on the WOMAC indicate worse pain, stiffness, and functional limitations); WOMAC pain scale (0-20); I=intervention group; C=control group; P=significance value; *Statistically significant change in favour of physical activity intervention; Unless otherwise stated, reported as: post intervention between group mean difference (95% CI=Confidence Intervals) or post intervention results, reported as mean (SD=Standard Deviation / SE=Standard Error / range) or change (95% CI); #=Raw mean change (standard deviation) from baseline to follow-up for I(intervention) and C(control) groups; NA=Not Applicable*

Table 4.2.5 Summary of function outcome findings

Study	Outcome measure	Post intervention mean ±SD or (SE) or (range) or mean change (low, high CI))		Post intervention between group mean difference (95% CI), P value	Other outcome reporting style	Notes
		Intervention	Control /comparison			
OA and obesity studies						
Casilda-Lopez et al., 2017	WOMAC PF 6MWT	28.50±14.03 301.99±50.17	29.25±10.04 246.22±48.43	NA	NA	PA vs PA
Christensen et al., 2015	6MWT	+38.48 (23.7, 53.2)	+22.89 (7.9, 37.9)	NA	NA	##
Jenkinson et al., 2009	WOMAC PF	-3.64 (1.21)	NA	NA	NA	NA
Messier et al., 2004	6MWT	472.73±13.12	429.89±12.77	3.31 (2.83, 3.80)	NA	NA
Messier et al., 2013	WOMAC PF 6MWT	17.6 525	17.7 502	0.26 (0.04, 0.49) -0.01 (-0.23, 0.22)	NA	NA
Miller et al., 2006	WOMAC PF 6MWT	15.2 (1.5) 510.0 (15.0)	23.8 (2.0) 459.0 (17.4)	0.48 (0.05, 0.90) -0.74 (-1.17, -0.31)	NA	NA
Schlenk et al., 2011	6MWT WOMAC PF	466.1±101.3 17.3±13.1	504.4±106.6 22.9±14.9	-0.37 (-1.14, 0.41) -0.40 (-1.18, 0.38)	NA	NA
Somers et al., 2012	WOMAC PF	36.0 (32.6to39.3)	37.5 (33.9to41.2)	NA	NA	NA
OA and T2DM						
Foy et al., 2011	WOMAC PF	9.0	10.77	NA	C: -0.73(11.32) I: -2.30 (9.92)	#
OA and multimorbidity						
de Rooij et al., 2017	WOMAC PF SF-36 6MWT	26.3±12.7 20.8±4.5 448.0±102.5	31.4±13.4 18.9±5.0 416.5±116.9	-7.43 (-9.99, -4.87)* 34.16 (17.68, 50.64)*	NA	NA
Mangani et al., 2006	6MWT	1=+12.2% (6.9, 17.5) 2=+0.7% (-2.9, 4.2)	+2.0% (-1.4, 5.3)	NA	NA	1 weight ex 2 aerobic ex

*OA=Osteoarthritis; PA=Physical Activity; ex=exercises; T2DM=Type Two Diabetes mellitus; WOMAC PF=Western Ontario and McMaster Universities Osteoarthritis Index (Physical Function) (Higher scores on the WOMAC indicate worse pain, stiffness, and functional limitations); WOMAC function=0-68; 6MWT=Six-minute walking test (distance covered over a time of 6 minutes (meters)); SF-36=36 item questionnaire which measures physical function (Lower scores on the SF questionnaires indicate worse outcomes); *Statistically significant change in favour of physical activity intervention. Unless otherwise stated, reported as: post intervention between group mean difference (95% CI=Confidence Intervals) or post intervention results, reported as mean (SD=Standard Deviation / SE=Standard Error / range) or change (95% CI); ##change in outcome measures from baseline to follow-up (mean (95% lower, upper confidence intervals); #=Raw mean change (standard deviation) from baseline to follow-up for I(intervention) and C(control) groups; NA=Not Applicable*

Table 4.2.6 Summary of QOL outcome findings

Study	Outcome measure	Post intervention mean ±SD or (SE) or (range) or mean change (low, high CI))		Post intervention between group mean difference (95% CI), P value	Other outcome reporting style	Notes
		Intervention	Control / comparison			
OA and obesity studies						
Christensen et al., 2015	SF-36 MCS SF-36 PCS	+0.1 (-1.7, 2.0) +3.8 (1.9, 5.7)	+1.3 (-0.5, 3.2) +4.4 (2.5, 6.4)	NA	NA	##
Lim et al., 2010	SF-36 PCS SF-36 MCS	1=38.8±7.7 1=54.8±8.8 2=40.4±7.9 2=52.9±8.3	36.9±9.6 48.4±14.3	NA	NA	1 aqua ex 2 land ex
Messier et al., 2013	SF-36 PCS SF-36 MCS	42.0 55.4	42.0 54.9	 0.23 (-1.47, 1.93)	NA	NA
Rejeski et al., 2002	SF36 MCS SF36 PCS	52.85 (1.26) 37.14 (1.25)	53.51 (1.20) 34.41 (1.09)	NA	NA	NA
OA and depression						
Yeol et al., 2013	SF-8	24.05±4.63	23.05±3.58	NA	NA	NA

*OA=Osteoarthritis; aqua=aquatic exercise; ex=exercises; QOL=Quality Of Life; SF-36=36 item Short Form questionnaire; SF-36 MCS=Mental Component Scale; SF-36 PCS=Physical Component Scale; SF-8=8-item Short Form questionnaire. Lower scores on the SF questionnaires indicate worse outcomes. *Statistically significant change in favour of physical activity intervention. Unless otherwise stated, reported as: post intervention between group mean difference (95% CI=Confidence Intervals) or post intervention results, reported as mean (SD: Standard Deviation / SE: Standard Error / range) or change (95% CI); ##change in outcome measures from baseline to follow-up (mean (95% lower, upper confidence intervals); NA=Not Applicable*

4.2.6 Meta-analysis

Each primary outcome measure in the obesity comorbidity meta-analysis are presented separately; (1) WOMAC pain, (2) WOMAC function and (3) 6MWT function.

4.2.6.1 WOMAC pain

The results of the random-effects meta-analysis for the three RCTs comparing WOMAC pain scores for the PA intervention and the non-PA control for OA patients with obesity are displayed in Figure 4.2.4. The pooled standardised mean difference (SMD) estimate suggests a potential small beneficial effect of PA on pain reduction, although this finding was not statistically significant -0.21 (95% CI -0.60, 0.17). The pooled SMD effect estimate is non-significant because the 95% confidence interval (CI) crosses the line of no effect (0). The study-specific estimates were substantially heterogeneous. This finding is supported by the I-squared test (percentage of variance attributable to study heterogeneity), which suggested the presence of considerable heterogeneity (I-squared = 78.35%). Lower I-squared values indicate less heterogeneity and higher values suggest substantial heterogeneity.

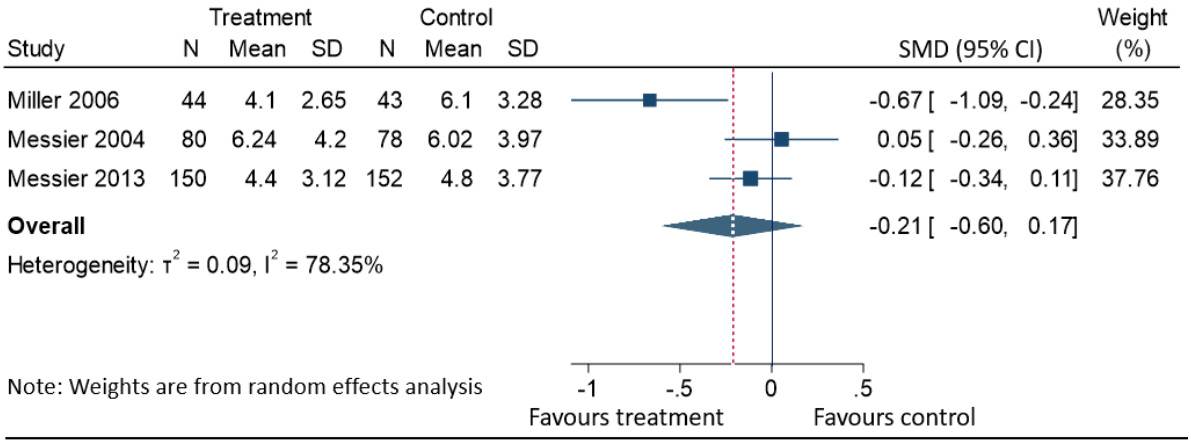


Figure 4.2.4 Forest plot of the effect of PA interventions on WOMAC pain: OA and obesity

OA=Osteoarthritis; PA=Physical Activity; SMD=Standardised Mean Difference; WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index; CI=Confidence Interval; N=Number; SD=Standard Deviation

4.2.6.2 WOMAC function

Figure 4.2.5 shows the results of a random-effects meta-analysis for the three RCTs comparing WOMAC function scores for the PA intervention and non-PA control for OA patients with obesity. The

pooled SMD estimate suggests a small beneficial effect of PA on physical function although this finding was not statistically significant (SMD) of -0.34 (95% CI -0.83, 0.14). There was substantial heterogeneity in the meta-analysis (I-squared = 73.39%).

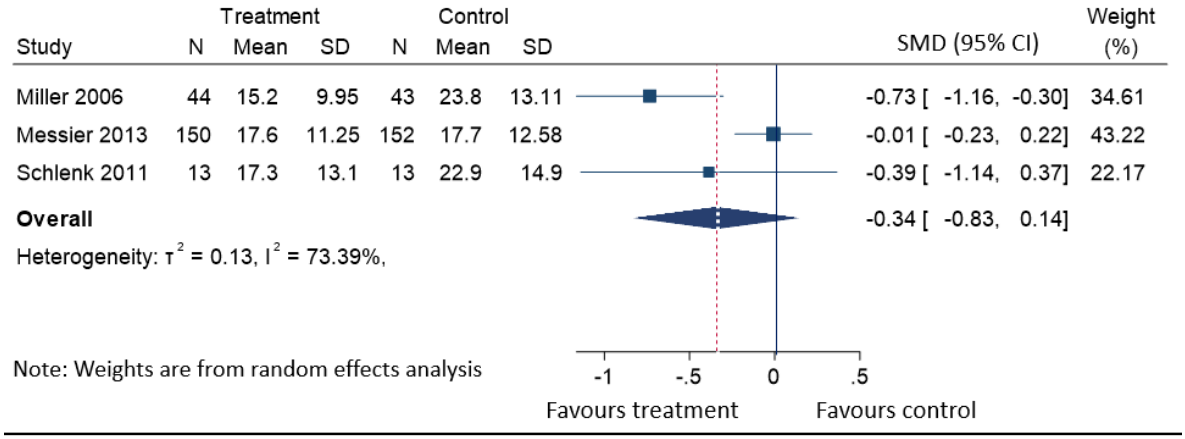


Figure 4.2.5 Forest plot of the effect of PA interventions on WOMAC function: OA and obesity

OA=Osteoarthritis; PA=Physical Activity; SMD=Standardised Mean Difference; WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index; N=Number; SD=Standard Deviation

4.2.6.3 6MWT function

The results of a random-effects meta-analysis for the four RCTs comparing 6MWT scores for the PA intervention and non-PA control for OA patients with obesity are displayed in Figure 4.2.6. PA had a small significant beneficial effect on 6MWT distance 0.29 (95% CI 0.13, 0.46). The heterogeneity between study estimates was very low (the CIs for each of the individual studies are similar and overlap), reflected in a low degree of statistical heterogeneity (I-squared = 0%), thus there is confidence in the precision of the results.

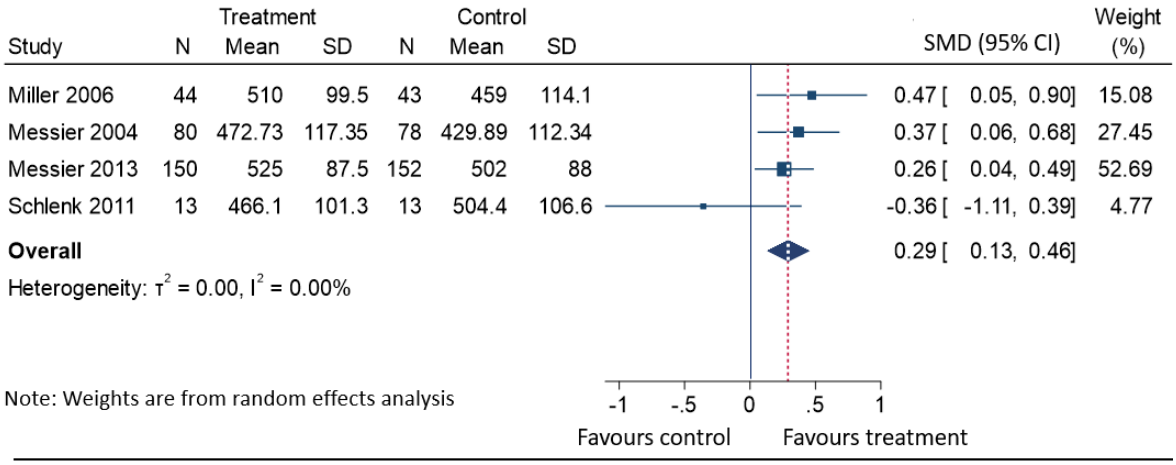


Figure 4.2.6 Forest plot of the effect of PA interventions on 6MWT function: OA and obesity

OA=Osteoarthritis; PA=Physical Activity; SMD=Standardised Mean Difference; 6MWT=6-Minute Walking Test; N= Number; SD=Standard Deviation

4.2.7 Narrative synthesis

The narrative synthesis is sub-grouped by comorbidity (obesity, T2DM, depression and multimorbidity) then within each comorbidity, the results for each primary outcome domain are described (pain, function, QOL). Finally, secondary outcome measures (long-term follow-up of primary outcomes and adverse events) are described when available. A large amount of heterogeneity was present in the reporting style of different studies. Most studies reported clinical outcomes as; post intervention between group mean difference (95% CIs) or post intervention results, reported as mean (standard deviation (SD) / standard error (SE) / range) or change from baseline (95% CIs). Also reported are adjusted mean change generated from mediation analyses (adjusted mean change (SE) and raw mean change (SD). Where available, P values are provided to back up statistically significant differences.

4.2.7.1 Sub-group 1: Osteoarthritis and obesity (n=10 studies)

The studies which included obesity comorbidity but where not included in the obesity meta-analyses were excluded for reasons including; lower BMI overweight / obesity ranges (Lim et al., 2010; Jenkinson et al., 2009); different outcome measurement scale, tool and reporting style (Somers et al., 2012; Christensen et al., 2015; Rejeski et al., 2002) and having a PA comparison group (Casilda-Lopez et al., 2017) (Appendix 8).

4.2.7.1.1 WOMAC Pain (n=3)

In all studies reporting knee pain that were not included in the meta-analysis, pain was measured by the WOMAC pain scale (Jenkinson et al., 2009; Somers et al., 2012; Casilda-Lopez et al., 2017). The study by Jenkinson et al. (2009) was not eligible for meta-analysis because of the actual mean BMI of the sample (>28), but there was a significant reduction in pain score from baseline over time between groups ($p<0.05$). The mean difference between PA and control was -0.91 (95% CI -1.7, -0.2) (Jenkinson et al*.,* 2009).

One study used the WOMAC pain visual analogue scale (VAS) (Somers et al., 2012). The range of scores on the subscale was between 0 and 100 with higher scores indicating higher levels of pain. Both control and intervention groups improved on pain scores, with the intervention group having a greater improvement and lower pain post intervention (35.5 (31.9, 39.0)) compared to control (38.0 (34.1, 41.8)).

The study by Casilda-Lopez et al. (2017) reported results for WOMAC pain. The results of this study showed an improvement in WOMAC pain in the aquatic dance-based PA group (5.8±4.8) compared with traditional aquatic PA (8.0±3.1) at the post intervention time point.

4.2.7.1.2 Function (n=3)

The study by Somers et al*.* (2012) used the WOMAC function VAS to measure physical function (ranging from 0 to 100, with higher scores indicating a worse condition), which meant it was not compatible to include in the meta-analysis. Both control and intervention groups improved on physical function scores between baseline and post intervention. The intervention group showed the most improvement in function score at post treatment follow-up (36.0 (32.6, 39.3)) compared with control (37.5 (33.9, 41.2)).

One study also reported 6MWT results for physical function (Christensen et al*.,* 2015). However, the results reported were given as mean change in outcome measure and 95% CIs from the baseline to

post intervention follow-up. From these results, both the intervention and control groups improved their walking distance (metres). The intervention group improved more (+38.5 (23.7, 53.2)) compared to control (+22.9 (7.9, 37.9)), but this between group difference was not statistically significant (p=0.27).

The study by Casilda-Lopez et al. (2017) reported improvements in WOMAC function post intervention for both the aquatic dance (28.5±14.0) and traditional aquatic PA groups (29.3±10.0). However, improvements were found only in the aquatic dance group and not in the traditional aquatic PA group for 6MWT (301.9±50.2; 246.2±48.4; respectively).

4.2.7.1.3 Quality of life (n=4)

Four studies reported QOL as measured by the SF-36 physical and Mental Component Scale (MCS), each scored from 0-100, with higher scores indicating better health (Christensen et al., 2015; Lim et al., 2010; Messier et al., 2013; Rejeski et al., 2002). Trends of improvements in mental health across groups (measured by the SF-36 mental health component) were reported within groups in all studies, although there was no improvement in overall QOL between groups. One study found no difference in the SF-36 MCS between the intervention group and control group post intervention (52.9, 53.5; respectively) (Rejeski et al., 2002). Lim et al., (2010) observed a difference on the SF-36 MCS in their aquatic PA group post intervention (54.8±8.8) which was higher compared with the control group (48.4±14.3) but not statistically significant. This study had a second land-based PA intervention which was also higher in the SF-36 MCS (52.9±8.3) than control (48.4±14.3) (Lim et al., 2010). In the SF-36 Physical Component Scale (PCS), Lim et al. (2010) found significant differences in their intervention groups, compared to control post intervention (38.8±7.7; 40.4±7.9; aquatic and land-based respectively) which were both higher post intervention compared with control (36.9±9.6). Rejeski et al. (2002) also found the SF-36 PCS to improve in favour of intervention (37.14) compared with control (34.4) (non-significant). The remaining two studies reported no significant difference between groups

on the SF-36 PCS. However, there were small improvements in both intervention and control groups over the study period (Christensen et al., 2015; Messier et al., 2013).

4.2.7.2 Sub-group 2: Osteoarthritis and type 2 diabetes mellitus (n=1 study)

4.2.7.2.1 Pain

The results for pain as measured by the WOMAC in the study by Foy et al. (2011) were provided as post intervention scores and adjusted mean change scores from baseline to post intervention (provided as means and SD). However, there was no difference post intervention between intervention and control (intervention group: 3.2 (mean change -0.5), control group: 3.6 (mean change -0.3)) (Foy et al., 2011).

4.2.7.3 Sub-group 3: Osteoarthritis and depression (n=1 study)

4.2.7.3.1 Quality of life

QOL was measured in one study (Yeol et al., 2013) using the SF-8 (a shorter version of the SF-36 consisting of eight items; body pain, general health, mental health, physical functioning, social functioning, role physical, role emotional and vitality). Scores range from 0 to 40, with higher scores indicating a better QOL. The SF-8 score of the control group did not show a significant difference in pre and post intervention (23.5±4.6, 23.1±3.6; pre and post respectively). The SF-8 score of the intervention group was slightly higher than the control group (24.1±4.6) and higher than pre intervention (22.5±3.5) but this change was not statistically significant ($p>0.05$) (Yeol et al., 2013).

4.2.7.4 Sub-group 4: Osteoarthritis and multimorbidity (n=2 studies)

4.2.7.4.1 Pain (n=1)

Knee pain was measured by one of the two OA and multimorbidity studies (de Rooij et al., 2017) using the WOMAC pain scale. There was a statistically significant difference in the reduction in pain score from baseline over time, between groups ($p<0.05$). The mean difference between PA and control was -1.78 (95% CI -2.7, -0.6) (de Rooij et al., 2017).

4.2.7.4.2 Function (n=2)

The studies in this sub-group investigated physical function outcomes using the WOMAC function subscale, the SF-36 physical function subscale and the 6MWT. In both studies, there was a statistically significant between group difference in change in WOMAC physical function ($p<0.05$). One study (de Rooij et al., 2017) found improvements from baseline to post intervention in both WOMAC score (-7.4 (95% CI -9.9, -4.9); $p<0.05$) and the 6MWT (34.2 (95% CI 17.7, 50.6); $p<0.05$) between intervention and control groups post intervention, without improvements in the SF-36 measure. One study measured two different interventions against control; aerobic training and weight training, and found those in the aerobic PA group showed significant improvement in the 6MWT (+12.2% (95% CI: 6.9, 17.5)) compared to the control group and the weight training intervention (+0.7% (95% CI -2.9, 4.2)) compared with control group (+2.0% (95% CI -1.4, 5.3)) (Mangani et al., 2006). This study found aerobic activity to provide the most consistent positive effects on study outcomes.

4.2.7.5 Adverse events (n=4 studies)

One study reported no serious adverse events (Miller et al., 2006). Otherwise, adverse events were only explicitly reported in three obesity RCTs (Messier et al., 2004; Messier et al., 2013; Somers et al., 2012). The reported adverse events were in the intervention groups, which all included a combination of aerobic and strength / resistance exercise. One study specifically reported that one participant fell off a treadmill while exercising, which caused wounding (Somers et al., 2012). One study reported one serious event where a participant tripped while exercising and sustained a head injury (Messier et al., 2004). Only one study reported more than one adverse event (n=2), which were both described as a trip or fall (Messier et al., 2013).

4.2.7.6 Long-term follow-up (n=1 study)

Only one study in this review reported long term follow-up results (>6 months post intervention) (Schlenk et al., 2011). For WOMAC function, the improvements in function at the post intervention time point diminished slightly at long-term follow-up (post intervention: 17.3 ±13.1, follow-up:

18.9±13.2). The intervention group showed greater improvement from baseline to the end of the six months follow-up in the mean distance (8.5% increase) compared with controls (2% increase) (Schlenk et al., 2011).

4.2.8 Heterogeneity of the studies identified

A high amount of between study heterogeneity was found within the papers identified within this systematic review. Few studies were identified within each different comorbidity category and the differences between sample size, intervention and control types, duration, intensity and frequency of interventions, delivery and follow-up, outcomes, measures and reporting statistics, made it hard to combine studies for analysis (Table 4.2.1).

4.2.9 Summary of results

In summary, 14 studies were included in this systematic review. All studies investigated knee OA, were mostly focused on obesity comorbidity (n=10) and included various PA interventions of which combined strengthening and aerobic exercises were most common (n=6). Synthesising the evidence from the included studies, the key findings were;

- In people with OA and obesity, pooled best estimates suggest PA interventions may improve pain and function (however only the statistically significant effects were found for 6MWT)
- One trial found no difference in pain outcomes between PA intervention and control in people with OA and T2DM
- One trial found no difference in pain outcomes between PA intervention and control in people with OA and depression
- In people with OA and multimorbidity, PA interventions improve pain scores ($p<0.05$) and improve physical function ($p<0.05$)

4.3 Discussion

4.3.1 Introduction

This discussion will firstly synthesise and evaluate the key findings of the review and the quality of the evidence. Following this, a discussion of each finding in the context of existing research is provided. The systematic review's strengths and limitations will then be discussed, and the clinical and research implications will be considered. Kraus et al. (2019) conducted a systematic umbrella review to evaluate the effects of PA on pain, function, QOL, in people with lower limb OA and found no systematic review included RCTs of participants exclusively with OA and comorbidity which highlights the novelty of this systematic review.

4.3.2 Aim and objectives

This systematic review investigated the clinical effectiveness of PA interventions in people with OA and comorbidity. The objectives were to (1) identify, (2) critically appraise and (3) examine the effectiveness of PA interventions for adults with OA and comorbidity.

4.3.3 Key findings

A total of 14 studies examining knee OA and four comorbidity types (obesity, T2DM, depression and multimorbidity) were included in the review. The most common OA comorbidity group type was obesity (n=10), and statistical pooling of a small selection of these studies was possible. A narrative synthesis approach was used to summarise the remaining studies as they were considered too heterogeneous to aggregate. Overall, the findings of this review are mixed with some studies suggesting that PA interventions have a beneficial effect on pain, function and QOL, but some showing no benefit over control in people with OA and comorbidity. Importantly, uncertainty exists due to study heterogeneity and meta-analysis imprecision. The overall ROB of the studies indicates that only a small percentage (3% of all ROB judgements) were at high ROB, but there was a large percentage of unclear judgements which is important to consider when interpreting the results.

4.3.3.1 Quality assessment

Overall, total ROB of all domains within the included studies was largely judged 'unclear' (48%). A large contributor to the unclear domains was blinding of participants to the intervention received, as this was not possible, and this domain was judged unclear for all studies. Blinding of participants is rarely possible in PA RCTs (unless "sham" PA groups are used) and placebo effects for self-reported outcomes in knee OA are possible (Zhang et al., 2010) which were not controlled for in the included PA studies. The remainder of unclear judgements were due to the inadequacy of the reporting on various domains within the study methods and results. Despite this, of those that did provide adequate detail, 49% were judged as 'low risk' and just 3% of all domains being judged as having a 'high ROB'.

Risk of attrition bias was low in approximately half of the studies within this review (47%). However, attrition bias was unclear due to incomplete attrition data in 40% of studies. The remaining 13% of studies were judged to have a high risk of attrition bias as the reasons for dropout were different between groups, and often related to the intervention received (Lim et al*.,* 2010; Somers et al*.,* 2012). It is important to know the attrition rates in RCTs as those who drop out may be systematically different from those who did not in terms of clinical outcomes, therefore clinical effectiveness findings may be biased if these participants are not included in the analyses.

Reporting bias was of some concern in this review as the majority of protocols for the studies were unpublished (n=10) and of those published (n=4), one was judged at 'high risk' of bias due to an inconsistency between the protocol and the study results paper (Casilda-Lopez et al., 2017). Without protocols, it cannot be determined whether specific outcomes were collected and not reported; thus, the results of this review could be skewed toward the favourable outcome results only. Overall, the ROB of the studies included in this review is relatively low with clearer methods in place for the remaining domains.

The studies by Casilda-Lopez et al. (2017), Schlenk et al. (2011) and Yeol et al. (2013) all had small sample sizes (n=<40) which could have affected the precision of their results.

4.3.4 Primary outcomes

The studies included in this review all measured at least one primary outcome of interest (pain, function, QOL). The outcomes reported and the outcome measures used varied between the studies and are discussed below.

4.3.4.1 Pain

Pain was reported by eight studies as measured by the WOMAC**.** Overall, the meta-analysis (n=3 studies) best estimates suggest that PA interventions for those with OA and obesity may result in a small mean treatment benefit for pain (SMD -0.21 (95% CI -0.60, 0.17)) although this finding was not statistically significant and the precision of this estimate was low as indicated by a wide CI. Heterogeneity in the pain effect estimate was primarily driven by one RCT (Messier et al*.,* 2004) where a healthy lifestyle education control arm performed similarly well to the PA intervention.

In those people with OA and T2DM, one RCT found no difference in pain outcome between PA intervention and control, however, one RCT of participants with OA and multimorbidity, found the PA intervention led to statistically significant improvements in pain compared to a control arm. These pain outcome results present a mixed picture suggesting PA may be beneficial for pain in some groups of people with OA and comorbidity but with best estimates indicating a smaller effect than estimates from systematic reviews of PA RCTs in other people with OA irrespective of comorbidity (Kraus et al., 2019; Fransen et al*.,* 2015; Uthman et al., 2013; Juhl et al., 2014; Fernandes et al*.,* 2013). For example, the review by Fransen et al. (2015) found pooled results of 44 RCTs demonstrated a statistically significant benefit of PA on pain, with a moderate effect size (SMD of 0.49 (95% CI 0.39 to 0.59)). The results of the current review were at best small in effect size across different comorbidities although more studies could change this finding and also improve estimate precision. The comorbid populations on average demonstrated more pain at baseline than those with general OA populations (de Rooij et al*.,* 2017) and this could be an important consideration when comparing the results to RCTs and reviews in populations of OA without comorbidity.

4.3.4.2 Function

Physical function was reported by 11 studies, using a range of measurement tools (WOMAC = 8, 6MWT = 8, SF36 = 1). Overall, the meta-analysis best estimates suggest that PA interventions for those with OA and obesity led to small improvements in physical function as measured by the WOMAC (n=3 studies) (SMD -0.34 (95% CI -0.83, 0.14)), however, this finding was not statistically significant due to individual RCT outcome heterogeneity. Once more, wide CIs highlight the current imprecision and uncertainty around this current best estimate. PA had a small significant beneficial effect on function as measured by the 6MWT (n=4 studies) (SMD 0.29 (95%CI 0.13, 0.46)). These findings are in agreeance with another systematic review of PA for knee OA (Fransen et al., 2015), which found pooled results of 44 studies demonstrated a moderate benefit of PA on function (SMD 0.52 (95% CI 0.39, 0.64)) although the magnitude of effect size appears to be smaller in those with OA and obesity compared to those in knee OA RCTs irrespective of comorbidity selection. Fransen et al. (2015) report statistical significance in their study, but their precision was downgraded because of the marked heterogeneity between the studies (similar to this review).

In the studies which included people with OA and multimorbidity, PA was shown to statistically improve function scores as measured by the WOMAC physical function and 6MWT. However, in one study (de Rooij et al*.,* 2017) improvements were seen in the WOMAC physical function and 6MWT results but not in the SF-36 function sub-scale. The WOMAC measure is specifically designed to measure physical function in people with OA, therefore may be more responsive to functional changes in OA populations compared to the general SF-36 function sub-scale. Within each outcome domain, the use of different outcome measures made it hard to make direct comparisons throughout various subgroups. The within study differences in outcome domain findings highlights the need to investigate the optimal outcome measures to accurately determine the effectiveness of interventions for this population.

4.3.4.3 Quality of life

QOL was measured in four RCTs of participants with OA and obesity and one study of participants with OA and depression (SF36-MCS = 4, SF36-PCS = 4, SF-8 =1). Due to the limited number of studies reporting QOL outcomes using the same measure, it was not feasible to perform meta-analyses for this outcome domain. None of the four studies found statistically significant differences in QOL between intervention and control arms. Fransen et al. (2015) found small QOL improvements in people with knee OA in their pooled results with statistical significance (SMD 0.28 (95% CI 0.15, 0.40)). Perhaps PA interventions alone do not change QOL in people with OA and comorbidity. Alternatively, QOL measures may be insufficiently responsive, or the presence of multiple LTCs could make QOL a harder outcome to improve. Despite this, research has suggested that symptoms that impact disability, QOL satisfaction and daily life are of more value and a high priority for patients (Muth et al., 2014; Young et al., 2016). However, QOL was less routinely measured than other outcome measures such as pain and function and global health was not measured. A possible explanation is a difficulty in any current QOL outcome measure to adequately accommodate for all multidimensional factors considered important to the QOL of an individual with OA and comorbidity (Goh et al., 2019).

4.3.5 Secondary outcomes

A minority of studies (n=4) included a secondary outcome of interest (long-term follow-up and adverse events), which are discussed below.

4.3.5.1 Long-term follow-up

Only one study in the current review reported long-term follow-up results and found that the benefits on the WOMAC function score reduced slightly but were still preferable to baseline values (Schlenk et al., 2011). This corroborates with a previous systematic review in terms of long-term pain and function outcomes (Fransen et al., 2015), which found both measures declined at time points past six months, and pain benefits were not sustained. PA types, intensities and modalities are often the focus of PA interventions (Juhl et al., 2014; Bennell and Hinman, 2013); however, the degree of adherence to the

PA program in the long-term has been suggested as a more important focus (Bennell and Hinman, 2013). Research suggests that it is only when PA is participated long-term that the benefits of a PA intervention can be fully realised and enhanced, particularly within comorbid populations (Mangani et al., 2006), therefore long-term follow-up may be important to report in RCTs. In OA, the review by Goh et al. (2019) found that the pain and function effects were reduced by at least half between two- and six-months follow-up. They found that one of the reasons for this was poor PA adherence (Goh et al., 2019). Previous RCTs of adults with knee OA have described better improvements in pain, function, QOL and overall level of disability for participants who adhere to the PA intervention (Ettinger et al., 1997; Van Gool et al., 2005). Secondary analysis of the ADAPT study by Van Gool et al. (2005), suggest a potential dose-response relationship between the level of PA adherence and greater physical improvements in overweight people with knee OA.

The study by Yeol et al. (2013) highlighted that PA intervention adherence rates are close to 50%; therefore, interventions with an adherence focus are necessary, to encourage maintenance of PA. There are several aspects which contribute to adherence, including personal beliefs, social support, provider support and ease of access (Goh et al., 2019; Bennell and Hinman, 2013). Also, Mangani et al. (2006) found that in the context of comorbidity, participants could need closer supervision, as common transitions from facility-based interventions to home-based interventions could result in lower adherence. Most patients across all LTCs require some form of monitoring or supervision to optimise the potential of PA (Foster et al., 2014; Fransen et al., 2015) and previous systematic review trends suggest booster sessions with a physiotherapist improve adherence to therapeutic PA in people with OA (Nicolson et al., 2017). This was also found in the intervention by Foy et al. (2011) which found a combination of group and individual counselling and regular feedback, encouraged progress, the achievement of goals and problem-solving strategies (Foy et al., 2011). A therapeutic relationship and ongoing communication between the provider and patient is likely to be important in OA and comorbidity, and a partnership that has ongoing engagement, involvement and accountability could improve PA adherence (Hurley et al., 2018).

In the current review, Casilda-Lopez et al. (2017) had low dropout rates within their aqua dance intervention for people with OA and obesity. This study found that by using an intervention that included social interaction and was considered fun, stimulated people to be more active and created lower rates of dropout (Casilda-Lopez et al., 2017). Similar results were found in the RCT by Lim et al. (2010) with improvements in clinical outcomes for both intervention arms, but with fewer injuries and less negative associated side effects, such as discomfort and pain in the aqua group, compared with land-based activity (Lim et al., 2010). Water-based PA, with its reduced weight-bearing when compared to land-based PA, targeted at people with OA who are overweight or obese appears to make PA more comfortable than full weight-bearing PA, potentially promoting PA participation in the long-term. Furthermore, previous findings have shown reductions in BMI may in part, explain adherence to PA interventions in people with knee OA who are overweight (Van Gool et al., 2005). Therefore, considering the prevalence of obesity in the population of OA, perhaps weight loss could be an optional intervention component for any group of people with OA and comorbidity.

4.3.5.2 Adverse events

In the current review, adverse events were generally not reported and were only reported in three studies. This mirrors the wider OA PA RCT literature (Quicke et al., 2015). In the studies within this review that did report adverse events they were only evident in the subgroup of OA and obesity and were all reported as a trip or fall (n=4), which resulted in minor injuries. A previous systematic review including 48 RCTs found consistent evidence that therapeutic PA did not cause serious adverse events and was safe for most older adults with knee pain, across various age groups and comorbidities including T2DM and obesity (Quicke et al., 2015). Furthermore, Quicke et al. (2015) found that out of 22 studies reporting adverse events, serious adverse events were absent, moderate adverse events were rarely reported and, like this study, mostly included falls (n=5).

Eleven of the RCTs within this review did not report adverse events. Although adverse events are uncommon, this finding is unlikely a true representation, due to the risk of reporting bias as above

discussed (section 4.3.3.1). It is important to know whether adverse events took place as this knowledge could indicate the requirement for comorbidity adaptation, or the use of a specific type of PA within a certain population or comorbidity. PA has many benefits in comparison to pharmacological treatments particularly regarding the likelihood of adverse effects such as medication interactions and side-effects (Bartels et al*.,* 2016). Nevertheless, the importance of tailoring PA to the person with OA and comorbidity which takes into account safety precautions related to comorbidity groups is necessary to avoid serious adverse events (de Rooij et al*.,* 2014). For example, those with comorbid conditions could experience additional adverse events relating to their LTCs, such as a cardiac event in CVD comorbidity or oxygen desaturation in people with COPD (ACSM, 2007; de Rooij et al., 2014).

4.3.6 Types of physical activity interventions

A key finding of this review was that the PA interventions identified were very heterogeneous. The PA interventions included different components ranging from specific types of PA alone (e.g. aqua dance or weight training) to lifestyle interventions (teaching and encouraging behavioural change strategies regarding nutrition and PA), PA with counselling and PA with diet. The PA interventions also varied greatly in mode, duration and supervision. This finding corroborates with previous reviews of PA interventions in OA populations; Fransen et al*.* (2015) found variability in the PA types, mode, and dosage, when specifically looking at land-based PA for OA and a recent review by Hurley and colleagues (2018) found huge variation and heterogeneity in PA interventions in OA populations. For example, previous RCTs on OA without comorbidity have included different forms of aerobic (Focht, 2005; Hurley, 2007), strength (Bennell, 2014), water-based (Bartels et al., 2016) and activities such as tai chi (Chen et al., 2016) and dance (Fransen et al., 2015). Furthermore, although effect sizes differ between RCTs, different systematic reviews have reached different conclusions as to whether categories of PA intervention type leads to different clinical outcomes (Fransen et al., 2015; Juhl et al*.*, 2014; Uthman et al., 2013).

It has been recommended that a holistic approach to the management of OA considers comorbidities (NICE, 2014), but there is no guidance on how to adapt PA for those with OA and comorbidities (NICE, 2014; Dekker et al., 2016). The interventions in the current review were complex and included multiple components which made it hard to distinguish whether benefits solely were gained from PA type alone or other factors such as delivery mode, nor what elements of the PA were influencing outcomes. For example, clinical outcomes and PA adherence may be influenced by behaviour change components or enhanced by reinforcement from other social and therapeutic interventions (Felson et al., 2000). Also, the differences in PA types would lead to different physiological responses and changes. For example, aerobic PA that focused on general fitness (Miller et al., 2006) might result in weight loss and improvements in cardiorespiratory fitness. In contrast, strength and flexibility PA (Jenkinson et al., 2009) may improve physical functioning and performance of daily tasks. Although both outcomes are desirable, whether they impact the specific outcomes of interest to this review, in the same way, is less certain.

In the current review, one study intervention had an alternative approach of tailoring the intervention delivered to the specific comorbid conditions to OA (de Rooij et al., 2017), which demonstrated how diverse populations could be clustered and receive tailored, but similar interventions, to optimise treatment. Findings from a previous meta-analysis of 4,000 patients found that focusing on one single mode of non-individualised PA, was more efficacious in reducing pain and disability than mixing several different modes of delivery and goals in the same intervention (Juhl et al., 2014). These results were also found in the review by Kraus et al. (2019) which found single-type PA programs were more efficacious than combined PA interventions for improving pain, function and QOL in people with OA.

Three of the studies did not exclusively use PA interventions. Caution is required in making inferences from these findings since the effect of the intervention may not be solely from the PA component alone. The three studies explicitly reported an intervention of PA and diet (Miller et al., 2006), PA plus lifestyle intervention (Foy et al., 2011) or PA including counselling (Schlenk et al., 2011). Previous

evidence has reported the effectiveness of psychosocial interventions on coping skills, and support to aid the maintenance of self-management in those with OA (Dixon et al., 2007), which could be further emphasised with the greater self-management demands of comorbidity. However, there is a lack of consensus on specific components, settings or delivery for optimal outcomes. Foy et al. (2011) found that in contrast to structured PA programs alone, interventions that combine an element of counselling allow for a more collaborative and independent approach for patients toward their care (Foy et al., 2011). NICE (2007, 2014: Public health guidelines [PH6, PH49]) suggests that interventions should incorporate a range of behavioural strategies, including goal setting, self-monitoring, building self-efficacy and support to aid intervention success. In the current review, the results from the intervention by Schlenk et al. (2011) complement this guideline, suggesting that not only was telephone counselling an effective addition to their intervention, but it was also a cost-effective strategy.

Educational coaching and teaching strategies were elements of the intervention in several studies (de Rooij et al., 2017; Somers et al., 2012; Schlenk et al., 2011; Foy et al., 2011). Teaching skills and encouraging self-management in combination with PA had a synergistic effect on enhancing participants ability to adhere with lifestyle changes in OA and comorbidity (Somers et al., 2012). However, different methods, such as PA and diet combinations and increased numbers of supervised sessions were found to be equally effective in a single RCT (Messier et al., 2004). Another review found that a combination of patient education or self-management intervention combined with PA intervention had a significant effect on pain, but less effect on physical function (Fernandes et al., 2013). The results of that review also found that PA interventions often consisted of varied combinations of components (Fernandes et al., 2013).

Other activities, such as exergaming (video game technology that tracks body movement and PA) were also employed in this review; such as in one study for participants with OA and depression (Yeol et al., 2013). However, they were less commonly used as the intervention compared to other forms of PA,

such as strength training. In the current review, the findings of an exergaming intervention in people with OA and depression showed trends of improved QOL scores but this change was not statistically significant between groups (Yeol et al., 2013). However, the study also had the shortest intervention duration (1 month) and had a small sample size (n=40), both of which could have influenced the results (Yeol et al*.,* 2013).

The findings from this review align with the previous systematic review by Fransen et al*.* (2015), finding that for both pain and physical function, interventions such as tai chi or PA involving coordination, stretching or balancing exercises, demonstrated smaller benefits and seemed to be less effective than strengthening and aerobic PA (Fransen et al*.,* 2015). However, other studies have found PA types including yoga and tai chi demonstrated the largest effect on QOL (Goh et al., 2019).

4.3.7 Control and comparison group types

The RCTs included in this review used different control and comparison groups, making it difficult to synthesise and make consistent comparisons across the studies. The control groups could be sub-grouped into usual care, healthy lifestyle, intensive diet, education / information, or different comparison PA intervention. It is important to consider control groups and what influence this may have had on comparing conclusions from the RCTs. Following guidance from the Cochrane Handbook (Higgins and Green, 2011), there is a distinction to be made between active and inactive control groups. One study included aquatic PA as the comparison group (Casilda-Lopez et al*.,* 2017). It was important to consider the control groups, whether they included education, information, a health program or usual care / current treatment. For example, individual RCT results suggest that a dietary intervention comparison in people with OA and obesity was an effective treatment (Messier et al., 2013), therefore, weight loss within the control group could reduce effect size of the PA intervention. Another challenge in considering control groups is that control reporting detail was lacking in many studies, which make it not possible to confidently evaluate between group effects (Karlsson and Bergmark, 2015).

4.3.8 Strengths of the review

This systematic review had a strict and clear protocol (PROSPERO Registration: CRD42017055582) which increases the review transparency and credibility. The review had a comprehensive search strategy to detect relevant studies and the search was performed with double reviewer screening, from title to full text. This was followed by piloted double reviewer ROB assessment, data extraction and result reporting, which will have minimised any individual reviewer bias in the selection of studies and outcomes. These strategies were employed to enhance the internal validity of the systematic review and allow accurate conclusions to be made about current evidence on the effectiveness of PA interventions in OA and comorbidity.

4.3.9 Limitations of the review

Despite the review following a comprehensive method, it was not without limitations. Firstly, the review was only designed to search for a limited selection of specific comorbidities and so may not have captured individual comorbidities other than those searched. Further, the search filter may have led to relevant RCTs being missed, due to a large number of terms and synonyms used to describe the conditions as comorbidities. It is also possible that various comorbidities and severity of comorbidity may have been excluded from individual RCTs due to contraindications to PA, such as those who have recently had a stroke or other major cardiovascular event. Another limitation of the systematic review was that the effectiveness of the PA interventions was only determined in terms of pain, function and QOL, although regular PA has demonstrated ability to improve other aspects of health and well-being. Therefore, this review may underestimate the overall beneficial effect of PA amongst the population of OA and comorbidity if PA is associated with additional health benefits.

A key limitation of this review is the dearth of evidence relating to other comorbidities other than obesity, which limits the generalisability of the findings and clinical implications, outside of OA and obesity. Linked to this, it was only possible to carry out meta-analyses for the effect of OA and obesity. However, this identifies a gap in the current literature. A further limitation was the small number of

total included studies (n=14). Within these studies, a wide range of reporting styles, heterogeneous condition definitions, methods, interventions, control group heterogeneity and outcome measures were used which made it hard to make direct comparisons between studies and comorbidity subgroups.

4.3.10 Clinical Implications

In the absence of clear and consistent evidence for the clinical benefit of PA in terms of pain, physical function and QOL, the mixed results suggest that PA interventions for people with OA and comorbidity should nevertheless be recommended, due to the existing extensive evidence base for PA in LTC management and other disease-specific clinical outcomes. However, the uncertainty around the findings, wide CIs, and within study result discrepancy, indicates more research needs to be done in this field. Although clinical uncertainty may exist in recommending specific components of PA interventions to populations with OA and comorbidity, some intervention results demonstrate statistical significance, and others do not. For example, almost all RCTs incorporated some form of aerobic PA and those in the statistically significant 6MWT test improvement all included some form of strengthening PA. Furthermore, the most consistently significant results were seen with the approach of heavily tailoring, and supervising the intervention delivered to specific comorbid conditions to OA (de Rooij et al., 2017).

4.3.11 Research Implications

The findings have contributed to the knowledge of PA interventions for those with OA and comorbidity and have identified important areas for future research such as; the need for studies on comorbidity in OA phenotypes outside of knee OA; common comorbidities other than obesity (for example depression and CVD); isolating intervention components (PA type or delivery mode); novel modes of PA intervention such as exergaming, with longer follow-up and more consistent outcome measurements and reporting styles, such as the OMERACT-OARSI recommendations for outcome measures (Smith et al., 2019). Future studies following a checklist of systematic, homogeneous

methods are needed to narrow down and simplify interventions to truly evaluate the impact of specific components of PA interventions to identify the optimal mode. For example, authors could use the existing TIDieR checklist (Template for Intervention Description and Replication) for reporting intervention details (Hoffmann et al., 2016). In addition, many RCTs did not specifically report adverse events. Monitoring and reporting adverse events in trials is important, and essential knowledge when ascertaining what interventions would benefit those with comorbidities. In summary, there is still a need to further develop and test PA interventions that can effectively improve outcomes in people with OA and comorbidity.

The beneficial effect on 6MWT in the current review (obesity and multimorbidity groups) could suggest that an objective measure could be more applicable to this patient group. Self-report measures such as the WOMAC function subscale are OA focused. Therefore, they may not be able to report how patient's comorbidities impact their functioning overall, alongside OA. Furthermore, it could be recommended that a standard QOL in OA and comorbidity tool is developed. Future research could determine the optimal outcome measure for each outcome domain in people with OA and comorbidity and then subsequent RCTs could be more consistent and comparable.

Further research should investigate the effectiveness of PA for people with OA and comorbidity that can offer additional evidence without the need for costly, time-consuming new RCTs, such as secondary data analysis of OA and comorbid subgroups (e.g. Mangani et al., 2006; Legha et al., 2020; Quicke et al., 2020) as well as individual patient data meta-analysis from existing RCTs that include both participants with and without comorbidity (Holden et al., 2017). For example, future research could explore mediators and moderators of PA effects to establish what works for whom and why.

4.3.12 Conclusion

In comparison to the wider PA literature in OA, relatively few studies have specifically targeted OA and comorbid populations, with 14 studies included in this review. In those studies, it is unclear to what extent existing interventions have benefit for people with OA and comorbidity, hence there is more

work to do in this area. The PA interventions led to mixed, mostly non-significant, small improvements in people with OA and; obesity (pain, function and QOL), T2DM (pain and function), and depression (QOL). PA interventions tailored to people with knee OA and multimorbidity, improved pain with statistical significance and function as measured by the WOMAC and 6MWT, but not SF-36 within the same study. Most of the evidence related to people with knee OA and obesity and the studies identified were heterogeneous in terms of; intervention components, outcome measurements and reporting, 'usual care' and control group types, countries, settings and populations.

More research is needed to determine the optimal PA for people with OA and comorbidity with secondary analyses and individual participant data meta-analysis of previous RCTs able to provide more evidence. This would then allow for a more informed analysis to determine whether certain aspects of the interventions are more efficacious in specific groups and in turn, may offer further insight into improving the care of people with OA and comorbidities. In conclusion, this systematic review has highlighted a dearth of evidence for the effectiveness of PA interventions for those with OA and comorbidities and highlighted areas for future research.

4.3.13 Chapter summary

This chapter described a systematic review that investigated the effectiveness of PA interventions on people with OA and comorbidity. There is a relative dearth of RCT evidence relating to OA and common comorbidity groups. It is still not certain what PA intervention components are optimal and for what specific comorbid patient subgroups. Uncertainty remains regarding the clinical effectiveness of PA for people with OA and comorbidity and further research focussed on OA and common comorbid populations is indicated. The subsequent chapter investigates the association between PA level and comorbidity in people with OA (chapter 5).

Chapter 5

Secondary data analysis study

Chapter 5. Comorbidity and physical activity levels in older adults with osteoarthritis: a secondary data analysis study

5.0 Introduction

This chapter is split into four parts. It begins with the research question, aim and objectives, followed by Part one, which describes the two trial datasets used within this second study of the thesis; The Benefits of Effective Exercise for knee Pain (BEEP) and The Management of OsteoArthritis In Consultations (MOSAICS) (Foster et al., 2014; Dziedzic et al., 2014). Following this, Part two of the chapter covers the analysis methods of the current study. Then, the chapter contains the results (Part three) and discussion (Part four).

5.0.1 Research question

Is comorbidity associated with PA levels in people with OA?

5.0.2 Aim and objectives

This secondary data analysis study aimed to examine the cross-sectional relationship between comorbidity and PA level in older adults with OA. Specifically, there were three individual objectives;

1. Is comorbidity presence associated with PA level?
2. Is comorbidity frequency associated with PA level?
3. Are different types of comorbidity associated with PA level?

5.1 Part 1. Introducing the datasets

Part one first provides a rationale for carrying out secondary analysis on the selected datasets, followed by an overview of the two datasets and the included participants. Key variables used to answer the study objectives are discussed, including how the data was prepared, cleaned and recoded. These steps are summarised in Figure 5.1.1.

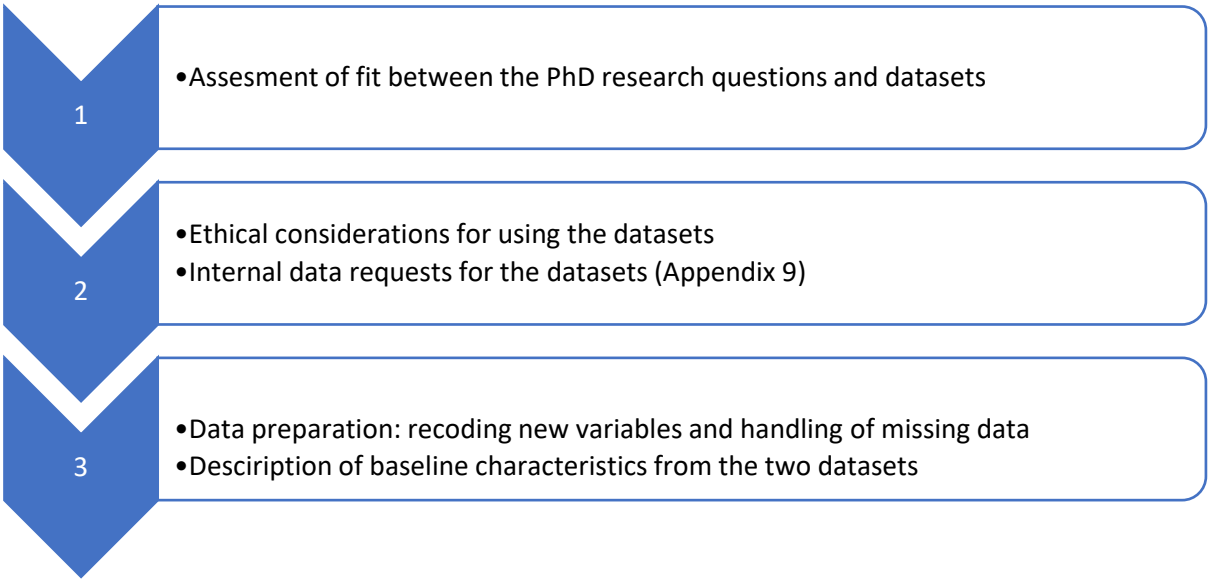


Figure 5.1.1 Preliminary stages of the secondary data analysis process

5.1.1. Rationale for choosing the BEEP and MOSAICS trial datasets

The two large RCT datasets were selected for quantitative secondary data analysis within this thesis because they contain appropriate data from the population of interest needed to address the research objectives. The two studies recruited adults with knee (BEEP), and peripheral joint pain attributed to OA (MOSAICS) and collected both PA and comorbidity data. In addition, the two study datasets included similar baseline socio-demographic and clinical measures including pain and function.

The BEEP dataset contained participant comorbidities collected via self-report. To identify the comorbidities of the participants within the MOSAICS cohort, a linked general practice Medical Record Review (MRR) using relevant health care condition Read codes was used. Using two separate datasets allowed for comparison of findings between different samples that include different OA phenotypes. Having the comorbidities measured in two different ways within the two datasets also allowed for the findings to be compared between recording methods. Also, the large number of participants in the datasets made them suitable for multivariable model building.

5.1.1.2 Ethical considerations

All participants signed a consent form which allowed for secondary use of the data. Following adequate ethical consideration, a formal internal data request was completed for both datasets, followed by approval from the study data custodians (Appendix 9).

5.1.2 BEEP trial dataset

The BEEP trial was a multicentre, pragmatic, parallel-group individually RCT of three exercise interventions undertaken between 2009 and 2014 (Foster et al., 2014 (full RCT report to be published) see Hay et al. (2018) for the NIHR grant report). The BEEP trial included 514 adults with pain or stiffness attributed to OA in one or both knees. The participants were recruited from 65 general practices in England and were identified in three ways; (1) examining medical records to identify patients consulting for knee pain in the previous 12 months, (2) conducting a population survey for older adults (aged 45 years and over) registered with participating GPs, which included the chronic pain grade scale to identify participants who had a chronic pain grade of 2-4 for recruitment, to ensure those participants had a mean level of pain and functional difficulty similar to those recruited by (3) identifying patients referred to physiotherapy from general practice for knee pain (Hay et al., 2018). The primary objective of the RCT was to test whether pain and function outcomes could be improved through changing characteristics of PA programmes in comparison to usual physiotherapy (PT) care in older adults with knee OA. The BEEP trial primary outcomes were self-report pain and physical function (WOMAC) (Bellamy et al., 1988).

5.1.2.1 Participant inclusion / exclusion criteria

To be eligible to participate in the BEEP trial, participants were required to be 45 years and older, with current knee pain and / or stiffness (i.e. a clinical diagnosis of OA) and chronic pain grade severity 2-4. Exclusion criteria were serious pathology (e.g. inflammatory arthritis or malignancy), history of hip or knee replacements or being on a waiting list for joint replacement, pain due to recent trauma, knee

joint injection in the previous three months or being unable to access physiotherapy treatment centres.

5.1.3 MOSAICS trial dataset

The MOSAICS study was a mixed methods study with a nested cluster RCT, undertaken between 2011 and 2013, of which this thesis used baseline data from the RCT and MRR data from Part three (Dziedzic et al., 2014);

1. A cluster RCT
2. A population survey
3. A consultation survey and MRR
4. An evaluation of the intervention and training

The primary aim of the MOSAICS RCT was to determine the clinical and cost-effectiveness of a model OA consultation (MOAC – implementing the core recommendations from NICE OA guidelines in primary care). 525 participants consented to take part, had MRR data available and were used for the current analysis. The MOSAIC trial primary outcome measure was general physical health (SF-12 PCS) (Ware et al., 1996).

5.1.3.1 Participant inclusion / exclusion criteria

To be eligible to participate in the MOSAICS trial, participants were required to be; 45 years and older, with current self-reported joint pain and / or stiffness (in the knee, hip, hand or foot), registered with a MOSAICS study practice in England, and to have completed the MOSAICS patient population survey. Exclusion criteria were screened by general practitioners including; a history of serious disease (malignancy or terminal illness), resident in a care or nursing home, inflammatory arthritis, or those who could not access their GP.

5.1.4 BEEP and MOSAICS variables used in this thesis

Baseline data from those participating in the BEEP RCT and MOSAICS RCT who also completed the consultation survey were included in this study. Table 5.1.1. displays the variables from the datasets considered for the analyses in chapter 5 Part 2.

Table 5.1.1 BEEP and MOSAICS baseline variables considered for analysis within this thesis

Variable name	Data type	Additional variable detail (BEEP)	Additional variable detail (MOSAICS)
Participant demographics			
Age	Continuous	Years	Years
Gender	Dichotomous	Female / male	Female / male
Body Mass Index	Continuous	Calculated from height (centimetres) and weight (kilograms)	Calculated from height (centimetres) and weight (kilograms)
Partner status	Categorical	Self-reported partner category (Married /separated /divorced /widowed /cohabiting /single)	Self-reported partner category (Married /separated /divorced /widowed /cohabiting /single)
Employment status	Dichotomous	Employed yes / no	Employed yes / no (retired /no categorised as no)
Clinical measures			
Anxiety	Continuous	GAD 7 0-21 (21=worst anxiety)	GAD 7 0-21 (21=worst anxiety)
Quality of life	Continuous	EQ-5D-3L -0.59-1 (1=better QOL)	EQ-5D-3L -0.59-1 (1=better QOL)
Physical & mental health	Continuous	N/A	SF12 V2 0-100 (100=better health)
OA measures			
Pain	Continuous	WOMAC 0-20 (20= worst pain)	0-10 (10=worst pain) (Pain intensity numerical rating scale)
Function	Continuous	WOMAC 0-68 (68=worst function)	WOMAC SF-PF 0-32 (32=worst function)
PA measure			
PA	Continuous	PASE 0-400+ (400+=higher PA level)	PASE 0-400+ (400+=higher PA level)
Comorbidity			
Comorbidity type	Dichotomous	Self-report of key comorbidities; • High blood pressure • Angina • Heart failure • Stroke • Heart attack • Depression • T2DM • Asthma	MRR to identify comorbidities; • Hypertension (including hypertension, high blood pressure) • CVD (including angina, heart failure, stroke, heart attack, heart disease) • Depression • T2DM • Asthma (including asthma, COPD, bronchitis) • Osteoporosis

- Bronchitis
- Osteoporosis
- Obesity

BEEP=Benefits of Effective Exercise for knee Pain; MOSAICS=the Management of Osteoarthritis In Consultations; OA=Osteoarthritis; PA=Physical Activity; PASE=Physical Activity Scale for the Elderly; T2DM=Type 2 Diabetes Mellitus; CVD=Cardiovascular Disease; COPD=Chronic Obstructive Pulmonary Disease; WOMAC=Western Ontario and McMaster Universities Arthritis Index; WOMAC SF-PF=Western Ontario and McMaster Universities Arthritis Index Short Form Physical Function; GAD 7=Generalized Anxiety Disorder 7; EQ-5D-3L=Euro Quality Of Life 5 Dimensions 3 Levels; SF12 V2=Short Form Version 12; PF=Physical Function; MRR=Medical Record Review; N/A=Not Applicable.

5.1.5. Variables used in the analysis

5.1.5.1 Comorbidity

Comorbidity was the primary independent variable of interest for this study. Comorbidity was captured through self-report (BEEP) and MRR (MOSAICS). To have consistency across the two datasets for future comparison, the comorbidities captured in BEEP were grouped to closely resemble those identified by the Read codes search in MOSAICS.

MRR is a method for identifying patients through electronic screening. "*Read code searches"* are pre-designed lists to most effectively capture specific comorbidities which may have synonyms or be recorded using different terms and Read codes within medical records. Read codes are the standard clinical terminology system that UK GPs use to identify patient's clinical symptoms and diagnoses. The Read code searches for the current study were derived from recent Keele University publications (e.g. Barnett et al., 2017) and all were compiled with the consensus of at least two primary care researchers who were also GP clinicians. Appendix 10 shows an example of the depression Read codes used in a MRR following a consensus exercise at Keele Versus Arthritis Primary Care Centre for The Consultations in Primary Care Archive (CiPCA) (Burton et al., 2013).

The individual comorbidities from the two datasets were originally collapsed into seven category types; high blood pressure (hypertension, high blood pressure), CVD (angina, heart failure, stroke, heart attack), depression, T2DM, respiratory (asthma, bronchitis, COPD) and osteoporosis. Obesity was calculated from BMI (calculated using height and weight (Kg/M^2)) and used as a dichotomous variable (obese (BMI≥30) yes / no).

5.1.5.2 Physical activity

PA level was measured by the self-report Physical Activity Scale for the Elderly (PASE) in both trial datasets (Washburn et al., 1993) and was the outcome of interest (dependent variable) in this study. Appendix 11 provides detail of the items included within the PASE and a description of the scale scoring instructions. The scale measures leisure, household and occupational PA with weighting specific to the

frequency and duration of each activity carried out over the previous week. The PASE scale gives a continuous score (0 to 793), with higher scores indicating higher PA levels. However, the PASE scale does not equate to minutes spent in intensity zones of PA or activity levels related to the PA guidelines (Washburn et al*.,* 1993). The PASE has shown strong validity and reliability useful for large epidemiological and intervention studies on the general population (Washburn et al*.,* 1993). Its use has been validated in hip OA with a standard error of measurement (SEM) of 31, retest reliability (ICC=0.77), and moderate correlation with other self-report PA scales such as the International Physical Activity Questionnaire (IPAQ) (r=0.61) (Svege et al., 2012). Washburn et al. (1999) further validated the PASE as a measure of PA suitable for use on the association between PA, health and physical function in older adults. The PASE tool has been shown to have a moderate correlation with other PA measures such as the 6MWT (r=0.35) and knee strength (r=0.41) in adults with knee pain (Martin et al., 1999; Prince et al., 2008).

5.1.5.3 Socio-demographics

Both the BEEP and MOSAICS trials datasets included several socio-demographic variables of interest to this thesis, including; age, gender and partner status (see Table 5.1.1).

5.1.5.4 Clinical variables

The clinical variables considered for the analysis included pain (as measured by the WOMAC pain subscale: 0-20 (BEEP), 0-10 (MOSAICS)), function (WOMAC function subscale: 0-68 (BEEP), 0-32 (MOSAICS)) (Bellamy et al., 1988), anxiety (Generalised Anxiety Disorder (GAD 7) (Spitzer et al., 2006)), QOL (Euro Quality Of Life-5 dimensions-3L (EQ-5D-3L) (EuroQol group, 1990) and general well-being (Short Form12 (SF12)) (Vilagut et al., 2008). These measures are widely used in OA clinical research, have shown to be reliable and valid (Spitzer et al*.,* 2006; Salaffi et al*.,* 2003; Bilbao et al*.,* 2017; Hawker et al., 2008) and may confound the association between comorbidity and PA (see Table 5.1.1 for further scale detail). Confounding in this context is the effect of uncontrolled variables that could distort or make a false result of association between comorbidity and PA (Skelly et al., 2012).

5.1.6 Variable recoding

Comorbidity variables were recoded into new variables to answer the three research objectives for this study. These were “comorbidity presence”, which categorised participants into either having or not having any of the five comorbidity category types (respiratory, CVD, depression, T2DM, obesity); “comorbidity frequency”, which counted the number of comorbidity types each individual participant had (0, 1, 2, 3+ (the frequency of four and five comorbidities were too small to use in separate analyses, therefore a 3+ category was formed) and “comorbidity type” (presence or not of respiratory, CVD, depression, T2DM or obesity comorbidity). At this stage, osteoporosis and hypertension were removed as individual comorbidity types, with five remaining comorbidity types included in analyses. Further detail of how comorbidity was coded into variables and the data informing the selection of comorbidity types can be found in Appendix 12.

A six-category “relationship status” variable was recoded to become a dichotomous variable. Those who were separated, divorced, widowed or single were coded as ‘no partner’ and those married, or cohabiting were categorised as ‘yes partner’.

5.1.7 Data preparation

This section focusses on the preparation of data for statistical analyses, including the handling of missing data and data analyses methods for each research objective.

5.1.7.1 Data cleaning

Data cleaning involved examining the properties of the variables and the way they were coded (nominal, ordinal, interval / ratio), including frequency distributions, e.g. histograms, frequency tables, mean, variance), and handling outliers and unexpected data (coding as missing). Following this, the data was prepared coding missing data and deciding on how to deal with missing values (case removed from analysis).

5.1.7.2 Missing data

ROB due to missing data depends on the amount of missing data as well as the reasons for the missing data (Taris, 2000). Comparing the participants with complete data and those with any missing revealed closely matched values for most variables (Table 5.1.2 and 5.1.3). For example, in BEEP, the mean GAD 7 was 3.3 for participants with complete data and those with incomplete data, and the mean BMI for participants with complete data was 29.7, compared with 29.3 in those with any missing data. However, in both datasets, the presence of any missing data was more likely in older participants, females and those without a partner. Complete case analysis was used in this study (Sterne et al., 2009). The level of missing data was relatively low in both datasets for other independent (<10%) and dependent (<20%) variables.

Table 5.1.2 Missing data across independent and dependent variables

Dataset	Total missing data	Age	Gender	Partner	WOMAC function	GAD 7	PASE
BEEP	124 (24%)	0	0	50 (8%)	10 (2%)	17 (3%)	51 (10%)
MOSAICS	136 (26%)	7 (1%)	0	2 (<1%)	9 (2%)	21 (4%)	93 (18%)

Total sample size: BEEP 514; MOSAICS 525
All values are number (% proportion of dataset sample); BEEP=Benefits of Effective Exercise for knee Pain; MOSAICS=the Management of Osteoarthritis In Consultations; PASE=Physical Activity Scale for the Elderly; WOMAC=Western Ontario and McMaster Universities Arthritis Index; GAD 7=Generalized Anxiety Disorder 7

Table 5.1.3 Descriptive data comparing participants with a) complete data and b) any missing data

Variable		BEEP		MOSAICS	
		Complete data N=390	Any missing N=124	Complete data N=389	Any missing N=136
Age	Mean	61.7	66.4	66.4	70.3
Female gender	N %	185 (47.4)	77 (62.1)	222 (57.1)	91 (66.9)
YES partner	N %	336 (86.2)	59 (79.7)	285 (73.3)	88 (65.7)
WOMAC	Mean	27.7	29.4	11.8	13.5
GAD 7	Mean	3.3	3.3	3.4	3.8
BMI	Mean	29.7	29.3	28.4	27.7
Comorbidity presence	N %	251 (64.4)	73 (58.9)	209 (53.7)	62 (46.6)
Respiratory	N %	68 (17.4)	20 (16.1)	39 (10.0)	16 (11.8)
CVD	N %	39 (10.0)	17 (13.7)	51 (13.1)	14 (10.3)
Depression	N %	85 (21.8)	29 (23.4)	28 (7.2)	10 (7.4)
T2DM	N %	46 (11.8)	20 (16.1)	52 (13.4)	14 (10.3)
Obesity	N %	142 (38.2)	42 (33.9)	128 (32.9)	34 (25.4)
PASE	Mean	176.9	177.2	144.0	130.7

Results are values as number (N) and percent (%) or Mean.

BEEP=Benefits of Effective Exercise for knee Pain; MOSAICS=the Management of Osteoarthritis In Consultations Study; OA=Osteoarthritis; PA=Physical Activity; PASE=Physical Activity Scale for the Elderly: 0-400+ (higher number=higher PA level); WOMAC=Western Ontario and McMaster Universities Arthritis Index: BEEP 0-68/ MOSAICS 0-32 (higher=worse function); GAD 7=Generalized Anxiety Disorder 7: 0-21 (21=worst anxiety); BMI=Body Mass Index; CVD=Cardiovascular Disease; T2DM=Type Two Diabetes Mellitus; N=Number

5.1.8 Variable selection for each objective

Variables were selected to investigate the association between comorbidity (presence, frequency and type) and PA levels in both BEEP and MOSAICS datasets. The dependent variable for all three objectives was PA level (PASE). The independent variable of interest was different for each objective; objective 1) comorbidity presence, objective 2) comorbidity frequency (0, 1, 2, 3+) and objective 3) comorbidity type as the independent variable. The potential confounding variables included age, gender, partner status, pain, function, anxiety and QOL.

5.2 Part 2. Secondary data analysis methods

This section describes the secondary analysis methods carried out separately on both the BEEP and MOSAICS datasets (Figure 5.2.1). All data analyses for this study were carried out using SPSS version 24 (IBM Corp. Released 2016. IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp).

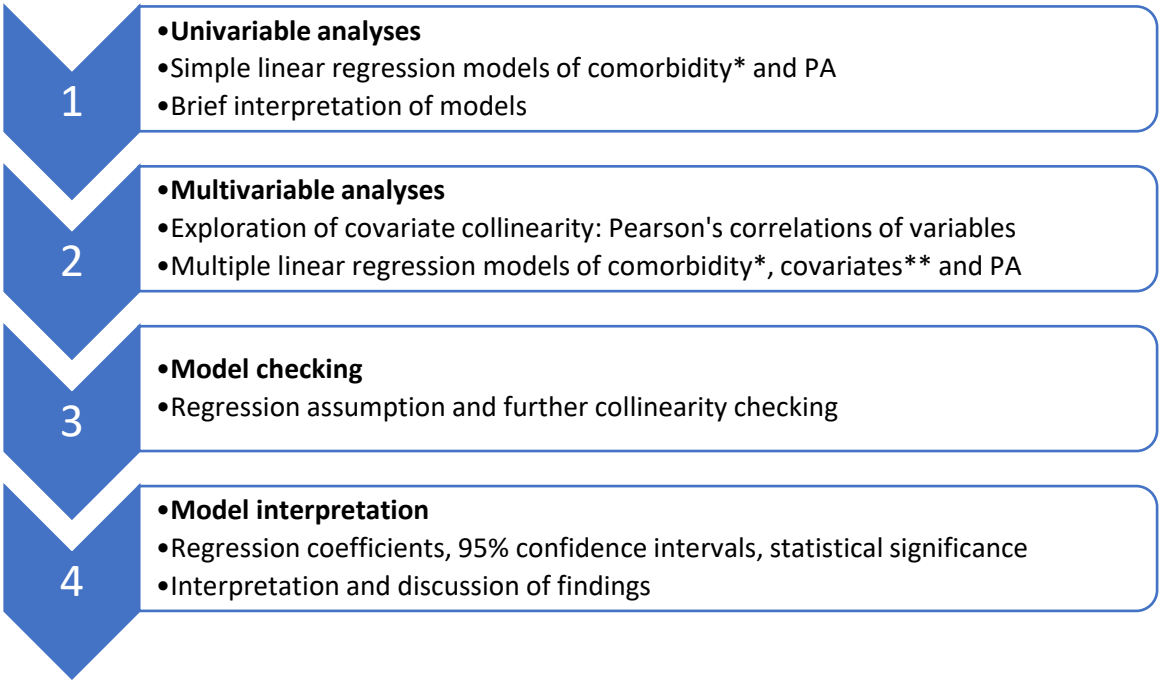


Figure 5.2.1 Stages of analysis

**Carried out for each of the three objectives using a different independent variable; objective: 1) comorbidity presence, 2) comorbidity frequency and 3) comorbidity type; **demographic: age, gender, partner; clinical: GAD 7 and WOMAC physical function. PA=Physical Activity*

5.2.1 Univariable analyses

Univariable analyses (unadjusted) allow an initial crude exploration of the relationship between the independent and dependent variables to demonstrate any associations (Szklo and Nieto, 2014). However, unadjusted analyses are at risk of confounding. By conducting unadjusted analyses, it is possible to subsequently compare unadjusted and adjusted models to understand the impact of confounding variables on the relationship between the independent and dependent variables (Katz, 2003). Table 5.2.1. describes the variables included in the unadjusted analyses.

Table 5.2.1 Variables included in the unadjusted analyses

Variable	Variable detail	Reference category / scale range
Independent		
Comorbidity presence	Dichotomous comorbidity presence (yes / no)	Reference: no comorbidity
Comorbidity frequency	Categorised comorbidity frequency: 0, 1, 2, 3 or more comorbidities	Reference: no comorbidity
Comorbidity type	Dichotomous comorbidity presence of Respiratory, CVD, T2DM, Depression, Obesity	Reference: no presence of the specified comorbidity
Dependent		
PASE	Continuous Physical Activity Scale for the Elderly	0-400+ (higher=higher PA level)
Socio-demographic		
Age	Continuous years	
Gender	Dichotomous (Male / female)	Reference: 0 male, 1 female
Partner	Dichotomous (Partner / no partner)	Reference: 0 no partner
Clinical variables		
GAD 7 anxiety	Continuous Generalised Anxiety Disorder	0-21 (higher=worse anxiety)
WOMAC PF	Continuous Western Ontario and McMaster Osteoarthritis Index	0-(32/68) (higher=worse function)

PA= Physical Activity; PASE=Physical Activity Scale for the Elderly; WOMAC=Western Ontario and McMaster Universities Arthritis Index; PF=Physical Function; GAD 7=Generalized Anxiety Disorder 7; CVD=Cardiovascular Disease; T2DM=Type Two Diabetes Mellitus

Simple linear regression is described as a mathematical equation (Marill, 2004);

$$Y = \beta_o + \beta_1 X_1 + e$$

'Y' is the observed dependent variable, β_o and β_1 are the regression coefficients, X is the independent variable and e is the error term. From this equation, the regression coefficients and error terms are estimated. The predicted value of Y takes the estimated value, β_o when X=0, while the estimated value of β_1 shows the slope and direction of the relationship (Marill, 2004).

For this analysis, the Y value represents the increase in PASE per one unit increase in X, the independent variable, comorbidity. For the dichotomous comorbidity variables, this was simply either 'no comorbidity' or one unit increase to 'yes comorbidity'. The regression beta coefficients show the strength and direction of the association between comorbidity and PASE score. A negative beta score

indicates an inverse relationship per unit increase in independent X with outcome Y. The association between the two variables was statistically significant if $p<0.05$.

In order to carry out linear regression modelling, the data was checked for assumptions of linear regression (Marill, 2004);

1. The dependent variable must be interval.
2. The relationship between the independent and dependent variables must be linear. This was checked with scatter plots of the independent variables against the dependent variable, which was also used to visually inspect outliers in the data.
3. The independent and dependent variables have normal distribution. This was checked through histograms and P-P plots. Visual inspection can determine a bell-shaped curve with vertically split symmetry.
4. There is little to no collinearity between independent variables. If independent variables within a regression analysis are highly correlated with each other, they may interact and alter the model outputs (Tu et al*.,* 2005). This was first assessed with all independent variables computed into a correlation matrix. Scanning the correlation matrix for any high pairwise correlations with other independent variables (Pearson's correlations ($r>0.7$) provides a warning of collinearity. Removal of one of the variables of those pairs highly correlated was the first step. Secondly, checking the Variance Inflation Factor (VIF) confirms low collinearity within the analysis (with results <10).
5. No autocorrelation in the data to ensure the residuals are independent of one another and are normally distributed. This was tested through the Durbin-Watson test. Durbin-Watson results closer to a value of 2 are best (<1 or >3 may indicate autocorrelation).
6. The data is homoscedastic. Homoscedasticity refers to the variance of the residuals being equal or constant. This was checked through a scatterplot of residuals against the predicted

values. Visual inspection was used to determine randomly distributed, evenly spread residuals (no funnel / linear relationships).

To calculate precise estimates of independent variable regression coefficients from linear regression models, an adequate sample size is required. There is a lack of consensus in the literature regarding the minimum number of cases (participant data) required per variable (e.g. PASE). For example, some authors suggest a minimum of two cases per variable would still guarantee accurate and unbiased coefficients (Austin and Steyerberg, 2015), whilst others suggest 10 (Harrell, 2015) or more (Schmidt, 1971). For this analysis, a minimum of 10 cases per independent variable (e.g. depression comorbidity) was chosen because it would make good estimates of the associations (Babyak, 2004).

5.2.2 Multivariable (adjusted) analyses

Multiple linear regression output provides information regarding the magnitude and direction of an association between two variables (β coefficient) and its statistical significance (p value) while controlling for all other independent variables (Katz, 2003). Multiple linear regression was used to investigate the association between comorbidity presence / frequency / type and PASE score while controlling for the confounding effects of socio-demographic and clinical variables or covariates (age, gender, partner, physical function and anxiety) (Nimon and Oswald, 2013; Field, 2013).

Multivariable (using more than one independent variable) analyses were carried out using multiple linear regression, denoted by the equation below:

$$Y = \beta_o + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 \ldots + e$$

'Y' is the dependent variable (PASE) and β_o is the intercept (if the independent variable (comorbidity), X=0), e is the error term, and the β values indicate the regression slope and direction while also controlling for multiple other independent variables ($\beta_1 X_1 + \beta_2 X_2 \ldots$).

5.2.3 Model building

Model building methods were carried out separately for both datasets and were repeated for each of the three objectives, with different comorbidity variables as the primary independent variable (see Table 5.2.2.). For each objective, the relevant comorbidity independent variable was first entered into the model followed by simultaneously entering all remaining independent variables (age, gender, partner, physical function, anxiety) which were selected a-priori. The dependent variable (outcome) in all models was PA (PASE). Results for each objective are presented as; beta-coefficient (lower, upper 95% CI limits).

The first step in the multivariable analyses was to explore all pairs of the independent variables for collinearity within the model using Pearson's correlations (Tu et al., 2005) (see Figure 5.2.1.). For example, the EQ-5D-3L measure of QOL was highly correlated with many other variables (e.g. WOMAC physical function r=0.664; SF12 r=0.639; SF physical r=0.591) and considered less clinically important, hence was not included in the model. WOMAC pain and WOMAC function were highly correlated in the BEEP dataset (r=0.798). Both measures are clinically important, however, MOSAICS only measured WOMAC function data. Therefore, to keep similar covariates in both datasets, the EQ-5D-3L and WOMAC pain were removed from the analyses. Further detail on this process is detailed in Appendix 13.

Table 5.2.2 An overview of the final models repeated throughout the analyses

Objective	Model	Variable	Reference
1. Comorbidity presence	1	Yes comorbidity	No comorbidity
2. Comorbidity frequency	2	1 comorbidity	No comorbidity
	3	2 comorbidities	No comorbidity
	4	3+ comorbidities	No comorbidity
3. Comorbidity type	5	Yes Respiratory	No Respiratory
	6	Yes CVD	No CVD
	7	Yes T2DM	No T2DM
	8	Yes Depression	No Depression
	9	Yes Obesity	No Obesity

9 univariable (unadjusted) models, executed for BEEP and MOSAICS separately (9x2) and repeated as 9 multivariable models (including the other covariates: age, gender, partner, anxiety and physical function) for BEEP and MOSAICS separately (18x2). Total models = 36. CVD=Cardiovascular Disease; T2DM=Type Two Diabetes Mellitus

5.2.4 Model checking

Once the final models were built, model assumption, further collinearity and specification checks, such as VIF (<10) were carried out (see assumptions list above) (Tu et al*.,* 2005). Further detail and example model assumption checking can be seen in Appendix 14.

5.3 Results

5.3.1 Introduction

This section presents the results of the quantitative secondary data analysis of BEEP and MOSAICS trials. First, descriptive statistics for the independent and dependent variables are provided for the separate datasets. The results are then presented by objective split by dataset. Where possible, tables present the results of both dataset analyses side-by-side to facilitate comparisons of associations between datasets. Unadjusted associations between independent and dependent variables for each of the 3 objectives are presented together with the adjusted multivariable models.

5.3.2 Participant characteristics

Descriptive statistics (frequency, percentage, mean and SD) for the independent and dependent variables are presented in Table 5.3.1.

Table 5.3.1 Summary of participants characteristics from the BEEP and MOSAICS trials

Characteristic	BEEP	MOSAICS
Total number	514	525
Age (years)	62.9 ± 9.8	67.3 ± 10.5
Gender (male)	252 (49.0%)	212 (40.4%)
Partner (yes)	395 (76.8%)	373 (71.0%)
GAD 7 score	3.3 ± 4.6	3.5 ± 4.7
WOMAC Function score#	28.1 ± 12.3	12.2 ± 7.3
Comorbidity presence	324 (63%)	271 (51.6%)
Respiratory	88 (17.2%)	55 (10.5%)
CVD	56 (10.9%)	65 (12.4%)
Depression	114 (22.2%)	38 (7.2%)
T2DM	66 (12.8%)	66 (12.6%)
Obesity	191 (37.2%)	162 (30.9%)
BMI	29.6 ± 5.7	28.3 ± 5.0
Underweight / normal	97 (18.9%)	135 (25.7%)
Overweight	209 (40.7%)	206 (39.2%)
Obese	191 (37.2%)	162 (30.9%)
One comorbidity	189 (36.8%)	184 (35%)
Two comorbidities	98 (19.1%)	67 (12.8%)

3+ comorbidities	37 (7.2%)	20 (3.8%)
PASE	176.9 ± 83.5	142.7 ± 80.3

All values are mean and standard deviation (±) or number and percentage (%).

BEEP=Benefits of Effective Exercise for knee Pain; MOSAICS=the Management of Osteoarthritis In Consultations Study; OA=Osteoarthritis; CVD=Cardiovascular Disease; T2DM= Type Two Diabetes Mellitus; PA=Physical Activity; PASE=PA Scale for the Elderly: 0-400+ (higher number = higher PA level); WOMAC=Western Ontario and McMaster Universities Arthritis Index: #BEEP 0-68 / MOSAICS 0-32 (higher = worse function); GAD 7=Generalized Anxiety Disorder 7: 0-21 (21 = worst anxiety); BMI=Body Mass Index; Underweight / normal (<25), overweight (25-29.9), obese (BMI ≥30)

5.3.2.1 BEEP participant characteristics

Of the 514 participants recruited for the BEEP study, there was a similar mix of gender proportions (49% male), mean age was 62.9±9.8 and most participants were overweight or obese (41% and 37%; in each BMI category respectively) with a mean BMI of 29.6±5.7. Most of the sample had comorbidity (63%); 37% of the population reported having one comorbidity; 19% reported having two, and 7% reported having three or more. The most common comorbidity type was obesity (37%) followed by depression (22%), respiratory (17%), T2DM (13%) and CVD (11%). Mean PASE score for the sample was 176.9±83.5.

5.3.2.2 MOSAICS participant characteristics

Of the 525 MOSAICS study participants, 40% were male with a mean age of 67.3±10.5 and most were overweight or obese (39%, 31%; respectively) with a mean BMI of 28.3±4.9. Just over half the participants (52%) had comorbidity, with 35% of participants having one comorbidity, followed by 13% having two comorbidities and 4% having three or more. The most common comorbidity was obesity (31%), followed by T2DM (13%), CVD (12%), respiratory (11%) and depression (7%). The mean PASE score for the sample was 142.7±80.3.

5.3.3 Differences between the datasets

The BEEP and MOSAICS trials had a similar number of participants, with a similar mean BMI, although MOSAICS participants were of slightly older mean age. BEEP had slightly more males and had a slightly higher mean PASE score than MOSAICS (Table 5.3.1.). BEEP had 11% more participants reporting the

presence of comorbidity (63% compared to 52%). The frequency of comorbidity across both datasets can be seen in Figure 5.3.1. The most common comorbidity was obesity in both datasets. The proportion of participants with individual comorbidity types was similar between datasets except for depression which was reported in almost a quarter of BEEP participants (22%), compared with 7% in MOSAICS (Figure 5.3.2).

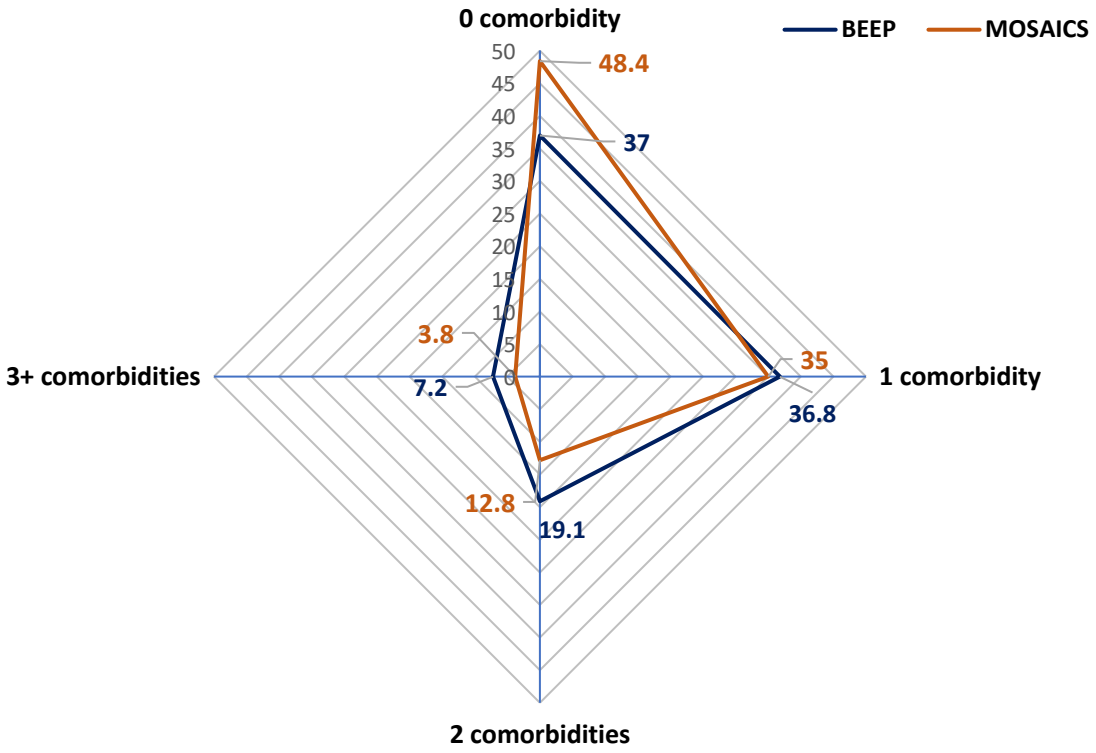


Figure 5.3.1 Proportion (%) of the BEEP and MOSAICS trial participants with different comorbidity frequencies (0, 1, 2, 3+)

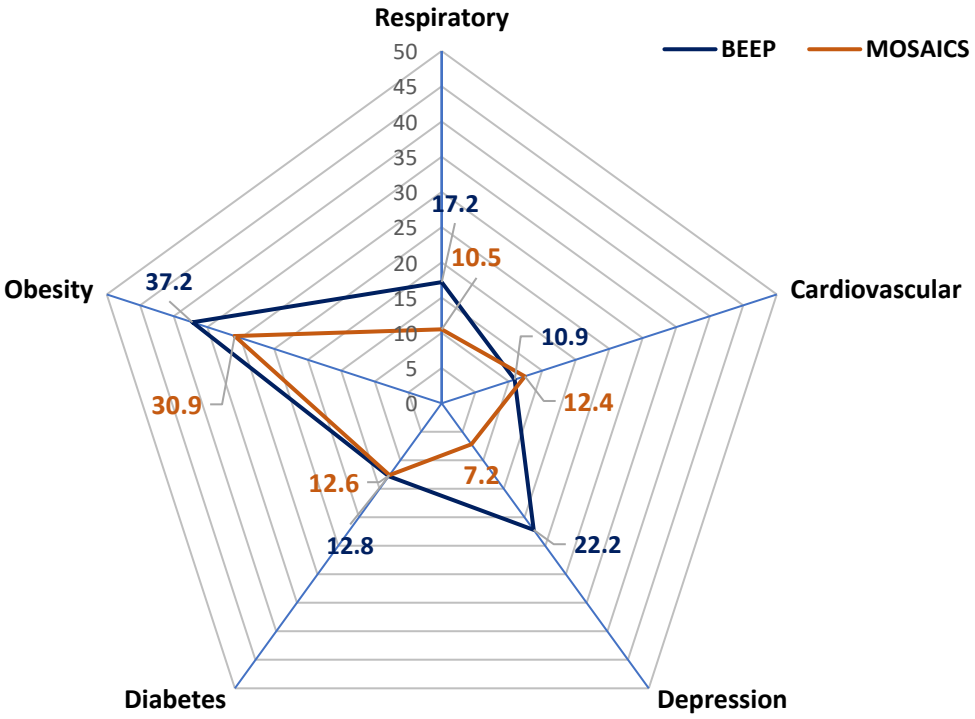


Figure 5.3.2 Proportion (%) of the BEEP and MOSAICS trial participants with different comorbidity types

5.3.4 Objective 1: Is comorbidity presence associated with physical activity level.

Table 5.3.2 shows both unadjusted and adjusted associations between comorbidity presence and PA. Unadjusted comorbidity presence was significantly associated with a decrease in PASE score in BEEP β=−27.93 (−44.10, −11.75) and MOSAICS β =−20.86 (−36.02, −5.70).

After adjusting for covariates (age, gender, partner status, WOMAC function and GAD 7), comorbidity presence remained significantly associated with a decrease in PASE score in BEEP β=−32.25 (−48.57, −15.93) and the strength of association increased. In MOSAICS, however, the association between comorbidity presence and PASE score attenuated after adjustment and was no longer statistically significant β=−6.50 (−21.11, 8.11). Increasing age and female gender were significantly associated with lower PASE score in both datasets. In the BEEP dataset having a partner was associated with an increased PASE score. In the MOSAICS dataset, worse function (WOMAC) and worse anxiety (GAD 7) were associated with lower PASE score.

Table 5.3.2 Objective 1: Unadjusted and adjusted models for BEEP and MOSAICS comorbidity presence and PASE score

		BEEP				MOSAICS			
	Independent variable	**(N)**	**β coefficient**	**95% CI**		**(N)**	**β coefficient**	**95% CI**	
				Lower	**Upper**			**Lower**	**Upper**
Unadjusted	Comorbidity presence	445	-27.93*	-44.10	-11.75	429	-20.86*	-36.02	-5.70
Adjusted	Comorbidity presence	390	-32.25*	-48.57	-15.93	405	-6.50	-21.11	8.11
	Age		-2.49*	-3.36	-1.63		-2.48*	-3.20	-1.76
	Gender(female)		-18.59*	-34.21	-2.97		-25.32*	-39.57	-11.06
	Partner (yes)		30.22*	7.73	52.70		14.89	-1.54	31.31
	WOMAC function#		-.24	-.92	.43		-1.58*	-2.69	-.46
	GAD 7		-1.57	-3.34	.21		-2.08*	-3.75	-.41

Unadjusted and adjusted models for objective 1 in the BEEP and MOSAICS datasets.
**denotes statistically significant at p<0.05.*
Footnotes: *complete case data, multiple linear regression adjusted for age, gender, partner, WOMAC function and GAD 7. β coefficient represents mean change in PASE score. Higher PASE scores indicate higher levels of PA. Age (increase in one year); Gender (reference: male); Partner (reference: no partner); Higher WOMAC function indicates worse function (one increase unit in WOMAC function score, # BEEP 0-68 / MOSAICS 0-32); Higher GAD 7 indicates worse anxiety (one increase unit in GAD 7 score, 0-21).*
Abbreviations: *CVD=Cardiovascular Disease; T2DM=Type Two Diabetes Mellitus; N=Number; β=unstandardized beta coefficient; CI=Confidence Interval; WOMAC=Western Ontario and McMaster Osteoarthritis Index; GAD 7=Generalised Anxiety Disorder Questionnaire*

5.3.5 Objective 2: Is comorbidity frequency associated with physical activity level.

Table 5.3.3 shows the unadjusted and adjusted associations between comorbidity frequency and PA. In the unadjusted BEEP model, each additional comorbidity was significantly associated with a lower PASE score; one comorbidity β= -19.85 (-38.11, -1.59), two comorbidities β= -32.72 (-53.91, -11.52), and three or more comorbidities β= -52.68 (-83.42, -21.94) compared to those with no comorbidity. After adjusting for confounding variables, comorbidity frequency remained significant and grew in association with lower PASE scores across all frequencies of comorbidity; one comorbidity β= -24.42 (-42.45, -6.38); two comorbidities β= -34.76 (-56.05, -13.48) and three or more comorbidities β= -73.71 (-106.84, -40.58).

In the unadjusted models for MOSAICS, having one comorbidity was not significantly associated with PASE score; β= -8.51 (-25.11, 8.08) compared to no comorbidity. However, having two comorbidities β=-45.06 (-68.45, -21.66) and three or more comorbidities β= -52.25 (-91.39, -13.11) were significantly associated with an incremental decrease in PASE scores compared to no comorbidity. In adjusted analyses associations attenuated. Having one comorbidity remained non-significant β= 1.39 (-14.30, 17.08). However, the presence of two comorbidities remained significantly associated with a decrease in PASE score β= -26.84 (-49.30, -4.38). Having three or more comorbidities was no longer significantly associated with PASE score β= -24.70 (-62.15, 12.76).

Table 5.3.3 Objective 2: Unadjusted and adjusted models for BEEP and MOSAICS comorbidity frequency and PASE score

		BEEP				MOSAICS			
	Independent variable	**(N)**	**β coefficient**	**95% CI**		**(N)**	**β coefficient**	**95% CI**	
				Lower	**Upper**			**Lower**	**Upper**
Unadjusted	1 comorbidity	445	-19.85*	-38.11	-1.59	429	-8.51	-25.11	8.08
	2 comorbidities	445	-32.72*	-53.91	-11.52	429	-45.06*	-68.45	-21.66
	3+ comorbidities	445	-52.68*	-83.42	-21.94	429	-52.25*	-91.39	-13.11
Adjusted	1 comorbidity	390	-24.42*	-42.45	-6.38	405	1.39	-14.30	17.08
	2 comorbidities	390	-34.76*	-56.05	-13.48	405	-26.84*	-49.30	-4.38
	3+ comorbidities	390	-73.71*	-106.84	-40.58	405	-24.70	-62.15	12.76

PASE score for each comorbidity category variable (reference 0 comorbidity).
**denotes statistically significant at p<0.05.*
Footnotes: *complete case data, multiple linear regression adjusted models adjusted for age, gender, partner, WOMAC and GAD 7. β coefficient represents a change in PASE score. Higher PASE scores indicate higher levels of PA.*
Abbreviations: *N=Number; β=unstandardized beta coefficient; CI=Confidence Interval*

5.3.6 Objective 3: Is comorbidity type associated with physical activity level.

Table 5.3.4 shows the unadjusted and adjusted associations between comorbidity type and PA. In the unadjusted BEEP model, respiratory, T2DM and obesity comorbidities were all significantly associated with a decrease in PASE score. Respiratory comorbidity had the strongest association with lower PASE scores β= -40.11 (-60.07, -20.14), followed by T2DM β= -26.68 (-48.82, -4.55) and obesity β= -25.78 (-41.06, -9.50). CVD comorbidity; β= -25.75 (-48.04, 0.54), and depression comorbidity; β= 3.12 (-15.53, 21.76) were not significantly associated with PASE score.

Respiratory β= -40.6 (-60.5, -20.35), T2DM β= -30.19 (-54.25, -6.12) and obesity comorbidities β= -27.72 (-44.08, -11.36) remained associated with lower PASE score in the adjusted models (Table 5.3.4) and CVD comorbidity was now significant β= -27.15 (-53.25, -1.05). Depression comorbidity remained non-significant β= -4.93 (-23.62, 13.76).

In MOSAICS, the unadjusted models showed CVD β= -43.00 (-65.08, -20.91) and T2DM comorbidities β= -34.42 (-56.64, -12.20) were significantly associated with a decrease in PASE score. Respiratory and depression comorbidities were non-significantly associated with PASE scores, but estimates suggest a negative association trend; β= -22.43 (-46.98, 2.12), β= -23.24 (-53.06, 6.58); respectively. Obesity comorbidity had the smallest magnitude of association and was non-significant; β= -7.62 (-24.12, 8.88).

After adjusting for confounding variables, only CVD comorbidity remained significant and had the strongest magnitude of association with PASE scores; β= -30.84 (-51.89, -9.80). Respiratory β= -11.82 (-34.95, 11.31), depression β= -10.27 (-38.45, 17.92) and T2DM β= -17.03 (-38.11, 4.05) were no longer significantly associated with PASE scores, with a weaker magnitude but still negative association trend, whilst obesity β=1.71 (-13.94, 17.35) was not significantly associated.

Table 5.3.4 Objective 3: Unadjusted and adjusted models for BEEP and MOSAICS comorbidity type and PASE score

		BEEP				MOSAICS			
	Independent variable	**(N)**	**β coefficient**	**95% CI**		**(N)**	**β coefficient**	**95% CI**	
				Lower	**Upper**			**Lower**	**Upper**
Unadjusted	Respiratory	463	-40.11*	-60.07	-20.14	432	-22.43	-46.98	2.12
	CVD	463	-23.75	-48.04	0.54	432	-43.00*	-65.08	-20.91
	Depression	462	3.12	-15.53	21.76	432	-23.24	-53.06	6.58
	T2DM	463	-26.68*	-48.82	-4.55	432	-34.42*	-56.64	-12.20
	Obesity	448	-25.28*	-41.06	-9.50	430	-7.62	-24.12	8.88
Adjusted	Respiratory	403	-40.60*	-60.50	-20.35	408	-11.82	-34.95	11.31
	CVD	403	-27.15*	-53.25	-1.05	408	-30.84*	-51.89	-9.80
	Depression	402	-4.93	-23.62	13.76	408	-10.27	-38.45	17.92
	T2DM	403	-30.19*	-54.25	-6.12	408	-17.03	-38.11	4.05
	Obesity	393	-27.72*	-44.08	-11.36	406	1.71	-13.94	17.35

*PASE score for each comorbidity *denotes statistically significant at p<0.05.*

Footnotes: *complete case data, multiple linear regression adjusted models adjusted for age, gender, partner, WOMAC and GAD 7. β coefficient represents a change in PASE score. Higher PASE scores indicate higher levels of PA.*

Abbreviations: *CVD=Cardiovascular Disease; T2DM=Type Two Diabetes Mellitus; N=Number; β=unstandardized beta coefficient; CI=Confidence Interval; WOMAC=Western Ontario and McMaster Osteoarthritis Index; GAD 7=Generalised Anxiety Disorder Questionnaire*

5.3.7 Summary of results

Table 5.3.5 summarises the findings which suggest comorbidity presence was associated with lower PA level. The findings suggest a potential dose-response relationship with PA levels decreasing as the number of comorbidities increases in people with OA. This was more pronounced in the BEEP trial than in the MOSAICS trial. Presence of respiratory, T2DM and CVD comorbidities were most strongly and consistently associated with lower PA levels.

Table 5.3.5 Summary Table of adjusted associations between comorbidity and PA level

	BEEP			MOSAICS		
	Adjusted β coefficient	**95% CI**		**Adjusted β coefficient**	**95% CI**	
		Lower	**Upper**		**Lower**	**Upper**
Objective 1						
Comorbidity presence	-32.3*	-48.6	-15.9	-6.5	-21.1	8.1
Objective 2						
1 comorbidity	-24.4*	-42.5	-6.4	1.4	-14.3	17.1
2 comorbidities	-34.8*	-56.1	-13.5	-26.8*	-49.3	-4.4
3+ comorbidities	-73.7*	-106.8	-40.6	-24.7	-62.2	12.8
Objective 3						
Respiratory	-40.4*	-60.5	-20.4	-11.8	-34.9	11.3
CVD	-27.2*	-53.3	-1.1	-30.8*	-51.9	-9.8
Depression	-4.9	-23.6	13.8	-10.3	-38.5	17.9
T2DM	-30.2*	-54.3	-6.1	-17.0	-38.1	4.1
Obesity	-27.8*	-44.1	-11.4	1.7	-13.9	17.4

Adjusted multiple linear regression models
Objective 2 reference category: 0 comorbidity.
***statistically significant association (p<0.05); β=Beta; CI=Confidence Intervals; CVD=Cardiovascular Disease; T2DM=Type Two Diabetes Mellitus*

5.4 Discussion

5.4.1. Introduction

This section discusses and interprets the main findings of this study and considers them in the context of existing research. It evaluates the strengths and limitations of the study before concluding with clinical and research implications and a summary. Increasingly, individuals with OA are living with comorbidity; however, the relationship between comorbidity and PA had not been thoroughly investigated. This study is the first to specifically investigate the relationship in detail using not just comorbidity presence and comorbidity frequency but also common comorbidity types and different methods of measuring comorbidity in people with OA.

5.4.2 Aim and objectives

This quantitative project aimed to examine the cross-sectional relationship between comorbidity and PA level in older adults with OA through secondary data analysis of two RCTs. The objectives were to investigate whether 1) comorbidity presence, 2) comorbidity frequency or 3) comorbidity type were associated with PA level in adults with OA.

5.4.3 Key findings

The results of this study found that comorbidity presence was associated with lower PA level. Furthermore, the findings suggest a potential dose-response relationship with PA levels decreasing with increasing comorbidity frequency in people with OA. Certain comorbidity types, such as T2DM and CVD had a stronger magnitude of association with lower PA levels, in both datasets. There were differences in the associations identified between the BEEP and MOSAICS trial data.

5.4.4 Comorbidity and physical activity levels in the two datasets

The participants in BEEP and MOSAICS, like other OA research, had a high prevalence of comorbidity (Stubbs et al., 2015; ARUK, 2013; Kingston et al*.,* 2018; Vos et al*.,* 2012; Kriegsman et al*.,* 2004). In the current study samples, obesity was the most prevalent comorbidity. The levels of comorbidity overall

are comparable to previous studies; with some notable difference by country, for example, in a knee OA PA trial (Ettinger et al., 1997) conducted in the USA, obesity was also the most prevalent comorbidity to OA (52.9%), whilst Reeuwijk et al. (2010) found obesity prevalence to be lower at 23.9% in a cohort of people with hip and knee OA in the Netherlands.

Comparing the participants in BEEP and MOSAICS revealed both similarities and differences in their comorbidity prevalence. Comorbidity was present in over half the participants in both RCTs (BEEP: 63%, MOSAICS: 52%). A recent international systematic review and meta-analysis of 23 observational studies found the pooled prevalence of OA and any comorbidity was 66% (Swain et al., 2019), closely matched with the BEEP trial comorbidity prevalence. However, fewer participants in the MOSAICS dataset reported multiple comorbidities, compared to BEEP (≥2 comorbidities BEEP: 26%; MOSAICS: 17%). These differences could be for several reasons. For example, due to the different methods used to measure comorbidity or the prevalence of comorbidity in different phenotypes of OA. For example, although 66% of people with OA have comorbidity (Swain et al., 2019), in hand OA, comorbidity prevalence is reported to be just 38% (Damman et al., 2016).

Within the BEEP and MOSAICS trials, the reported levels of comorbidities such as obesity, T2DM and CVD, that have clear diagnostic features, appear to be similar for both self-report and MRR. This could be because of concordance between the documentation in MRR and patient recall in conditions that have distinct or objective diagnostic procedures, for example, having height and weight measured or the cut-offs for BMI (Noble et al., 2019). However, there was some inter-dataset variation in terms of sample proportion with other comorbidity types (e.g. depression). Self-reporting of LTCs, especially in the older population, with the potential additional risk of declines in cognitive ability and recall may be both under and overestimated (Noble et al., 2019; Barber et al., 2009; Harris et al., 2009). Furthermore, GP's can use a variety of codes in MRR for recording symptoms associated with some conditions, such as depression (Barber et al., 2009), which may not explicitly provide a diagnosis of the condition through MRR, and therefore underestimate comorbidity prevalence.

These differences in comorbidity recording could explain why depression comorbidity prevalence was distinctly lower in MOSAICS (7.2%) compared to BEEP (22.2%). Previous studies have compared the accuracy of GP judgements of depression with standardised tools, structured interview, or through MRR (Freeling et al., 1985; Wilhelm et al*.,* 2008). Studies found that medical records are inaccurate or incomplete (Joling et al., 2011; Mitchell et al., 2011), and assessment usually based on depressive symptoms scales have arbitrary cut-off points (Sanchez-Villegas et al*.,* 2008) which may not reflect patient self-report of depression. Also, research has shown that the stigma of reporting depression may make people reluctant to seek professional help; although 20-40% of community-dwelling older people show signs of depression, fewer than 10% consult a GP (Barney et al*.,* 2006; CPA., 2009). An interview study by Coventry et al. (2011) with HCPs, patients and carers, found that in the presence of other LTCs, depression often becomes normalised.

The overall levels of PA as measured by the PASE tool were comparable to other similar international datasets (Dunlop et al., 2011; Svege et al., 2012). It should be acknowledged that the lower PA levels and prolonged inactivity due to OA could in turn increase risk factors for comorbidities (Felson et al*.,* 2000). The slightly lower level of PA in the MOSAICS dataset compared to the BEEP dataset may, in part be explained by the older mean age of the MOSAICS participants and the gender differences between the datasets, both of which can be associated with lower PA levels (Stubbs et al., 2015; Zullig et al., 2015).

The SMILE (Study of Medical Information and Lifestyles in Eindhoven study) cross-sectional study investigated the presence of pairs of co-existing LTCs associated with PA, and found that out of 3,386 participants (52.9% female, mean age 67.5) the cohort had; no comorbidity (47%), one (28%), two (14%), three (7%), four (3%) and five comorbidities (1%) (Dorenkamp et al*.,* 2016), which aligns with the current trials comorbidity frequency (Foster et al., 2014; Dziedzic et al., 2014).

5.4.5 Objective 1 findings

In the cross-sectional analyses, crude associations were found between comorbidity presence and reduced PA level in both datasets. This finding suggests that the independent variable (comorbidity) is associated with a change in the dependent variable (PASE) in people with OA. When adjusted for potential confounding variables, the relationship only remained statistically significant in the BEEP dataset with a non-significant trend in the MOSAICS dataset. Although the adjusted association between comorbidity and PA in MOSAICS was not statistically significant, best estimates suggest a relationship. A possible explanation for the difference in the findings could be that potential confounding variables affect people with different joint site OA phenotypes in different ways, although this is unclear.

Within the datasets, the magnitude of confounding in the relationship between comorbidity and PA level can be seen by comparing the adjusted and unadjusted regression coefficients. For example, age was higher, there were more females, and fewer people with a partner in the MOSAICS dataset. Age and female gender have previously been associated with lower PA (Dunlop et al*.,* 2011; Veenhof et al., 2012; Stubbs et al*.,* 2015; Chad et al*.,* 2005; Parkinson et al*.,* 2017; Bauman et al., 2012) and could act as confounders to different degrees between the datasets.

The association within the BEEP dataset supports previous studies suggesting that OA combined with another LTC, increased the likelihood of lower PA levels (Dorenkamp et al., 2016; Stubbs et al*.,* 2015; Tamari et al*.,* 2010; Herbolsheimer et al*.,* 2016; Wallis et al*.,* 2013). Comorbidity presence may contribute to the accumulation of symptom and physical impairment barriers, but also psychological barriers, such as negative outcome expectations, motivations and fear of movement and harm (Qin et al., 2015; Campbell et al., 2001). Previously, the presence of comorbidity has been found to have a significant association with social restriction, psychological distress and work limitation, which is further worsened if one condition is arthritis, which may lead to reductions in overall PA (Qin et al., 2015).

Comorbidity could act as a barrier by reducing motivation to do PA in people with OA. A qualitative investigation by Campbell et al. (2001) explored the reasons for adherence and non-adherence with PA interventions in people with knee OA. Comorbidity was linked with reduced patient motivation to adhere with PA, due to the perceived severity of knee symptoms (Campbell et al., 2001). The impact of comorbidity has previously been reported to reduce the physical ability and the desire to do PA (Hurley et al., 2018). A higher prevalence of diseases such as T2DM, respiratory disease and CVD are associated with worse pain and function in OA patients (Caporali et al., 2005), which could all negatively influence motivation to participate in PA.

Previous studies have reported negative PA outcome expectations, illness beliefs and fear of movement and harm in people with OA (Mackichan et al*.,* 2013; Holden et al*.,* 2014). Negative physical symptom outcomes from PA can translate to an enhanced fear over the safety of PA for people with OA and comorbidity (Campbell et al*.,* 2001; Holden et al*.,* 2014). In a recent cross-sectional analysis of people with OA, 62.1% of the participants had comorbidity, which was found to be associated with worse OA symptom severity, fear of pain, worse QOL and lower PA level (Muckelt et al., 2020). Fears about undertaking PA in people with OA such as worsening the condition and falling, could, therefore, be heightened with the addition of comorbidity (WHO, 2015).

5.4.6 Objective 2 findings

In the current study, across both datasets, as comorbidity frequency increased, PASE score decreased (indicating decreased levels of PA). In BEEP, the addition of one, two and three or more comorbidities was incrementally associated with a greater magnitude of difference in PASE score in both unadjusted and adjusted models. A similar pattern was observed in the MOSAICS dataset, but with a plateau in the effect from two comorbidities upwards. Unadjusted and adjusted models in both datasets had a significant reduction in PASE score when two comorbidities were present. Overall, a potential dose-response pattern of increased comorbidity frequency and lower PA level can be seen.

These findings corroborate with previous research; a previous review by Xu et al. (2017) showed an association between the presence of OA with a higher number of non-communicable-disease comorbidities, increased disability and reduced PA level. Increased comorbidity burden has also previously been associated with reduced odds of reporting moderate to high levels of PA in participants with rheumatic diseases (including OA) (Slater et al., 2011). Murphy et al. (2017) explored the weighted prevalence among US adults with arthritis meeting the 2008 PA guidelines for Americans. In their findings, 75% of adults with arthritis had comorbidity, and the proportion (95% CI) of people meeting the recommended PA level decreased with comorbidity frequency; arthritis alone: 49.9% (46.4, 53.4), one or two comorbidities: 42.1% (38.6, 45.7), and three or more comorbidities: 19.5% (14.6, 25.5) (Murphy et al., 2017).

Potential interactions and antagonisms exist in populations with comorbid conditions that interfere with, and restrict treatment and patient abilities, in turn potentially reducing PA ability (Slater et al., 2011). Therefore, a higher frequency of comorbidities may lead to greater physical and psychological barrier interactions, emphasising the importance of considering comorbidity status when considering OA treatment options.

A higher frequency of comorbidities could influence key psychological factors associated with PA level such as self-efficacy for PA (Quicke et al., 2017; Dobson et al., 2016; Cuperus et al., 2013). Low self-efficacy for PA is also associated with lower levels of PA in people with other LTCs such as T2DM (Thomas et al., 2004) and heart failure (Klompstra et al., 2015) and it is possible that living with multiple LTCs may have a cumulative negative effect on self-efficacy for PA which in turn may contribute to lower levels of PA.

A negative cycle may occur whereby reduced PA levels lead to a reciprocal increase in comorbidities and, in turn, further barriers. For example, reduced PA levels in COPD have not only been associated with increased physical limitations but also increased morbidity (Liao et al., 2014). Low levels of PA and more sedentary time are key risk factors for multiple LTCs such as T2DM, obesity and CVD (De Souto

Barreto, 2017). Shared risk factors could increase the likelihood of disease pairings; therefore, pairs could more commonly co-exist with OA or could have a greater effect on PA. For example, obesity has previously been shown to exacerbate symptoms such as pain and stiffness in OA (Rejeski et al., 2002), but also contributes to the development of several other medical conditions such as T2DM and CVD (Sedjo et al*.,* 2016; Foy et al*.,* 2011).

5.4.7 Objective 3 findings

In the comorbidity type models, BEEP had a greater number of comorbidity types significantly associated with lower PASE score (indicating lower PA levels) in both the unadjusted and adjusted models. Specifically, in the BEEP adjusted models, the presence of respiratory, CVD, T2DM and obesity comorbidities were all significantly associated with a decrease in PASE score. Furthermore, although the same comorbidities were associated with PASE in the MOSAICS dataset, the magnitude of association was much smaller and non-significant, except for CVD comorbidity. Several reasons could explain the lower PA levels in specific comorbidity types, both disease-specific factors (physical and psychosocial) and HCP specific factors (e.g. concerns of exacerbating conditions).

CVD comorbidity was consistently significantly associated with a reduction in PASE scores in both datasets. The presence of CVD comorbidity has been associated with reduced PA levels, over and above other comorbidities in people with Inflammatory Rheumatic and Musculoskeletal Diseases (IRMDs) (Cook et al., 2018). In primary care, patients with OA have twice the rate of CVD than those without OA (Van Dijk et al., 2008) and people with CVD have been found to be less physically active than those without CVD (Jeong et al., 2019). One reason for this could be that people with CVD are most likely to experience the complex accumulation of barriers to PA. Recent studies have found that those with CVD were more likely to have a higher BMI (Van Den Oever et al., 2014), and have more comorbidities (Jeong et al., 2019). This could lead to an accumulation of physical barriers including; greater OA pain, symptom burden and functional limitations (Hawker et al., 2014). OA and CVD are associated with chronic inflammation (Skou et al., 2018), which plays a role in OA symptoms such as

joint pain, swelling and stiffness (Alkatan et al., 2016). CVD is also associated with more intrapersonal barriers to PA such as perceived poor physical condition, lack of motivation and interest (Fleury et al., 2004), low perceived benefits of PA and a low sense of personal control (Reges et al., 2013).

Other comorbidities in the study could also contribute to the accumulation of barriers to PA. For example, symptoms such as pain and functional limitations are known barriers to PA participation in many LTCs (Osthoff et al*.,* 2018; Coventry et al*.,* 2011; Theis et al*.,* 2016). Conditions such as COPD increase levels of fatigue, muscle weakness and pain, all of which may add to the symptoms already experienced from OA, further reducing mobility, physical ability and PA tolerance (Wshah et al., 2018). From a psychological perspective, the fear-avoidance model applies well to the complex relationship between OA related pain and PA behaviours (Vlaeyen et al*.,* 2000). However, in people with comorbidity, the addition of further fears, such as aggravating symptoms, causing more harm or falls could exacerbate the avoidance of PA.

Fears regarding the safety of PA (both in patients and HCPs) are known barriers to PA participation in many diseases (Osthoff et al*.,* 2018). The HBM (Becker and Maiman, 1975; Janz et al*.,* 1984) could be used to explain part of the relationship. In brief, this model describes a balance between the perceived threat of disease, risks and benefits as well as other cues that are key to health behaviours. In a person with OA and comorbidity, there could be an additional perceived threat of disease, more risks associated with PA participation (e.g. increased OA pain and fear of bronchoconstriction in respiratory comorbidity) (Mancuso et al., 2006)). Combined, these may outweigh the perceived benefits of PA and reduce the likelihood of PA being undertaken.

Respiratory conditions and T2DM had a negative association with PASE scores in the current study. Safety concerns from HCPs regarding comorbidity specific factors (e.g. hypoglycaemia in T2DM), symptoms (e.g. breathlessness in respiratory conditions) and adverse events during PA (Beckwee et al*.,* 2015; Tamari et al*.,* 2010) could make them cautious and reluctant to prescribe PA. It is possible that people with CVD, T2DM or respiratory conditions may not be recommended PA, or are

recommended PA at an intensity and dose that is suboptimal, leaving patients unsure of how PA is beneficial to them and what the optimum levels of PA are for them as an individual (de Rooij et al., 2017).

In the BEEP dataset, following model adjustment, people with OA and obesity had lower levels of PA. Obesity-related lifestyle barriers to regular PA have been reported including time, low motivation and knowledge, but also the combination of OA and obesity has been associated with both low adherence to PA (Kearns et al*.,* 2013). Additionally, the intrapersonal impact of obesity comorbidity as a barrier could also impair people's motivations to do PA (Campbell et al*.,* 2001; Hendry et al*.,* 2006), such as experiences of negative body image, identity, discomfort when carrying out PA, perceptions of poor health and embarrassment (Rech et al., 2016; Ball et al., 2000).

The lower levels of PA in those with obesity as a comorbidity observed in the BEEP dataset was not matched in the MOSAICS dataset. This could be explained by the different OA joint sites included in the MOSAICS sample. MOSAICS included participants with OA at different sites, including knee, hip, foot and hand. There were fewer significant associations in the MOSAICS dataset between each comorbidity and PA level, which could be due to an interaction between the site of OA with the comorbidity and PA levels. For example, obesity may have a bigger role in reducing PA levels in BEEP as this dataset only included those with knee OA. Obesity may have a larger effect on weight-bearing joints such as the knees than non-weight-bearing joints such as the hand (Rejeski et al*.,* 2002; Roubille et al., 2019).

The study findings suggest different LTCs could pose different barriers to PA in people with OA, both through their symptomology and also through their associations with additional comorbidities.

5.4.8 Strengths

Several strengths of this study are associated with the use of the two large RCT datasets, which were from existing peer-reviewed studies. The dataset strengths included the different OA joint phenotypes

and two different methods for the measurement of comorbidity (self-report and MRR), which makes the results more generalisable to different OA populations. MRR has strengths such as; being measured at multiple time points and retained records of historic diagnoses.

Within the study, the range of comorbidities investigated are those that most commonly exist alongside OA and are likely to influence PA behaviour (Louati and Berenbaum, 2019; Davis et al*.,* 2002). The BEEP and MOSAICS trial samples were representative of people with OA in primary care and community settings in the UK. Also, the use of multiple linear regression meant that we could adjust for known confounders in the models. Levels of missing data were generally low in both datasets with levels of outcome PASE missing data 10% in BEEP and 18% in MOSAICS. However, it is acknowledged that missing data may influence the findings by reducing the statistical power or contributing to biased estimates.

5.4.9 Limitations

This study is not without limitations. First, it was not possible to investigate all comorbidities or severity of comorbidity that may influence PA, nor adjust for confounding variables not captured in the original datasets. For example, medication use for specific comorbidities could act as either confounders or effect modifiers, and further socioeconomic variables, such as deprivation and ethnicity, could potentially influence the results. Also, causation cannot be inferred in our findings due to the cross-sectional nature, and a reciprocal relationship could possibly exist where comorbidities may be both risk factors for, and a result of, reduced PA level.

Objectively measured PA (e.g. accelerometer or pedometer measures) is seen as the preferred method of measurement (Prince et al, 2008), therefore the use of a self-reported PA measure in both trials could be criticised. Further, in people with hip OA, the PASE has a relatively large SEM of 31, and it may be prone to self-report bias including recall bias, misclassification the over / underestimation of PA level (Harris et al*.,* 2009; Prince et al*.,* 2008; Smith et al*.,* 2019). Also, generalisability is limited to the eligibility of both study protocols; these datasets excluded people with joint replacements, those

unable to access physiotherapy or General Practice and those residing in nursing homes, who may be older or have a higher frequency of comorbidities.

5.4.10 Clinical implications

The PA levels of those with comorbidity in this population were lower than those without. People with OA both with and without comorbidity should aim to increase their PA levels to gain benefits for their LTCs, for general health benefits and potential to improve clinical outcomes such as pain, function and QOL. People with OA and comorbidity may be a greater risk of the consequences of insufficient PA and may represent a specific group to target with tailored PA interventions. Clinicians need to be supported to be able to tailor optimal interventions for people with OA inclusive of their comorbidities, assessing the frequency and type of comorbidity to extrapolate how they may need to adapt and tailor their recommendations. Furthermore, OA and CVD as a comorbidity pair could be targeted in tailoring future PA interventions.

5.4.11 Research implications

Although the findings of this study showed comorbidity to be associated with self-report PA in people with OA, it did not investigate *how* and *why* this might be the case. Hence, qualitative explanatory research exploring attitudes, beliefs and experiences of PA in the context of people with OA and comorbidity is indicated. Further work aiming to identify barriers to PA and ways to overcome these barriers to PA in the presence of OA and comorbidity is also warranted. The findings also suggest that interventions tailored to and focused on improving PA in people with OA and comorbidity are required since this group is at high risk of low PA levels and associated poor health outcomes due to the existence of their comorbidity.

5.4.12 Conclusion

In conclusion, in patients with OA, comorbidity is associated with lower PA levels, and this association grows in magnitude with increasing comorbidity frequency. People with OA and certain types of

comorbidity, such as CVD may be important to subgroup in terms of PA interventions since they appear to have the lowest levels of PA.

5.4.13 Chapter summary

This chapter described a quantitative secondary data analysis study to investigate the relationship between comorbidity and PA level in older adults with OA. This was achieved through linear regression modelling of baseline data from two RCTs in older adults with OA. The findings from this study provide evidence for the association between comorbidity presence, frequency and type with PA level in people with OA. It also highlights the need for further work in this field to understand the reasons why comorbidity may influence PA levels in people with OA. The next study within this thesis will seek to understand people's attitudes towards, and beliefs about, PA in the context of OA and comorbidity and how they can be encouraged to uptake and maintain PA levels.

Chapter 6

Qualitative interview study

Chapter 6. The attitudes towards, and beliefs about, physical activity in people with osteoarthritis and comorbidity: a qualitative investigation

6.0 Introduction

The previous chapters have provided a quantitative description of the effectiveness of PA in people with OA and comorbidity, demonstrating the relationship between OA, comorbidity and PA, and shown how comorbidity presence is negatively associated with PA levels. This chapter (study three) of the multi-method thesis, provides a qualitative interpretation of a sample of people's experiences of PA in the context of having OA and comorbidity. This chapter complements the use of quantitative data analysis by further exploring how and why people with OA and comorbidity have lower levels of PA than those without comorbidity. The chapter begins with a rationale for the qualitative study, with the aim and research questions provided. Following this, the chosen methods are described, including the data collection and analysis process. The subsequent parts of the chapter then present the results and discussion of the qualitative investigation.

Although NICE guidelines recommend advising about PA in the form of strengthening and aerobic exercises to people with OA, irrespective of comorbidity (NICE, 2014; 2016), they do not specify if and how advice should be tailored for those with comorbidity. The guidelines further state that clinicians need to make a judgement in each case on how to effectively ensure participation in PA and that this will depend upon the person's individual needs, circumstances and self-motivation, and the availability of local facilities (NICE, 2014). However, there is a gap in current research to determine the influence of OA and comorbidities on PA (Theis et al., 2016) and understand in more detail how patients experience PA in the context of OA and comorbidity.

6.0.1 Research question

How do people with OA experience PA in the context of comorbidity?

6.0.2 Aim and objectives

This qualitative investigation aimed to investigate the attitudes towards, and beliefs about, PA in people with OA and comorbidity using qualitative methodology. To inform understanding of how interventions can be designed and delivered to motivate this group to take up and maintain PA, there were two specific research objectives;

1. What are people's attitudes towards, and beliefs about, PA in the context of OA and comorbidity?
2. How can people with OA and comorbidity be encouraged to uptake and maintain PA levels?

6.1 Methods

With human subjects involved in this research study, the application of appropriate ethical principles was important. Therefore, an application was reviewed and approved by the Ethics Review Panel at Keele University (Ref: ERP3128) (Appendix 15).

6.1.1 Semi-structured interviews

Semi-structured interviews can provide meaning to participant experiences and an interpretation of the social construction and interaction between the researcher and the participant perspectives narratively reported with support from direct quotes (Bhattacherjee, 2012; Creswell, 2009). Individual semi-structured interviews were preferred to focus groups since they may be at less risk of social desirability bias and groupthink (Charmaz, 2006). Interviews provide detailed information; however, this information is filtered through the view of the researcher and therefore it was important to understand my perspective and appreciate my presence and role in the interview results (see section: My research experience).

Having an interpretive approach meant the interview method was used to generate theory inductively from the data to explore a range of in-depth experiences about PA in patients with OA and comorbidity (Creswell, 2009). Face-to-face semi-structured interviews were preferred over structured interviews as they offer flexibility in addressing and exploring the topic as they emerge from participant responses

but also allow for the researcher to focus on different topics of interest, within a wider interview guide (Creswell, 2009; McNamara, 1999). Therefore, the semi-structured interview guide allowed for key topics (described in section 6.1.8) to be explored, whilst allowing for the flexibility to pursue emergent ideas in more detail (Gill et al*.,* 2008; Creswell, 2009). A meeting with members of the PPIE group at Keele University helped shape the interview guide and study documentation (e.g. recruitment poster) used for this study and is detailed in Appendix 16. For example, the PPIE members suggested that their employment status was an important factor to consider, to explore how their conditions impact upon their daily life and routine and, finding out what activities they miss being able to do.

6.1.2 Sampling approach

There are different types of qualitative sampling, such as purposeful, snowballing and quota sampling, chosen on their appropriateness for the research (Creswell, 2009). Criterion purposive sampling was used (which is an appropriate technique when participants are selected based on characteristics), to select a diverse sample regarding gender, comorbidities, and age range (Palys, 2008). Also, Snowball sampling was used (initial respondents referring other potential participants believed to meet the criteria of the research) to access more participants such as those of a younger age and male (Johnson, 2014)). This was to encourage as much variation in the sample and diversity in interview responses, and a better understanding of the experience of PA in a range of people with OA with a range of comorbidities. However, the main disadvantage of this sampling technique is the probability of researcher bias, as the sample selected to answer the research questions has been chosen by the judgement of the researcher (Palinkas et al., 2015).

6.1.3 Sample size

Qualitative studies do not require the same prediction of a minimum sample size required for statistical significance like quantitative studies. The size of the sample was planned to be continued until data saturation within the sampling frame was reached (Saunders et al*.,* 2017). Glaser and Strauss (1967) recommend saturation within all types of qualitative studies, however, the exact number required

varies between studies. Based on previous qualitative research and experience from the study team, it was estimated that 15-20 participants would be required for data collection (Creswell, 2009; Morse, 1991).

6.1.4 Study population

The study population was composed of adults who self-reported OA and at least one other condition, attempting to sample a range of comorbidity types (e.g. psychological and physical comorbidities).

6.1.4.1 Inclusion criteria

- Age 45 years and over
- Males and females
- Self-reported OA
- Self-reported existence of one or more comorbidities
- Location in the North West of England and West Midlands

6.1.4.2 Exclusion criteria

- Under the age of 45
- Inflammatory arthropathy
- Inability to communicate in English
- Inability to provide fully informed written consent

6.1.5 Recruitment

Participants were recruited from specific local community groups and third sector organisations (e.g. Arthritis Action, Green Door activities and the College of the Third Age) and through advertising within the local community such as the local library, local shops, cafés and leisure centres. Multiple recruitment strategies aimed to reach a range of different potential participants. A preliminary list of possible locations was identified, which was then extended through contact made with recommended groups and snowballing through group leader contacts (Appendix 17).

6.1.5.1 Recruitment process via community groups.

- Community group leaders were contacted via phone / email.
- A suitable date was found to attend community groups.
- A brief face-to-face talk was given to the group members.
- The poster advertising the research (Appendix 18) and a prepared PowerPoint presentation when requested (Appendix 19) were also taken to the group meeting along with the study summary and a reply slip for potential participants to return if they wanted to receive more information about the study.
- Potential participants could fill in the reply slip there and then or send it back via post (pre-paid envelope provided).
- Those who indicated they would like more information were then sent the study documents in the post including; an invitation letter (Appendix 20), participant information sheet (Appendix 21), reply slip (Appendix 22) and consent form (Appendix 23) regarding preferred contact time to arrange a time and date for an interview.
- An interview was arranged.

6.1.5.2 Recruitment process via community advertising.

- Contact was made with each location to discuss whether a poster could be displayed.
- Posters were displayed in the agreed locations.
- The poster allowed participants to learn about the study and use a reply slip to agree to be contacted and sent more information.
- Those who wanted more information were sent the study documents; invitation letter, participant information sheets, a reply slip and consent form (Appendices 20 to 23) regarding preferred contact time to arrange a time and date for interview.
- An interview was arranged.

The recruitment period was between February 2018 and May 2018. Figure 6.1.1 demonstrates the process for recruiting participants once initial contact had been made.

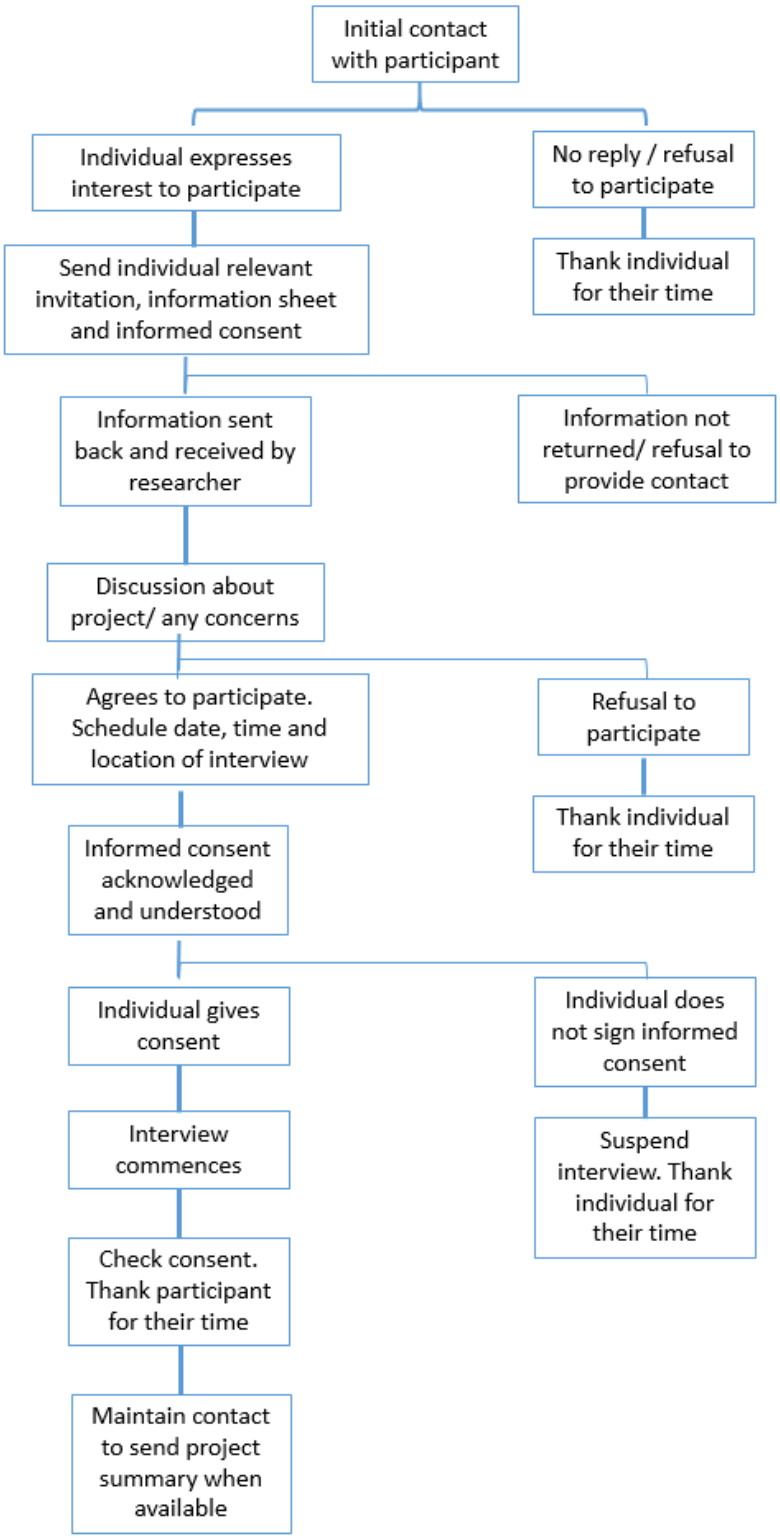


Figure 6.1.1 Participant recruitment flow diagram

6.1.6 Study setting

Participants were asked to choose a convenient location (e.g. phone, home, community group, local café) and interview time. Possible interviewer safety risks were mitigated by adhering to the Keele University Lone Working policy, based on the 1974 Health and Safety at Work act and the 1999 Management of Health and Safety at Work Regulations.

6.1.7 Consent

Informed consent was obtained from potential participants before starting any data collection (Appendix 23). This process of informed consent began with potential participants contacting me after they had the opportunity to read the letter of invitation and participant information sheet. These documents identified the nature and objectives of the study, what involvement meant, participatory rights, withdrawal options, confidentiality and anonymity, data storage and dissemination. On the day of the interview, it was ensured that the participant understood the information, had the opportunity to raise any queries, and then was invited to sign the consent form before the interview commenced. Consent was checked again verbally at the end of the interview.

6.1.8 Data collection

6.1.8.1 Interview guide development

The interview guide was drafted following a literature review on OA, comorbidity and barriers to PA and input from the PPIE group. A literature search was conducted on electronic databases; MEDLINE, EMBASE, AMED, CINAHL, and SportDiscus in May 2017 covering medical, clinical, treatment, physiotherapy and rehabilitation, and sports medicine records. The search was comprised of terms relevant to the topic of enquiry; OA, comorbidity and PA, and use of qualitative methods. This led to the identification of articles dating from 2000 to 2016 which indicated relevant themes and research questions about how adults with OA and comorbidity experience PA. Following this, a discussion with the supervisory team (CJ, JQ, EH) led to the development of key topics. For example, some key topics identified included; general challenges of comorbidity and PA, prioritising conditions and where PA

situated in participant priorities, the impact of OA and comorbidity on sedentary time, and facilitating PA.

The interview guide consisted of open-ended questions and prompts, where necessary, to ensure the participant had the opportunity to share in-depth perspectives on the topic of OA, comorbidity and PA. A pilot interview was carried out between myself and the supervisory team (CJ, EH and JQ) to ensure the interview flowed, the topic guide was relevant, and that I was prepared for participant involvement. This was also a chance to practice questioning style, for example, asking open questions to avoid leading the interviewee, ensuring a conversation through listening and responding, and expressing a positive body language that signals assurance. From the pilot interview, a few amendments were made to the interview guide, such as emphasising the comorbidity aspect of the questions and adding additional probing, which largely included asking 'why?' to the individual responses to gain a richer insight into the reasoning behind an answer.

The first few interviews (n=3) were conducted, transcribed and initially examined by myself and the supervisory team to ensure the interview guide was yielding relevant data. This led to the interview guide being modified prior to the continuation of the data collection. For example, questions which yielded similar responses were condensed and more prompts were added to encourage participants to expand and elaborate on their first responses, such as; 'can you tell me more about that?'. Appendix 24 shows the tracked changes in the final interview guide. Furthermore, the supervisory team noticed from the responses and characteristics of participants in upcoming interviews, that certain participant groups were underrepresented at this stage, such as males and people of working age, therefore, these groups were actively sought in further recruitment.

6.1.8.2 Interview procedure

Participants were invited to participate in a single face-to-face or telephone interview lasting approximately 60 minutes. All interviews were conducted by myself, as the lead researcher. Firstly, the dictaphone was introduced, which was used to record the interviews so they could be transcribed prior

to analysis. The interviewee was also made aware of the purpose of field notes, to capture any non-verbal communication or memos that I wanted to capture during the interview. The interviewee was informed when the dictaphone was switched on followed by the confidentiality statement and beginning the interview. Demographic data was first collected and some general questions about the participant were posed to provide insight into the population sample and ease the participant into the conversation. Then, I followed the predetermined interview guide themes and questions, allowing for elaboration and prompting when necessary. The dictaphone was turned off after the final question and appropriate closing of the interview with more opportunity to ask questions and converse outside of interview conditions. After concluding each interview, the dictaphone and any field notes were taken directly to a secure storage facility in Keele University and were all independently transcribed by myself.

6.1.8.3 Data protection

To ensure data protection and patient confidentiality, the Data Protection Act 2003 (https://ico.org.uk/for-organisations/guide-to-data-protection/) was followed, as well as Keele University Ethics requirements (REF: ERP3128) for data collection, storage, transfer and archiving of all data. I and my immediate academic supervisory team were the only persons with access to the data. Transcripts of the interviews were uploaded and stored in a secure, password-protected network drive located within the Research Institute's server.

Hard copy documents containing identifying information such as signed consent forms, were stored in a separate locked filing cabinet in an office at the Research Institute. Anonymised data (transcripts) will be archived for five years after the publication of the main results paper, to enable possible reuse (part of the participant consent form, Appendix 23), by other members of the Research Institute of Primary Care and Health Sciences (now the School of Medicine) at Keele University and other collaborating researchers.

6.1.9 Data analysis

I adopted a flexible framework approach to data analysis (Ritchie et al., 2013). The framework method is situated amongst methods of thematic and content analysis (Gale et al., 2013) to capture and interpret meaning within data (Ritchie et al., 2013). Thematic analysis is based on the constant comparison method to identify and develop themes from patient responses (Braun and Clarke, 2006), and allows for exploration of pre-identified themes in the data as well as emergent themes from individual interviews (Ritchie and Spencer, 1994).

The framework approach to analysis is a valid method to analyze interview data as it involves systematically applying the basic principles of thematic analysis with explicit analysis stages to guide the process (Ritchie et al., 2013; Smith and Firth, 2011). Having a framework approach promotes an inductive and interpretive process to identify patterns and descriptions for the development of meaningful themes (Ritchie and Spencer, 2002; Smith and Firth, 2011). The defining feature of the framework approach to analysis is the matrix output which provides structure to reduce the data and systematically analyze it by individual case, or code (such as in thematic analysis) (Ritchie and Spencer, 2002). The words and experiences of the participants' accounts are used to holistically identify patterns and themes framed under the research questions (Gill et al*.,* 2008), with focus on a transparent approach of linking, exploring and describing themes (Gale et al*.,* 2013; Smith and Firth, 2011).

The framework approach is most commonly utilized within qualitative research that employs semi-structured interviews (Gale et al., 2013; Ritchie and Spencer, 1994). Adopting this method allows for a systematic process (Figure 6.1.2), whilst having flexibility in applying the method to suit the research questions and data (Braun and Clark, 2006). This way, it was possible to gain an in-depth view of the data and individual interviews, before exploring themes and findings across interviews, with an iterative stance to link back and forth to the raw data (Gale et al*.,* 2013). The framework method is suitable to this study especially with the involvement of multiple members of a team with varying

experience of qualitative data analysis (Gale et al., 2013) as it provides structure to identify and develop themes with a transparent audit trail.

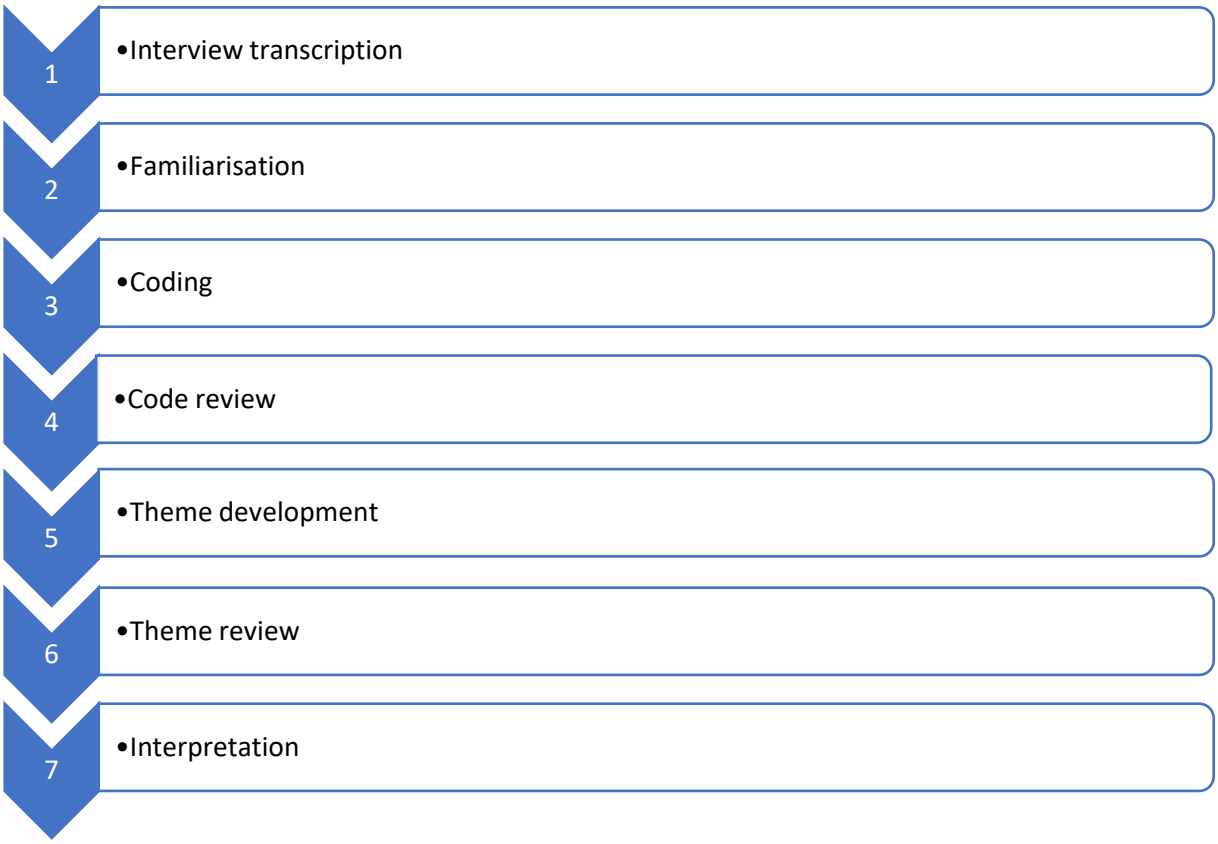


Figure 6.1.2 Overview of the Framework approach used in the qualitative data analysis

6.1.9.1 Stages of Framework approach analysis

The seven stages of the analysis process are detailed below, and examples of stages are provided in Appendix 25.

1. Interview transcription: Analysis began with the transcription of the interviews. This allowed revisiting the interviews and maintaining a close connection with the raw data.
2. Familiarization: The process of reading and re-reading the transcripts and reflecting upon each interview. Immediate thoughts and impressions were noted regarding any key issues within the transcripts. The supervisory team (CJ, JQ, EH) also read a selection of transcripts (n=3).
3. Coding: The choice was made to manually code the data by Word and hand owing to this method providing a more engaged and methodical process, with emphasis on flexibility to focus on depth and meaning in the data. Each transcript was studied and coding the data

began. This phase involved generating labels to identify important portions of text within the interview transcripts. Two interviews were coded by members of the supervisory team (CJ social scientist; JQ physiotherapist) and discussed. The codes were then collated as well as the relevant data extracts (quotations) to support the concepts. A code book was developed and used as an additional technique in the analysis. Generating an initial code book assisted with a reflexive stance to aid the transparency of the framework approach. The code book consisted of code names, detail of what each code did / did not include, additional information and example extracts from the raw data to describe the meaning of codes and what each code did and did not encompass.

4. Code review: Regular contact between myself and supervisor CJ allowed for discussion of the interview codes, including; style of coding (descriptive vs interpretative), tracking changes made and giving examples how a code may have changed and been refined. Individual interviews were examined in more depth simultaneously to coding review by creating participant diagrams to display the key focus points within each individual interview and potential links between codes (see example Figure 6.2.4). This allowed further exploration and discussion of the data, particularly the context and meaning to the participant's voice. From the discussions and diagrams, the individual interviews were cross-checked to see if the participant perspectives were depicted accurately by the codes. This process continued until the codes were agreed amongst the team to be reflective of the participant responses and were not redundant or interchangeable. The reviewed codes list was edited and re-applied to the full dataset.
5. Theme development: The finalised code list was examined to identify significant patterns, groups and potential themes across the interviews. This began with grouping and moving codes, then clustering into groups around specific topics or collections of codes that seemed to be related in some way. Subthemes were identified and used as a building block for themes, organised around a central concept and core idea and discussed with supervisor CJ.

6. Theme review: The themes were discussed in regular supervisor meetings and developed to create a thematic map showing how key themes were linked to the subthemes and codes, and each other. This phase tested the referential adequacy (constantly returning to the raw data to ensure conclusions were firmly grounded in the data (Lincoln and Guba, 1985)). This involved checking the proposed themes against the dataset, to ensure that each code and supporting extract sat comfortably under the theme, that each theme captured the essence of the codes it contained, and that each theme was independent and described a unique part of the data. The findings were discussed and developed further. The data was iteratively compared and analysed across participants in a process of constant comparison, which ensured initial topics, as well as emergent themes, were explored across all interviews. This process determined the scope and focus of each theme and eventually lead to a consensus of an appropriate informative name for each theme. Diagramming and note keeping was used to make sense of theme connections about the development and hierarchies of concepts and themes.
7. Interpretation: The final themes provided a framework for organizing and reporting the analytic observations of the data. The framework matrix was generated in Word and was the last stage of organising the data. The final themes and accompanying data extracts chosen to depict them were charted into the framework matrix. The matrix allowed for a transparent systematic structure to collate and reduce the data, through themes, cases and codes. This then allowed for the analytic process to have a good balance between interpretive narrative and illustrative extracts to tell a convincing and well-organised story about the data. The interpretation of the data was a recursive process to ensure that the results weaved together the analysis and interpretation in the context of the research questions and existing literature, to tell a coherent story. The interpretation was discussed and refined further with the supervisory team.

6.1.10 Ensuring credibility of the methods

Thematic and framework analyses are not without disadvantages and the flexibility of the methods could lead to inconsistency when analysing data (Braun and Clarke, 2006). Therefore, it is necessary to adopt strategies for coherence and consistency (Braun and Clarke, 2006). Lincoln and Guba (1985) outlined the concepts trustworthiness, credibility and dependability within qualitative research. Credibility in this context refers to the 'fit' between the participant responses aligned with the views depicted by the researcher (Lincoln and Guba, 1985). It is important to acknowledge and critically reflect on my role within the research process. This is necessary to understand that it may affect the investigation and methods used as well as the findings and framing of the conclusions made (Malterud, 2001). Reflexivity is a central, self-critical account of the research process whilst accounting for the researcher's personal values, interests and influences (Lincoln and Guba, 1985). By being reflexive, I acknowledge that I may have a different view and understanding of the research to another, but that all understandings are equal and valid. Throughout this reflexive stance, the iterative process of checking findings and interpretations back and forth against transcripts ensured the findings were still representative of the raw data and tested the conclusions drawn (Malterud, 2001).

To further strengthen the rigour of the study and dependability of the findings, the use of multiple coders was employed for inter-coder reliability. Discussions of each stage of the coding process was a vital aspect of the analysis, which not only encouraged transparency and clarity of the analysis process but also highlighted discrepancies, assumptions and exposed new and alternative explanations. Once again, this process encouraged the analysis to step away from the subjective and be inclusive of multiple views, reflecting the diversity that exists around the topic (Malterud, 2001).

6.2 Results

6.2.1 Introduction

This section will first describe the study sample, in terms of participant characteristics. A summary of key findings of the qualitative investigation is presented and findings are then described in detail.

6.2.2 Study sample

From the recruitment process described in the methods of this chapter, 17 participants attended an interview. All interviews were conducted between March and September 2018. Interviews were conducted either in a community setting (e.g. library, café), Keele University premises, or the participants home. None of the participants opted for a telephone interview. Participant characteristics are presented in Table 6.2.1. Participants included both males and females ranging between 49 and 95 years of age, with differing OA joint sites and severity, and a range of comorbidity types (e.g. obesity, depression) and frequency (1-4+ comorbidities). Figure 6.2.1 gives further detail on the extent of comorbidity in the interview sample.

Table 6.2.1 Interview participant characteristics

ID	M/F	Pseudonym	Age	Marital status	Education	Occupation	Work status	Comorbidities
1	M	John	75	MA	S18	Driver	R	Diabetes, AF, Had Cancer, Depression
2	F	Mary	59	WID	Nurse training	Nurse	R	Depression, Bilateral Uveitis, Underactive Thyroid, Crohn's disease, OP
3	M	Tim	79	MA	S16	Mortuary	R	High Blood Pressure, Obesity
4	F	Karen	75	WID	S18	Tills	R	Had Cancer, Depression
5	F	Rachel	70	DIV	Degree	Teacher	R	Obesity
6	F	Jackie	76	DIV	S15	Nurse	R	Back Pain, Neuropathy, Spondylitis, Diabetic, Blind
7	M	Bill	58	SING	Degree	Teacher	R	Depression, OCD
8	F	Alice	49	MA	PhD	Academic	NR	Coeliac, Chronic Migraines, Asthma
9	F	Laura	92	WID	S14	Retail	R	High BP, Underactive Thyroid
10	F	Ann	95	WID	S14	Nursery nurse	R	Cystitis, Anaemia
11	F	Vera	77	WID	A	Teacher	R	OP, Hypertension
12	F	Debbie	80	WID	S16	Telegraphist	R	Bronchiectasis, RA
13	F	Holly	86	SING	Teacher training	Teacher	R	OP, Back Pain, Heart Arrhythmia, Carpal Tunnel Syndrome
14	F	Jane	82	WID	S15	Retail	R	Heart Disease, Had Heart Attack
15	F	Clare	90	-	S14	Retail	R	Sciatica, Cystitis, RA, OP
16	M	Dave	54	SEP	A	Police	R	Acid Reflux, High Blood Pressure
17	F	Kate	77	WID	A	Nurse	R	Underactive Thyroid, Palpitations, Raynaud's disease

M/F=Gender; M=Male; F=Female; MA=Married; WID=widow, DIV=divorced, SING=single; SEP=separated; S(N)=educated at school (age), A=A-levels; R=Retired; NR=Not Retired; AF=Atrial Fibrillation; OP=Osteoporosis; OCD=Obsessive Compulsive Disorder; BP=Blood Pressure; RA=Rheumatoid Arthritis

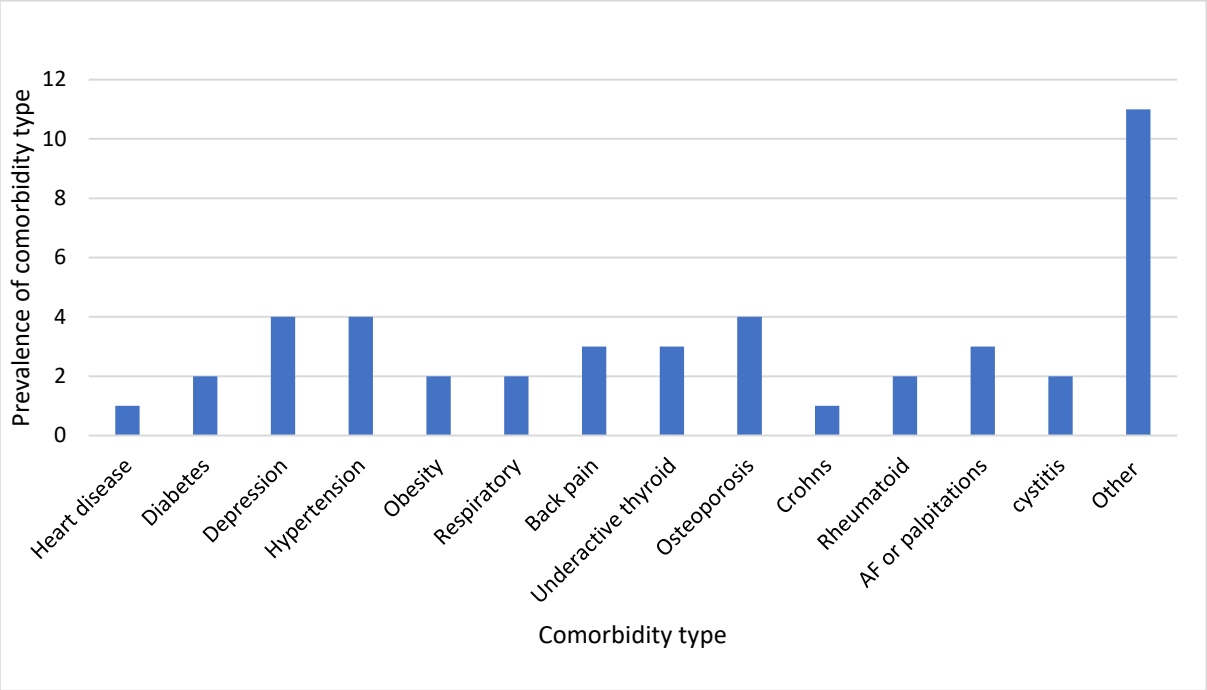


Figure 6.2.1 Comorbidity prevalence in the participant sample

Other: 1 case of each (Bilateral uveitis, neuropathy, spondylitis, blind, obsessive-compulsive disorder, coeliac, chronic migraines, anaemia, carpal tunnel syndrome, acid reflux, Raynaud's).

6.2.2.1 Physical activity levels in the sample

All participants indicated that they engaged in some form of PA. However, the definition of what constituted PA varied. Some participants were actively engaged in sports, group classes and walking, whereas others indicated housework, gardening and shopping as their PA. 15 of the 17 participants engaged in walking activities, be that purposeful, walking their dog, social or commuting regularly. Often, participants indicated they were 'always moving' or keeping their 'limbs moving' throughout the day, as opposed to structured PA. Beyond walking, approximately half of the participants were regularly engaging (approximately weekly) in PA formats such as; yoga, swimming, tai chi, cycling, climbing and crown green bowling. However, only a small proportion of the participants were active past light-moderate levels, with reported moderate-vigorous intensity PA ranging from lifting weights regularly at the gym to running their own dance class. Approximately half of the participants were regularly engaging (approximately weekly) in a structured PA class group for adults, with two participants leading a voluntary PA class for older adults of their own. Figure 6.2.2 displays the PA types currently being undertaken within this sample, with the dashed line demonstrating the decrease in PA popularity, as it increases in intensity.

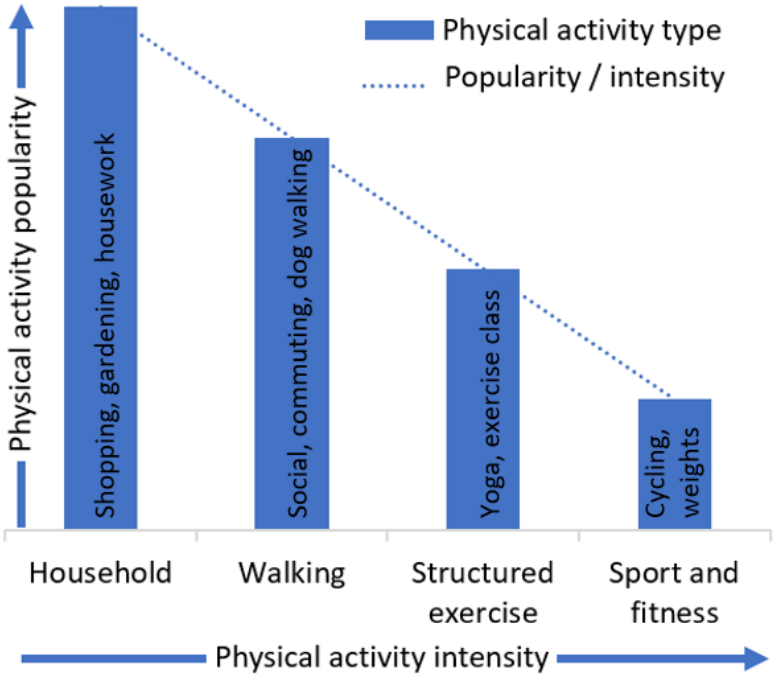


Figure 6.2.2 Popularity and intensity of physical activity types (with examples) in the sample

6.2.3 Presentation of findings

Two themes emerged as key findings; (1) barriers to PA and (2) facilitators of PA, with all subthemes and codes related to these. The themes and subthemes are presented in Table 6.2.2 below and the links between themes and subthemes are displayed in the thematic map (Figure 6.2.3).

First section 6.2.4 presents the results related to barriers to PA in people with OA and comorbidity. This section begins with specific barriers to PA that appear inherent in the general experience of living with OA and comorbidity including; a lack of talk about "comorbidity" as a concept; self-prioritising of conditions; uncertainty about how to manage health conditions, and uncertainty of PA effectiveness for conditions in general; and, negative perceptions of LTCs and ageing, and negative perceptions of PA. Next presented are the multiple biopsychosocial barriers to PA that exist and how these are dynamic, meaning that barriers operated at different levels. Participants talked about barriers, identified solutions to barriers, but then identified subsequent barriers to the solutions previously mentioned.

Section 6.2.5 then presents the results related to facilitators of PA in people with OA and comorbidity. This section outlines two main types of support mechanisms to PA; knowledgeable HCPs that could instil confidence and teach participants skills to self-manage PA; and, social support that encouraged shared learning, through a homogeneous group. Finally, the PA modes and type that facilitates PA participation in people with OA and comorbidity, are described. Throughout the results section, extracts with pseudonyms are used to conceal participant identity.

Table 6.2.2 Two main themes and subthemes about PA in people with OA and comorbidity

Main theme	Subthemes
1 Barriers to PA	1. Lack of concept of "comorbidity" and LTC prioritisation 2. Uncertainty about the management of health conditions and PA effectiveness 3. Negative perceptions concerning LTCs and ageing, and PA 4. Multiple co-existing biopsychosocial barriers to PA 5. Solutions to barriers and barriers to solutions
2 Facilitators of PA	1. Social support through shared learning and homogeneity 2. Healthcare professional support to facilitate self-management of PA 3. PA mode and type that is intermittent, adapted, and fits into daily life

PA= physical activity; LTC=Long-Term Condition

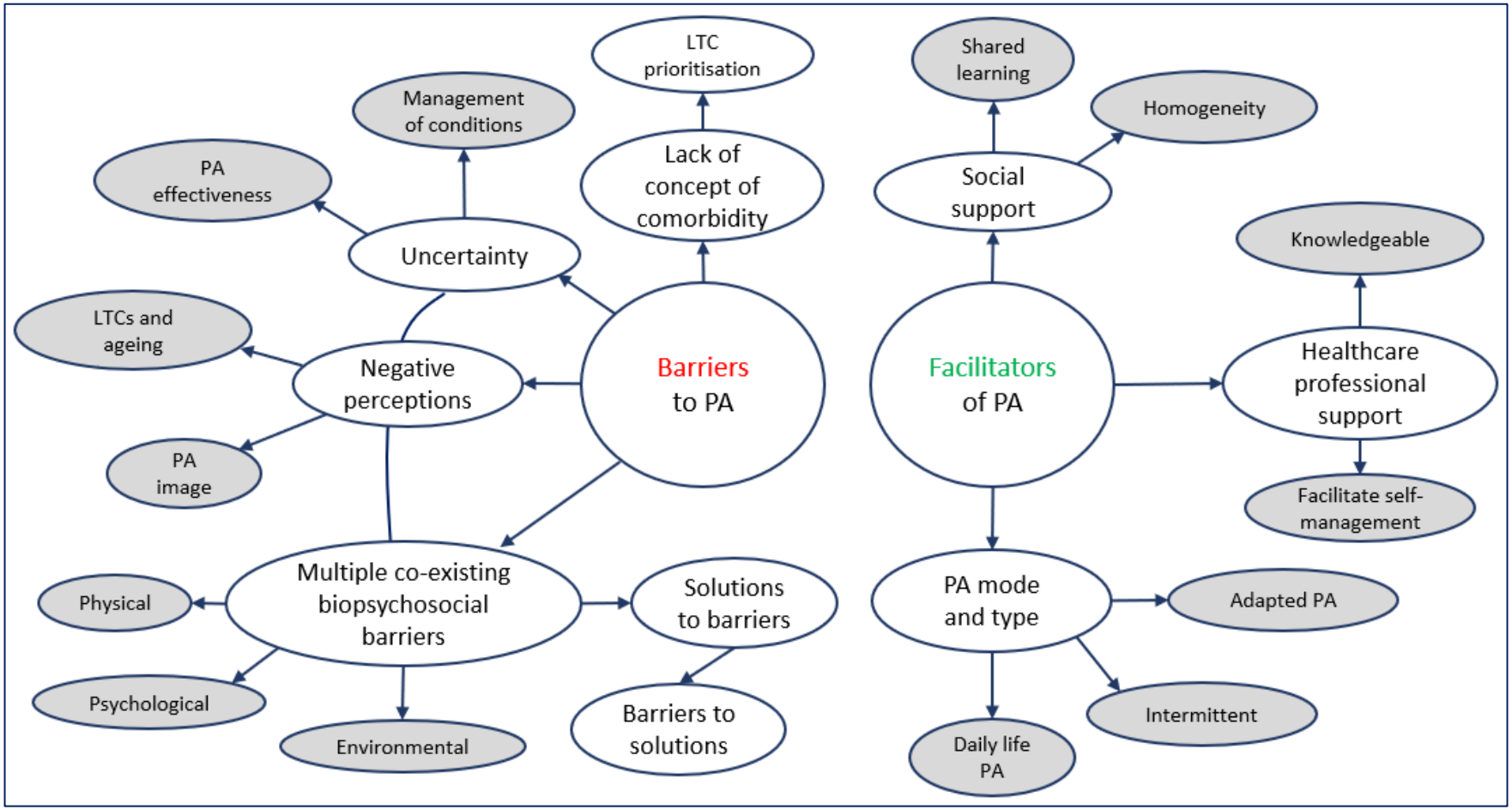


Figure 6.2.3 Thematic Map with links between themes and sub-themes

PA=Physical Activity, LTC=Long-term condition

6.2.4 Barriers to physical activity in people with osteoarthritis and comorbidity

6.2.4.1 Lack of a concept of comorbidity and long-term condition prioritisation

Participants in this study largely talked about their conditions in isolation and did not conceptualise having OA at the same time as other health conditions as a different construct of "comorbidity". Instead, participants saw their conditions as separate entities and prioritised individual conditions, based on what they perceived to be the most disabling and the level of disruption created for daily life. This meant that OA was often thought to be a priority. OA was prioritised over life-threatening conditions for several reasons including the level of pain it caused, impact on walking mobility and disruption to social functioning:

> *'You see I forget that I've got other conditions, I always just think it's my arthritis that hurts me' (Laura)*

> *'The problem with umm, me walking condition (OA), is what bothers me mostly and me balance….it impacts a lot on me physical activities, because I haven't got the energy and I can't do things…Well the heart condition I could, I could just cope with that alright it didn't, didn't seem to bother me but the walking is, very detrimental to me' (Jane)*

> *'I think my OA is the most important…it's because it's going to impact on my life, as to how much I can get about…meet friends and do the things I want to do really isn't it…In fact I'm quite frustrated now because of my hip, I can't get up and go' (Kate)*

> *'I think the arthritis is the most important, in that it's the one that stops me doing more things' (Vera)*

In contrast, it was rare for a participant to prioritise other non OA conditions which posed the most serious health threat, due to the control they felt they had over other conditions, in comparison:

> *'My cancer returning, that's a condition…that sort of up there on the top of the list, my other is my AF, if I can keep that under control' (John)*

The symptoms from OA, such as pain, loss of function and reductions in QOL were often discussed by participants as the reasons why OA was the most important condition for them, which could be

important in tailoring PA interventions. Other conditions, in comparison to OA, were less problematic because of their perceived predictability and manageability:

> *'That affects everything (OA) that's the overriding thing…umm the others, I manage with tablets…I don't feel they affect me very much on a day to day basis…I don't really think about the hypertension at all, because I'm on the medication, that stabilized it. Yes, it's another tablet you have to take every day' (Dave)*

> *'I've got hypertension but that doesn't affect me at all because it's now under control with medication' (Vera)*

> *'I don't think about, I mean the osteoporosis I have to take a tablet once a week, with a glass of water, I hate it, but if it's going to help, I'll take it you know' (Holly)*

Furthermore, the experience participants had from healthcare consultations mirrored their own lack of conceptualisation of comorbidity. Despite participants having combinations of conditions and condition priorities, during healthcare consultations they often found their HCP was only aware / focussed on one condition at a time. This lack of coordination and single disease focus is important, as it made it hard for participants to do the PA they were prescribed; for example:

> *'I've been shown one lot of exercises and that was for me knees. But what she was expecting me to do, I couldn't do because of the pain in me back…When they come to give me exercise for me knees, all they know about is me knees, they don't even know about me back…she was showing me these exercises…I couldn't do it…she seemed quite surprised as though she didn't know anything about me back' (Jackie)*

Although participants in this sample tended to prioritise their OA over other health conditions (due to the pain and impact it had on mobility and valued activities), their priorities also fluctuated according to the episodic nature of many comorbid conditions, particularly at the time of an acute attack or flare:

> *'I daren't do anything if it kicks off, it's when it kicks off (IBS) it's with vengeance… If we go out for a meal or anything I'm thinking where the toilets is, and if we're too far away from them I start panicking' (Mary)*

'The erratic heart thing, that, if you have an attack of that, you feel ghastly while it lasts, but it doesn't last all that time.' (Holly)

'When I have the cystitis bad that really does, when I'm up, at least about 6 times in the night going to the loo…the next day I am, you know, I feel really tired' (Clare)

6.2.4.2 Uncertainty about the management of long-term conditions and physical activity effectiveness

Participants were often uncertain about their condition management, which was an initial problem before tackling how they could manage their conditions with PA. Participants often felt they received mixed messages about the best approach to manage their conditions and availability of treatment options:

'I did go and see that physiotherapist…and she did give me these movements…but when I went to see the specialist, he said he doesn't' think, because my hip is so degenerated, he says he honestly doesn't think that exercises would do me any good' (Bill)

'I get medical stuff coming through now and some of the things they suggest…you get so much, and you find it difficult to find what's good and what isn't' (Tim)

Some participants had the perception that HCPs had a preference for pharmacological, and surgical treatments, rather than endorsing PA as an option for treating OA, which led to uncertainty about the effectiveness and importance of PA for their conditions:

'When I went to the specialist, I just felt, he was pushing me for this hip operation, you know, that seemed to be his number one thing…They especially seemed obsessed with booking me in for this hip op, and I felt as if I was on this conveyer belt going into it and I thought well no' (Bill)

'I'd been about this to the doctor before, and then again, 'take some paracetamol…Nobody's ever said to me like, you know, you ought to try (PA)' (John)

'They put me on the morphine tablets, and nobody has ever recommended anything else for it' (Jackie)

'Even if the doctor said, I want you to go (PA class), you know, but they don't' (Karen)

'I mean doctors don't give you anything other than pain killers and rubbing stuff' (Laura)

The lack of PA endorsement from HCPs contributed to an overall lack of knowledge about what PA was appropriate and uncertainty about PA effectiveness in people with OA and comorbidity:

'To have guidance as to what I should do…otherwise you're working in the dark, you just don't know what you're doing…the Alexander Technique person, she is so good because she explains what muscles you're using and why you're using them' (Holly)

'Knowing what I ought to be doing, I haven't got any, I don't know what I should be doing, I've always just done what I do…they can pinpoint exercises for you…look at how you are now…with a physio leading…about what kind of exercises need to do and how, how to isolate muscle groups to do those exercises and all that sort of thing… instruction from someone that's easy, if they just say to you these are the exercises to do' (Dave)

'I had a NHS physiotherapist who…was rubbish…he gave me one set of exercise for my knees…and then he says to me, and that's as much as I can do for you […] It's knowing what to do…actually knowing what you're doing and then actually doing good. Like I say its knowledge you need to know about your complaint and what works best…that would be the perfect answer for me, learn to do it… Knowing what exercise would benefit me the best…it comes down to physiotherapy…' (Tim)

'I need to know, what is going to help, the condition…I don't know enough about it sort of what would make things better, what would make things worse, so knowledge, knowledge is really important…this is recommended, but this isn't, or this could make it worse, you know' (Rachel)

6.2.4.3 Negative perceptions concerning long-term conditions and ageing, and physical activity

Participants had negative perceptions of their conditions which they believed would lead to an inevitable decline in health. They also had low PA expectations with ageing. These perceptions meant participants were less inclined to participate in PA to relieve something that they deem inevitable. For example, participants largely connected their health status with feelings of succumbing to age, deterioration of their health and inevitable decline in QOL:

'I expect to slow down at this age…I'd love to do more than I'm doing but I'm learning to live within the confines of my condition. Which isn't a good thing' (Tim)

> *'well you can't bend the same when you've got the arthritis, practically all over your body, in your joints and that, but you wouldn't at my age duck, would you?... I used to be able to just stand on the chair and if I wanted to do my curtains, I could, I can't do that, but I put that down to my age as well' (Laura)*

> *'Because it's not going to get better, its slowly going to get worse, isn't it…I don't know how long I can drive for though do I, once I can't drive, that's finished it, that's another door closed to me' (Kate)*

> *'I'm always aware of the fact that age is against me…I'm getting older, I must be thankful, for what I can do' (Holly)*

Participants indicated they expect to worsen; they seemed to think of ageing and worsening of their QOL as normal and these thoughts were being reinforced by how they perceived HCPs viewed their health status:

> *'She come she said, 'it's just arthritis I'm afraid it's just something at your age, something you've got to live with' (Ann)*

> *'A terrible lack of empathy over the experience of a chronic condition and my, as I said, my experience with physios and chronic condition is absolutely useless […] ''oh they're 80 years old we must try to get the poor dear moving", you've lost already' (Alice)*

Also, there was an overarching negative perception of PA, due to lack of positive experiences or references, fears about safety, a perceived focus on weight loss, and negative perceptions of the gym and PA classes. Negative perceptions were created because participants expressed a lack of positive reference of PA from peers:

> *'I've never seen anybody with a condition, come out of it any better, with any activities or special classes…I've never known anybody to benefit in any real terms' (John)*

> *'I don't want to belittle the NHS, but I have friends, experiences…but the other friend had, emm, issues…her opinion was it was pointless' (Dave)*

Furthermore, despite recent literature reporting the safety of PA in people with OA (Quicke et al., 2015), in the responses in the current study, fear of damage from PA was still evident, perhaps heightened due to the existence of comorbidity. For example, many participants identified fear of

worsening their health, a fear of pain and the risk of ending up in the hospital, making participants more cautious, and less confident in participating in PA:

> *'If I went on one of these physical things…it'd probably do more harm than good' (John)*
>
> *'I'm frightened of it doing me any more damage to be truthful' (Karen)*
>
> *'I'm frightened of slipping down…you become almost overprotective of yourself, because I don't want to end up in the hospital again' (Kate)*

Also, participants expressed a shared a fear of falling. Falls were therefore perhaps more likely in OA and comorbidity or had a more detrimental impact on the participants. This fear was from bad experiences falling and a lack of trust in their bodies:

> *'My balance mainly, stops me doing things, which I am frightened, I'm very frightened of falling over again you know' (Jane)*
>
> *'I'm worried that I'm going to fall. Because the pavements in some parts are really bad' (Mary)*
>
> *'I've been always frightened of falling, my legs are sort of…they haven't much going' (Ann)*

Participants that were overweight or obese, indicated how the image of PA only to achieve weight loss, didn't appeal to them. They indicated that a more all-encompassing general health target would be preferred to a weight target:

> *'You can really put people off exercise if you tell them they have to lose weight first…Ways to motivate yourself when you aren't getting the the kinds of rewards that a lot of the popular media tell you should get from exercise' (Alice)*

There was also a negative perception from some participants of the gym environment and classes; that it was not their lifestyle or a waste of their time and energy:

> *'I don't enjoy being in a gym… I don't want to go to the gym because I find it boring…sitting on a machine looking at a screen is not my lifestyle' (Dave)*
>
> *'Zumba and all that thingy I think you know, what are they doing that for? Wasting energy like that for!' (Mary)*

> *'I suppose you could go to these classes where you sit around in a circle and you go waaay ehh ohh! (swings arms) …I'm not going to get to that stage' (John)*

The image of PA, physiotherapy and PA classes didn't fulfil goals that matter most to the participants, such as functional, social or enjoyment, which one participant vocalised; they would rather be hoovering for PA and health, than pointless gym exercises:

> *'when you go see somebody about moving your arms and that, physiotherapy…you know listen, if I could lift my leg up there, lift my arm up there I wouldn't need physio! but I know that…but I class that as me getting up and doing a bit of hoovering and whatever you know, rather than just stand in a corner and do that (lifts arms and legs) (jokes) and you know I take the tablet, paracetamol or whatever' (John)*

6.2.4.4 Multiple co-existing biopsychosocial barriers

Participants spoke of how they encountered multiple barriers to undertaking PA. For example, common barriers, such as pain, function loss, fear, fatigue, a lack of support and environmental factors were experienced by the participants and often co-existed. This confirms findings from previous studies that people with OA experience multiple barriers to PA (Petursdottir et al*.,* 2010; de Rooij et al*.,* 2014; Dobson et al*.,* 2016; Jack et al*.,* 2010) but could be due to OA, their comorbidities and other biopsychosocial factors (Kanavaki et al., 2017; Dobson et al., 2016; Egerton et al., 2017; WHO, 2001).

Throughout each interview, participants experienced these barriers concurrently, for example, a participant could have a physical barrier (e.g. pain) alongside a psychological barrier (e.g. low confidence in their ability to carry out PA). Examples of the multiple concurrent barriers can be seen as participant diagram illustrations in Appendix 26. One example can be seen below, from Dave, who had OA and hypertension and experienced multiple barriers in his attempts to undertake PA. Dave experienced pain, episodic flares in his conditions, negative aftermaths of PA, access problems, a stigma attached to disability, mental fatigue and a lack of confidence in his ability, outlined in the excerpts below and shown in Figure 6.2.4. Dave's barriers to PA included;

Pain:

'actual burning pain from having done too much, the soreness within the joint, that's when you're standing there and it's hurting you […] my knee is, if it is really sore, and I can't get that pain to go away […] it's coping with or managing the pain that's the overriding block'

Condition flares:

'I get a flare-up because I've done something that's flared it up […] And I'm waiting for it to ex, to blow up so to speak, as much flare up and say 'no you can't walk on it today! You can't do anything!'

PA aftermath:

'with the cadets I've still got to walk from one place to another…you have to kind of work through that, and then you know that it's going to take maybe two weeks to recover…or get it back to normal, after that […] after being on my feet, I had to come away and stop'

Access:

'maybe I should start doing the gym because it's maybe more controllable, I can stop, get in the car and go home. Whereas if you walk, you've still got to walk home […] even getting in and out of a car is a problem'

Disability stigma:

'people don't see me as a disabled person…And saying that in itself is quite a big thing, because I don't you know, but I am'

Fatigue:

'pain and that level of will power is quite tiring and quite fatiguing'

Lack of confidence:

'I have got very little confidence in my knee and the only thing I am confident in is if I do something, it's going to hurt […] I haven't got uhh, confidence in knowing what I ought to be doing, I haven't got any, I don't know what I should be doing'

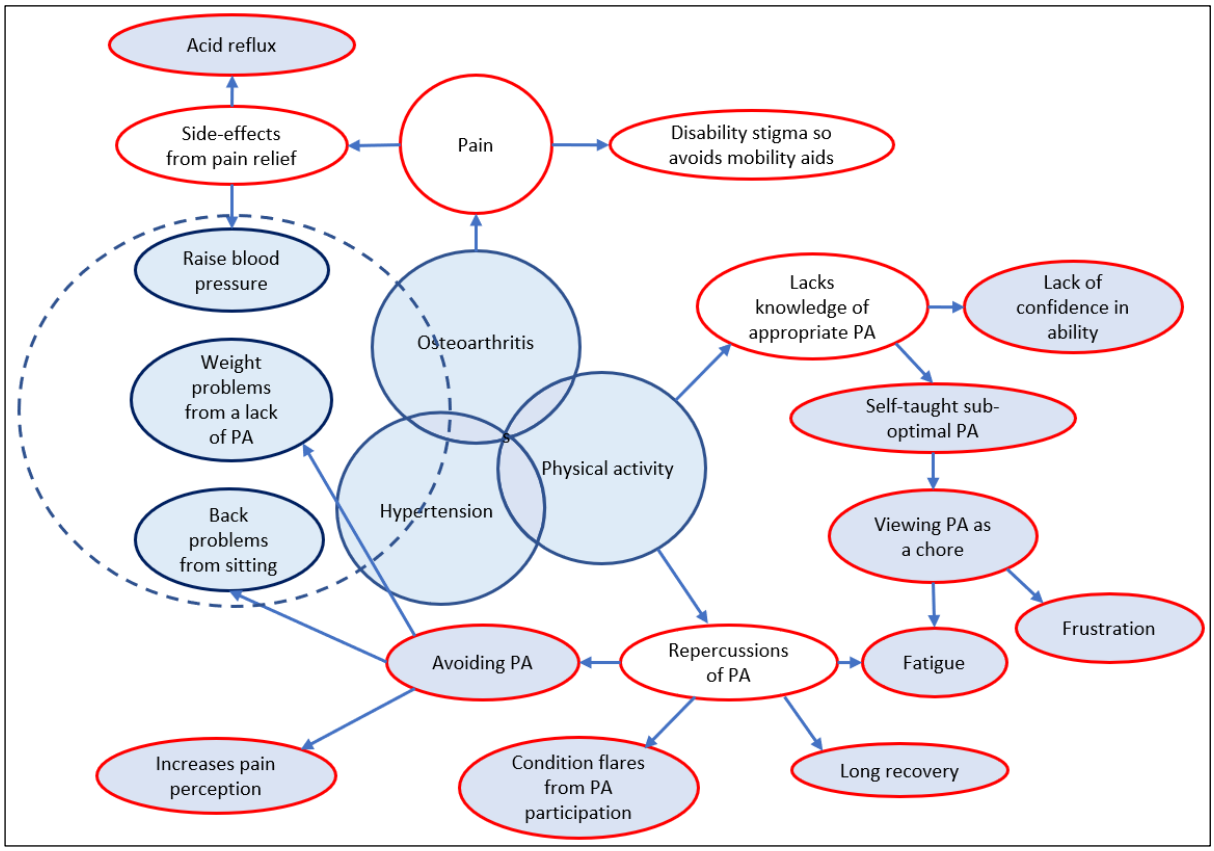


Figure 6.2.4 A summary of Dave's experience of barriers to PA

Barriers to PA also impacted on participants in multiple ways. For example, pain was the most common barrier experienced by participants in the interviews. However, pain impacted PA for different reasons. For example, pain created physiological barriers including ceasing PA ability and fatigue:

> *'It's not like your muscles, if you're cycling and your muscles get tired, you turn back. With cartilage, you can be perfectly happy for an hour and suddenly you can't cycle' (Alice)*

> *'That level of pain and that level of will power is quite tiring and quite fatiguing' (Dave)*

However, pain could also create behavioural barriers including fear avoidance and demotivation:

> *'I won't do anything that gives me pain' (Rachel)*

> *'It's having the motivation to do it that's difficult, because you know it's going to hurt, and you know it may not hurt on the day you do it, but you know it's going to hurt in the long term, so it has to be something you want to do' (Dave)*

Further, pain also affected psychological domains, by creating feelings of hopelessness and doubt in ability in participants:

> *'Mental as well because you think, oh I can't, I can't do anything you know, and it hurts too much and a lot of people give in' (Vera)*

> *'I have got very little confidence in my knee and the only thing I am confident in is if I do something, it's going to hurt' (Dave)*

6.2.4.5 Solutions to barriers and barriers to solutions

6.2.4.5.1 Solutions to barriers to physical activity in people with osteoarthritis and comorbidity

As described above, multiple barriers to PA exist preventing participants from engaging in and maintaining PA. However, after identifying barriers to PA, participants in this study also identified possible solutions to the barriers that they had encountered. This goes beyond previous work in OA studies, by demonstrating that participants went beyond the initial articulation of barriers and recognised there were solutions available. For example, some participants indicated that despite the disruption often experienced by conditions, a solution to cope was to maintain routines and patterns of behaviour that could encompass PA in their daily life:

> *'Daily routine itself is activity, getting up, going shopping…sometimes, I have to plan when I'm going to go shopping' (Dave)*

> *'I set out errands each day to make me do it…it's why I shop daily, its why on a Tuesday when the cleaner is there I pack my books and go down to café Nero and on the way I got to the gym…deliberately pick longer routes' (Alice)*

> *'Built-in routine, we know where we're going to walk to and where we've got to come back' (John)*

> *'I have patterns…Sunday walk, Mondays yoga, Tuesday the friendship group…things that I enjoy' (Rachel)*

For some participants, barriers such as episodic condition flares, and anticipating PA side-effects, could be solved by being prepared and equipped. For example, participants made sure they had an

alternative transport mode available, they rested in preparation for PA, and took pain relief as a preventative measure:

> *'I have to put enough money in my purse, now, if I've walked to town and I'm not well, I need enough money to get a taxi to bring me back home again (Kate)*
>
> *'If you've got activities that you particularly want to do, I end up resting it before those' (Dave)*
>
> *'Getting up and doing a bit of hoovering...I take the tablet, paracetamol or whatever' (John)*

For other participants, having someone to support them, in both daily life and for specific tasks such as transport, was a solution:

> *'Absolutely bloody awesome husband…he's very supportive about what I can and can't do' (Alice)*
>
> *'My cousin, comes and picks me up and takes me, and I want to spend time with her as well' (Kate)*

Participants indicated that enjoyable activities were a solution to behavioural barriers such as a lack of motivation. For example, participants reminisced on previous activities or emphasised interests and skill development to foster a positive PA experience, rather than focussing solely on the biomedical aspects such as weight loss or disease progression:

> *'we used to walk a lot…we really did enjoy that; it was a day out' (Tim)*
>
> *'I used to play things like squash, but we are going back a number of years, and table tennis which I love…so I really ought to find somewhere that does table tennis and get back to it…Dancing me say would be enjoyable, table tennis I would enjoy…I tried tai chi but I didn't get on with that really. I prefer yoga' (Rachel)*
>
> *'You've got to keep yourself interested in things and keep going…you've got to try and master it a bit, do something, be yourself' (Laura)*
>
> *'Weights…force you to see your body as a machine rather than what it looks like, and that turned out to be really psychologically good for me' (Alice)*

6.2.4.5.2 Barriers to the solutions to overcome low levels of physical activity

Participants endured a complex process of overcoming barriers to reach the goal of PA. As seen in the previous two sections, participants identified barriers and solutions to these barriers. However, a further, subsequent barrier then appeared as a *barrier to the solution*. The way participants in this study problematized PA was, therefore; initial barrier, a solution to the barrier and, a barrier to the solution.

Karen is a good example of participants presenting barriers to solutions for being more physically active. Karen has OA, cancer, depression and back pain and illustrates how participants problematize the barriers they face when considering PA. She perceives there are initial barriers to PA, but also some solutions to these barriers. However, she then perceives further barriers to her solutions. This is outlined in the excerpts below:

> *'I daren't, I'm frightened to go like, Kathleen, goes to a gym and she's asked me go there and I daren't just because of the pain in my back, I just daren't, I'd like to go out, do it, because as I say with Kathleen, because my back, um, because as I say, you know even if I walk around a lot, I'm in that much pain, I'd be frightened of my back' […] 'I wouldn't mind going in the hydro pool again, things like that, if it was suggested to me that it could help me, that's the main thing. I don't want to go things that will do me damage. I think up here, well if I go, it's probably going to make my back worse, that's what I'm frightened of' [...] 'I haven't got the confidence to go on my own'*
>
> *'If somebody's with me, I'd have a go at anything really…I've never been a gym in my life… I'd like to go…I wouldn't like to go on my own' […] 'I could go with Kathleen, you know. Yeah. Yeah. you see, there again going this keep fit' [….] 'I'd like to go to the keep fit class, yeah, because a lot of the girls form the craft club go as well'*
>
> *'But. Yeah. Nobody comes, lives up here you know' […] 'I've got a motorized scooter, and I'm frightened of it! a little boy walked out in front of me, there's no breaks on them, you just have leavers…I've got no confidence on it' […] 'If I had a taxi, it would cost me 6 pound to go…we pay so much for transport but I think for where I've got to go it's a lot of money, if I could, depend on the buses, I would, I can go on a bus there and a bus home, but it's getting there*

and back…I daren't go and wait for a bus, the time to wait for bus, because my legs give way underneath me, unless you know the bus, and sometimes they don't turn up you know' (Karen)

Karen has a fear of damaging her back and lacks the confidence to go to the gym or other PA opportunity on her own, which are her initial barriers to PA participation. Karen's friend goes to the gym, and her other friends go to a PA class, which appeals to Karen, as friends are a support mechanism for her and it would be run by a professional, which could instil confidence in the safety and provide a socially supportive environment, the solutions to her initial fear barriers. However, she identifies a new barrier to participation, in the form of access and transport. She is frightened of an accident on her mobility scooter, she can't wait for buses, taxis are expensive and there's no one to provide her with other transport.

Participants identified clubs and group activities that they would like to attend but couldn't get to, before suggesting modes of transport to help with access, but then spoke about reasons why that would not help, as illustrated from the excerpts from Jackie below:

'there's all these lunch clubs…and all sorts of activity going on, but I can't get there and I can't get back' […] 'and you know I've even thought of a taxi' […] 'but then I thought, I can't do that because I don't know where a taxi is taking me. And It's frightening…I need a wheelchair to go any reasonable distance…but I've got nobody to push the wheelchair so I can't go' (Jackie)

The complexity of tackling barriers to PA, such as transport, was also illustrated by Kate. Kate was initially hindered by her function and mobility, but her granddaughter helped her to get out by providing transport. However, this made her dependent on her granddaughter, and she did not want to use walking sticks as an alternative, to help her function with independence, so instead, she suggests she could do a PA class, but, her cousin doesn't like that and without her cousin, that seems unattainable:

'I feel a bit depressed about it almost because I know I can't function…where I want to function […] 'at the moment, you see, I'm not even, I was making myself go for a walk into town, but I haven't done that for a little while…'

'my granddaughter is coming around tomorrow, she'll take me to the shops, so I'll walk around the shops then…but other than that, I'm walking round the house, perhaps up the stairs, down the stairs, things like that'

'I don't want to be walking down the road with sticks, and that probably sounds silly to you, but I don't, I don't like to do it…I don't want to be seen as some poor old weak old thing that needs sticks to get down from A to B'

'I could join umm, I could join umm a group…I want to do aqua aerobics as well, because I think that'd be very good for my condition…to do some physical movement' […] 'I would've been better off going to the church and doing the exercise' (keep fit group)

'but because of my cousin, comes and picks me up and takes me, and I want to spend time with her as well and she doesn't necessarily want to do that, keep fit thing' (Kate)

Another example from Jane, who was a participant that experienced the fear of falling previously described. Jane realised a solution for her fear of falls and lack of transport could be the use of PA equipment at home but was confronted by uncertainty and a lack of knowledge:

'what worries me is falls, because my balance now is very bad…I do wish somebody could invent something that they could give you so it'd help your balance' […] 'there's a class along London road…But I feel as though it's just a bit out of my reach…Because I don't drive and everything that I do I've got to make my way on foot'

'after I'd had my heart attack, I went on a 6-week course up at the hospital, eh an exercise course…it was on various machines you know… I have thought about getting an exercise machine of some kind'

'but I'm not sure what kind of machine I would have to get' (Jane)

It is important to highlight that the multiple, co-existing barriers to PA and barriers to solutions, were vocalised by the participants, but they did not collate them as an integrated experience. From threading the interview barriers together, as depicted in the example diagrams of analysis (appendix 26), it is clear that the multiple barriers were from the experience of having multiple LTCs (bold text), but participants did not seem to connect them together;

*'I could walk that, but I couldn't walk there, do the activity and get back home again […] I don't want to be walking down the road with sticks…seen as some poor old weak thing […] and I definitely can't drive…my **visions** not brilliant […] I did go to the hospital for a little while…to do exercise because I had a **frozen shoulder**…but because my **hip** was getting worse, it was too difficult for me really […] because of my hip, I can't get up and go…there's something you want to do and then you're waiting and waiting, the moment's gone […] pain does impact but I don't like taking pain killers…cocodamol has other side-effects like **constipation** […] if you've got **Raynaud's**…all you can think about it keeping warm isn't it…but if I had medication for my Raynaud's, apparently it will impact (negatively) on my **blood pressure** […] my blood pressure bothers me because obviously I could fall over at any given time […] **palpitations** when they happen, they frighten me…I think, oh, I feel a bit dizzy now […] my **thyroid**, I don't know whether that makes me tired…I am exceptionally tired…' (Kate)*

6.2.5 Facilitators of physical activity in people with osteoarthritis and comorbidity

6.2.5.1 Social support

Social support has been included in some guidance for the management of OA (e.g. ACR, 2012). The interview findings concur with the need for this, as social support was a facilitator for engaging in PA and appeared as general encouragement, confidence booster and shared learning from others:

'Having other people…you encourage one another, you can lift your knee a bit higher you know? You can encourage one another' (Tim)

'You can learn so much…from other people… it's meeting them, and speaking with them' (Kate)

The key aspect of social facilitation for this group was having a homogeneous group of people together (e.g. with similar experiences of their conditions). Participants felt that having a group of people who could empathise with each other, and positively compare relatable PA experiences, would facilitate learning specifically according to their conditions and instil confidence in their current and future abilities. This made the typical aspects of social support relevant to their specific circumstance:

'The opportunity to exercise with people with the same complaint…There's got to be a lot more than me, with exactly the same problems that I've got…getting that group of people

together…for that particular complaint…'Oh I can lift me knee this far' and 'I've started doing this one and that one'' (Tim)

'People, with the same kind of condition…how they manage things, I think that would be useful, and what kind of things they did' (Rachel)

'Most of the people in the exercise class are my age…most of them have got something wrong with them…it helps me socially…and umm, you know the exercise helps me besides' (Jane)

'Well people with a like condition, people who share your misery basically!... it might spur you on to do more, or you might think I'm doing jolly well here, because they aren't doing so good! So, on two levels!' (Kate)

'People will actually listen to people who are only a few steps ahead of them, where they won't listen to somebody who appears to be something they couldn't possibly aspire to be' (Alice)

6.2.5.2 Healthcare professional support

Although the participants emphasised the need to be in a group of homogeneous people, they also needed the instructors to be knowledgeable of them as an individual, capable of advising PA inclusive of their conditions and unique circumstance:

'They just have to come see me and say, right that's your condition, if you do this, you know' (Tim)

'An instructor who, understands your condition…better than somebody who hasn't got a clue what it's all about…so they would know your limitations…to devise a programme around, various conditions that existed within the group' (Kate)

'Tailored to the people who would come to the class, and you can't really make a program until you have met everyone' (Vera)

'I think the prescription idea for exercise is excellent…I'd want to know that whoever was taking it, actually, understood chronic pain' (Alice)

Learning how to do PA that was best for the individual person, came down to the instruction and guidance. Participants valued both relatable, and professional opinion and input, especially through face-to-face contact, to instil confidence in their ability to participate in, and self-manage PA;

> *'Mentor programmes maybe…you could actually start to set things up, so you start people on a kind of conveyor belt at which a certain point you ask them to come and be a mentor' (Alice)*

> *'There would be someone there from the NHS…just to make sure you're alright…If there's a professional doing it, yes, I would certainly consider it and give it a go…someone who knows what they're talking about…a physician or…I mean the people that run the, our, they're volunteers, they've been trained but they're not professional' (Debbie)*

> *'Start with is a first meeting in person, and maybe a meeting in person once a week…talking you through it…but something about that interacting with somebody else helps you think about it, helps you embed it…so it's that focusing on the interaction' (Alice)*

6.2.5.3. Physical activity mode and type

The mode of PA was important to the participants in overcoming barriers identified in 6.2.4 above, such as having multiple appointments, time-consuming treatments, exhaustion from conditions, symptoms and treatments. For example, making a routine that fitted PA into daily life (as a mode of treatment) was a facilitator of PA:

> *'I set out errands each day to make me do it…it's why I shop daily, its why on a Tuesday when the cleaner is there I pack my books and go down to café Nero and on the way I got to the gym…deliberately pick longer routes' (Alice)*

> *'I have patterns…Sunday walk, Mondays yoga, Tuesday the friendship group…things that I enjoy' (Rachel)*

The interview responses also indicate that participants had a preference for an intermittent mode of PA. That is, PA that took on shorter duration, but could be done more regularly, focussing on more general movement and breaking up sedentary time:

> *'There's a tendency for fitness classes to assume three quarters of an hour or an hour and that's actually long for me…I don't often tend to do a whole workout in the sense of stopping and*

doing a workout, I'll do 10 minutes, and then I'll do 10 minutes later, and 10 minutes later on and that's the way to move around…I'd want to focus on small and often' (Alice)

'I have to do a little bit, and then sit, then do a little bit more and then sit' (Jackie)

'I've got a certain amount of exercise and a certain amount of sitting; it was well balanced' (Tim)

'I'd probably have to just do it, ten minutes and then rest a bit you know?' (Karen)

Another common barrier example was access to PA, as described in section 6.2.4 above. Therefore, a key feature of facilitating PA in people with OA and comorbidity was providing access to more readily available, appropriate PA opportunities. For participants in the current study, appealing PA was adaptable to suit their needs. Participants felt that the duration, type of PA, environment and equipment could all be adapted to enable participation:

'If there was like a fun dancing, like a Zumba for seniors' (Rachel)

'If you can't move a lot then chair based activity' (Vera)

'There is a tai chi class locally, but I can't do tai chi as it is, real tai chi, the one that I went to, she adapted…and it makes a big difference' (Debbie)

'Having the equipment to be able to do set exercises…a step, a pole to balance on…walls to lean against' (Dave)

'The treadmill that's it, where you can hold on because it makes a big difference…when you are outside like me, you have to watch where you're walking' (Debbie)

6.2.6 Summary of results

In summary, responses from interviews with 17 participants with OA and a range of comorbidities, resulted in two themes. The first theme was barriers to PA, including key findings of a lack of "comorbidity" conceptualisation and subsequent self-prioritisation of their LTCs, the uncertainty about management of conditions and PA effectiveness for their conditions, negative perceptions about their health, ageing and PA and finally, the co-existence of multiple biopsychosocial barriers, solutions to barriers, and subsequent barriers to solutions. The second theme; facilitators of PA, included support

mechanisms, with focus on social homogeneity and confidence instilled from knowledgeable HCPs, coupled with an adapted PA type that fits into the daily life of living with OA and comorbidity.

6.3 Discussion

6.3.1 Introduction

This section discusses the main findings of the qualitative study and considers them in the context of existing research. The qualitative study's strengths and limitations are outlined before the chapter concludes with clinical and research implications.

6.3.2 Aim and objectives

This qualitative study investigated the attitudes towards, and beliefs about, PA in people with OA and comorbidity. The research questions were designed to provide an understanding of the current experience of PA and how to encourage the uptake and maintenance of PA, in people with OA and comorbidity.

6.3.3 The sample

The participants varied in demographic characteristics including age and gender, as well as comorbidity frequency, type and PA levels. The variation in the sample characteristics allowed for diversity in the interview responses and deeper understanding of PA in OA and comorbidity. The sample comorbidity types included common comorbidities such as obesity and diabetes as well as those less extensively described in the literature such as hypothyroidism and Crohn's disease. This range of conditions is expected, for example, OA is more common among adults who are obese than those of a healthy weight (Turkas, 2012; Dhalwani et al*.,* 2016) and having OA as a condition often results in immobility and increased risk of developing several other LTCs such as T2DM and CVD (Nüesch et al*.*, 2011; Sedjo et al., 2016 Foy et al*.,* 2011; Leite et al., 2011; Rosemann et al., 2008).

All participants indicated that they engaged in some form of PA, but this ranged greatly from household chores to adapted tai chi and organised exercise classes for older adults. Although WHO (2015) state that PA encompasses activities such as household chores, other guidance suggests that people with OA should aim for the recommended 150 minutes moderate activity to gain health benefits (DOH, 2019; WHO, 2015; McAlindon et al., 2013). Participants in the current study were often engaging in activity that was less than moderate intensity, lower than recommendations. This aligns with previous research on the low PA levels of the OA population (Wallis et al., 2013; Herbolsheimer et al., 2016; Holden et al., 2014). Furthermore, most participants had OA and at least two comorbidities. This aligns with the comorbidity frequency results from chapter 5 and with previous research, suggesting that increased comorbidity burden is associated with more limitations in PA and reduced level of PA (Juhakoski et al., 2013; Reeuwijk et al., 2010; Xu et al., 2017; Murphy et al., 2017), which could be why the participants preferred light, household PA, rather than moderate-vigorous level activity.

6.3.4 Barriers to physical activity in people with osteoarthritis and comorbidity

Barriers to PA often originated in the experience of living with OA and other LTCs. A novel finding from this study is that participants didn't talk about comorbidity as something relevant to them (lacked a conceptualisation of comorbidity) and talked about their health conditions overall as existing separately. This has relevance to care as it means that PA is viewed largely as a management technique for each condition in isolation, inhibiting more holistic and joined-up care. LTCs were prioritised by participants based on the impact on their life and this meant OA was often the condition that was brought to the fore. The study found that participants lacked knowledge and were left uncertain about how to manage their conditions together, and of the effectiveness of PA. This experience led to negative perceptions regarding health status, ageing and PA was experienced in the context of this.

6.3.4.1 Lack of concept of comorbidity and long-term condition prioritisation

In the current study, participants found it hard to talk about their conditions together as a combined concept of 'OA and comorbidity' (section 6.2.4.1). A recent report from the Richmond Group of

Charities (Aiden, 2018) raised awareness of drawing upon people's lived experience to understand issues of having more than one LTC, and the need to increase the patient and public awareness of this issue.

Instead of comorbidity, other terms like multimorbidity, complexity and burden, have been readily used by many HCPs and academics (Taskforce, 2018; Shippee et al., 2012). However, such terminology has little functional use in addressing patients with multiple conditions, yielding only a descriptive explanation, without practical applicability for treatment (Taskforce, 2018; Shippee et al., 2012). Furthermore, although some patients with multiple health conditions may find identity in this diagnosis (Møller et al., 2018), most patients do not understand or accept multimorbidity as a concept, can associate it with negative connotations, and report worse experiences with healthcare and negative psychosocial outcomes from diagnosis (Chew-graham et al., 2019; Møller et al., 2018; Paddison et al., 2015).

Therefore, the current study findings support the need for an improved conceptualisation of comorbidity and the need to find ways to talk about PA in light of this. Development of more practical language for this circumstance could provide a better understanding between patients and clinicians, improving communication and shared understanding of patient needs (Chew-Graham et al., 2019). The interview results suggest that HCPs and patients need to work together at the outset, to actively engage patients into conceptualising their conditions together. This may require stepping back in the design and adding this discussion as a component of PA interventions. This aligns with the HOC model, by starting first to understand the person at the centre of the care, before then approaching PA advice and treatment accordingly. Improved comorbidity conceptualisation could subsequently offer a platform for improved patient experience and engagement with healthcare, better organisation of patients' healthcare needs and targeting of interventions such as PA leading to better health outcomes and improved self-care (Chew-Graham et al., 2019; Nardi et al., 2007).

In the current study, patients prioritised their conditions and treatment, to manage daily life. Previous research has shown that patients prioritise conditions themselves, in order of which they deem as the main condition (Morris et al*.,* 2011). Despite the participants in the current study having several LTCs, they mostly perceived OA as their priority, due to a lack of condition control and disruption from pain. The participants also reported OA as a priority because of the interference with mobility and partaking in PA, and subsequent influence on their normal social functioning. Previous studies have found similar results; the results from a survey in primary care found patients described OA as more disabling in life than conditions such as diabetes and hypertension (Alami et al., 2011).

In contrast to patient priorities, HCPs tend to prioritise other conditions above OA (Alami et al., 2011; Egerton et al., 2017; Christiansen et al., 2020). A recent qualitative interview investigation (n=12) found from the HCP perspective, there was difficulty in managing multiple conditions and a tendency to prioritise the other conditions over OA (Christiansen et al., 2020). Furthermore, a previous systematic review from eight qualitative studies, found that the lower priority of OA was a key barrier to its management in primary care because it tends to be trivialised as inevitable by GPs and perceived as a non-serious problem (Egerton et al., 2017).

The lack of conceptualisation of OA and comorbidity and subsequent differences in priorities between patients and HCPs could, in part, be a result of non-holistic healthcare. Specialised areas of healthcare expertise defined around specific conditions, lacks tailoring to patients with comorbidity (Valderas et al., 2011) and may often result in complex and contradictory recommendations (Schoenberg et al., 2009). A consequence of this is fragmented primary and secondary care delivered by specialists who may not be communicating as effectively as they could (Barnett et al., 2012, Smith et al 2013), leaving patients feeling like a ‘shuttlecock’ between various referrals and suboptimal communication (Paskins et al., 2014).

There is a case for addressing the conceptualisation of OA and comorbidity, through conversations and shared decision making, so that patient and HCP priorities could be better aligned (Reuben and Tinetti,

2012). Treatment could then be better synchronised to meet patient needs, but also make patient treatment more manageable from a HCP perspective (Mold et al., 1991; Shippee et al., 2012).

The current study found that although participants prioritised conditions based around which interfered most in their life, these priorities could fluctuate. Previous studies have reported the episodic nature of comorbidity and how this creates burden in having priorities (Simonik et al., 2016; Morris et al., 2011; Cheraghi-Sohi et al*,* 2013). Despite participants focussing on OA, as seen in the results, comorbid acute conditions could create a need for reprioritisation and as such, patient priorities shift. A study by Morris et al. (2011) found patients to identify priorities based on their perceptions of predictability and manageability, and priorities fluctuate according to the episodic nature of many comorbid conditions.

This shifting of priorities, managing various conditions and daily life responsibilities has been previously described as a burden of 'work' (Cheraghi-Sohi et al., 2013). The participants in the current study showed similar patterns of effort and exhaustion from their condition's fluctuations and disruption to priorities and routine, which could overall make PA more burdensome. In OA, similar 'work' from fluctuations in pain, forces patients to change day-to-day routines, which is further compounded by the uncertainty and treatment burden of comorbidity (Simonik et al., 2016). Simonik et al. (2016) found the episodic nature and fluctuating levels of well-being and health crises, negatively influenced patient motivations and decreased PA as a priority (Simonik et al., 2016). This could mean that the burden of comorbidity reprioritisation distracts from a routine of PA and may lead to therapeutic PA being dropped (Cheraghi-Sohi et al., 2013). Therefore, HCPs need to understand patient priorities, strategies and routines in daily life (Morriss et al., 2011) before supporting them on how best to integrate sustainable PA.

In part, a result of the lack of conceptualisation of comorbidity, and conflicting and fluctuating priorities could force HCPs to improvise care (Iserson et al., 2012; McKenna et al., 2013). "Improvised medicine" is a result of circumstances that force HCPs beyond their comfort level (Iserson et al., 2012), such as

healthcare systems that don't accommodate a predictable trajectory and treatment plan for each patient's LTCs (McKenna et al., 2013). Therefore, although the participants often related their PA experiences with their perception of the HCP and communication, the reasons behind could stem further back to the current structure of healthcare systems (Salisbury, 2011; Barnett et al., 2012; Alami et al., 2011; Paskins et al., 2014), which does not accommodate consistent and specific HCP guidance to manage OA and comorbidity. Attempting to follow combinations of guidelines may be excessively burdensome, inefficient and ineffective from both the HCP and patient perspective (Salisbury, 2011). Therefore, with a lack of comorbidity conceptualisation, self-improvised and fluctuating priorities that may not align with HCPs, participants are left with an increased burden of work to self-manage and live successfully with their conditions (Watt, 2017). Furthermore, particularly in the presence of multiple comorbidities and the associated contraindications of certain medications, PA and self-management interventions are even more important in addressing OA symptom relief (Murphy et al., 2017).

6.3.4.2 Uncertainty about the management of health conditions and physical activity effectiveness

Throughout the interviews, there was a theme of uncertainty, about the management of OA and comorbidity, and, uncertainty regarding the clinical effectiveness of PA. Participants reported a lack of endorsement and mixed messages about the benefits of PA for their conditions, which likely impacted on their volition to undertake PA as a treatment for their OA and comorbidities.

The patient-perceived lack of PA endorsement from HCPs as a barrier to PA has been reported before (Paskins et al, 2014; Cuperus et al., 2013), and the patient view that HCPs hold a preference for pharmacological approaches, and a lack of discussion of PA has been referred to as a 'blinkered approach' (Hunt and Papathomas, 2019) which seems to be common amongst the participants with comorbidity. Similarly, a study by Holden et al. (2009) explored physiotherapists' attitudes and beliefs regarding PA and knee OA. Their study found the biomedical view of OA as a degenerative joint disease

may impact on beliefs about the potential benefit of PA in managing conditions and subsequently impacts PA advice (Holden et al., 2009).

Several other reasons could in part explain the lack of PA endorsement by HCPs. For example, Petursdottir et al. (2010) found HCPs had not emphasized the importance of PA because they needed more education about PA for OA and lacked understanding of the factors that pose as internal and external barriers influencing PA behaviour (Petursdottir et al., 2010). This suboptimal guidance about PA for HCPs has been found elsewhere; a UK based survey of 2000 physiotherapists found they were uncertain of the benefits of PA for OA patients (Bennell et al., 2014). This uncertainty was explained by a lack of familiarity with current research and clinical guidelines which left HCPs unsure of what exercises were best, or the optimal type or dosage of PA (Bennell et al., 2014). In a Canadian qualitative study, a lack of PA prescription was principally explained by limited knowledge of PA for OA and a lack of training on PA treatment or delivery (Christiansen et al., 2020). Therefore, the HCP may be ill-equipped to realign uncertainty that patients have in managing their conditions and PA as they do not have the resources to perform effectively in these uncertain situations (McKenna et al., 2013). An implication of this could be that the HCPs are needing to adopt improvised care (as mentioned in 6.3.4.1), due to their own uncertainty, which makes it harder to address and reduce patient uncertainty regarding PA.

Uncertainty in HCPs attitudes and beliefs about PA as a beneficial treatment for people with OA and comorbidity may be a result of deficiencies in the healthcare system, deficiencies in guidance and a lack of relevant evidence for PA in OA and comorbidity. Recent research has defined the clear clinical benefits of PA interventions for OA (Fransen et al*.,* 2015), that PA as long-term treatment is safe (Quicke et al., 2015). In contrast, other studies have explored the risk of PA for the onset of OA, differing across the lifespan (Urquhart et al., 2008). Therefore, it is perhaps understandable that with mixed messages coming from a dearth of research and evidence for OA and comorbidity, some healthcare providers are uncertain about the role of PA and therefore do not actively endorse a

treatment they believe could be ineffective, or even adverse for OA, let alone OA and comorbidity. In relation to the HOC framework (Coulter et al., 2016), HCPs are unsure about giving advice for PA for OA, therefore, some fundamental components in developing care for OA are missing, which precedes the delivery of PA advice when OA patients also have comorbidity.

6.3.4.3 Negative perceptions concerning long-term conditions and ageing, and physical activity

The uncertainty abovementioned, contributed to participants having negative perceptions about whether they could manage their LTCs, a view of ageing that normalises reduced functioning and low levels of PA, and negative perceptions regarding outcome expectancies and self-efficacy for PA as a treatment.

The participants in the study seemed to lack the confidence in their ability to manage their health conditions and PA, which could be due to a lack of knowledge. Many older adults deem PA as inappropriate because of their age, because of their pain and because of the PA setting (Holden et al., 2012). Supporting these findings, the results of a recent focus group study exploring barriers to, and influences on, PA in 22 people with OA found a key theme was a gap in knowledge (Webber et al*.,* 2018). Their findings suggest that it is important to first address intrinsic factors to the individual, such as ageing, personal preferences and their comorbidity status with patient education, to then implement behaviour change techniques, and increase PA levels (Webber et al*.,* 2018).

The participants in the study had a negative view of ageing and normalised their conditions, symptoms and reduced QOL as a result of an inevitable decline in health. This has been found elsewhere; in a systematic review of qualitative studies about the experience of PA in people with OA (Kanavaki et al., 2017), participants expressed a resigned attitude toward PA, due to feelings of helplessness and that nothing could be done to help their condition. This could be important as, in another study, participants were found to rationalise their decisions to reduce and alter activity due to normative ideas around ageing (Mackichan et al., 2013). In that study, pain and functioning increased limitation, impairments and restrictions, but were viewed as normal experiences of increased age and therefore

legitimised reduced activity levels (Mackichan et al., 2013). Therefore, HCPs could have a key role in exploring and challenging patients' negative perceptions of ageing and the symptoms associated with OA and comorbidities, and reduce this important barrier to PA. This could be a challenge, as the current participants, reflective of the general population, had high comorbidity frequency, which could exacerbate this negative perception link between LTCs, ageing and PA.

Furthermore, the participants expressed negative perceptions regarding outcome expectancies and low self-efficacy for PA as a treatment. This ranged from negative views of PA environments such as the gym, perceptions that classes were ineffective, fears of participating in PA, and a negative association with non-functional or unfulfilling PA goals (e.g. weight loss). These negative views of PA could, in part, be due to the perceived dismissive attitude HCPs had toward PA in the study. A previous study also identified a similar finding of a lack of PA and behavioural counselling delivered to patients (Schutzer and Graves, 2004). Patients in that study reported being told to 'be more physically active' rather than being provided with specific guidance (Schutzer and Graves, 2004). A possible consequence from the lack of positive PA endorsement could mean participants are less likely to get the encouragement and communication needed to instil positive perceptions, but rather develop negative beliefs toward PA (Hunt and Papathomas, 2019).

In the current study, a lack of knowledge of the benefits of PA and thus the belief in its treatment effect seemed to be a barrier for participants, presenting as a fear. However, the fear was not often due to the existence of a threat, but rather the inadequacy of PA treatment to cater to the specific needs of those with OA and comorbidity. Concern about the safety of PA has been reported elsewhere (Campbell et al., 2001; Hendry et al., 2006; Holden et al., 2012). Patients with OA can associate the pain following PA participation as negative, worsening their symptoms, and furthering a process of 'wear and tear' (Campbell et al., 2001). Many patients with other LTCs often perceive the symptoms associated with PA as negative (Schutzer and Graves, 2004), but for people to engage in PA, they must believe that the behaviour is both safe and achievable (Hurley et al., 2010) and of benefit to their

conditions and symptoms (Quicke et al., 2017). Previous studies have highlighted the patient need for the accurate understanding of PA participation in OA, acquired through endorsement from HCPs (Hammer et al., 2016; Petursdottir et al., 2010). Therefore, in OA and comorbidity, a link could exist between improving both condition knowledge and PA knowledge, to raise awareness regarding the interpretation of PA side-effects, such as fatigue and muscle soreness, which may be more debilitating with the existence of comorbidity.

This was also found in a recent study, whereby psychological barriers such as depressive symptoms, low self-efficacy for managing OA, pain catastrophising and fear of movement, were experienced by people with OA (Iijima et al., 2018). However, after controlling for pain levels, Iijima et al. (2018) found fear of movement and pain catastrophising were still found to be associated with PA level (Iijima et al., 2018). This could suggest that it is the attitude toward and perception of pain, rather than the pain itself, that is related to PA, which strengthens the need to reconceptualise symptoms of PA as positive, and improve patient ability and self-efficacy to manage their conditions and associated symptoms, to improve PA treatment (Iijima et al., 2018).

In the current study, a negative perception of generic PA participation targets (e.g. weight loss focus), perhaps adds to the non-patient centred, unfulfilling focus of PA participation. For example, the negative perception of PA with a weight loss focus has been reported in the general population (Bruce et al., 2008; Jackson and Steptoe, 2017). A study by Jackson and Steptoe (2017) found that those individuals who had perceived weight discrimination compared to those who did not, led to them being less physically active. This study found that weight discrimination had an adverse relationship with weight-related behaviours such as worse diet and lower PA (Jackson and Steptoe, 2017).

In OA and comorbidity, PA interventions could focus on a range of outcomes other than those such as weight, as independent of weight loss, participants can still gain improvements in health and mobility (Bruce et al., 2008). This is important, as a study by Williams et al. (2018) found that PA became a burden when participants thought of PA as something they ‘have to do’ for their health. In the case of

OA and comorbidity, this situation could be exaggerated as there is so much focus on health outcomes, such as weight loss, that the other positive experiences of PA could be stifled. Too much emphasis on health outcomes could negatively impact on PA participation by weakening personal motivations such as enjoyment, replacing them with additional burden (Beckwee et al., 2015).

6.3.5 Multiple, co-existing and multi-level barriers to physical activity experienced by people with osteoarthritis and comorbidity

In the current study, participants experienced multiple barriers to PA, which co-existed and impacted upon their lives and PA in multiple ways. Numerous barriers to uptake and maintenance of PA in those with OA have been described previously (Petursdottir et al*.,* 2010; de Rooij et al*.,* 2014; Dobson et al*.,* 2016; Jack et al*.,* 2010) including pain, mobility, a lack of knowledge, belief in treatment effect, outcome expectations, perceived importance and PA self-efficacy (Cuperus et al*.,* 2013; Schutzer and Graves, 2004; Paskins et al*.,* 2014; Sperber et al*.,* 2014; Marks, 2012). Also, previous research has suggested similar patterns and combined effects of several co-existing and complex barriers to PA, amplified by, and linked with, the presence of comorbidity (Wilcox et al*.,* 2006).

Biopsychosocial barriers to PA have previously been described as being complex and having interactions among physical, personal-psychological and socio-environmental domains (Kanavaki et al., 2017) which corresponded with the barriers to PA in people in the current study. Figure 6.3.1 demonstrates how in the current study, a common barrier to PA, pain, presented as a barrier to PA in multiple ways. This is important to first acknowledge, as it highlights the challenge of addressing this type of barrier alone, and the need to better understand how just one barrier can impact simultaneously on levels of PA in an individual.

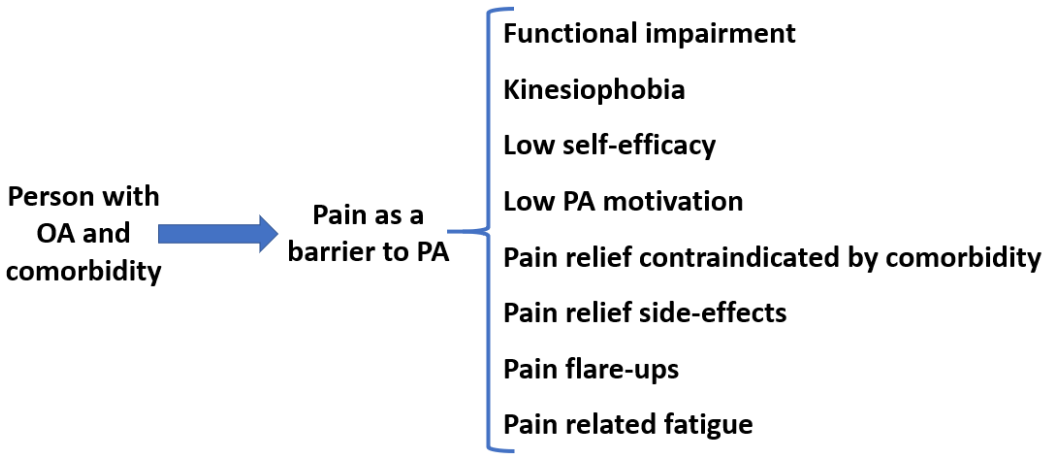


Figure 6.3.1 The different impact of barriers to PA, for example, pain

People with arthritis have also been shown to make 'trade-off' decisions in daily life, as common barriers such as pain, fatigue or competing responsibilities interact, thus reducing regular PA participation (Der Ananian et al., 2008) and increasing drop out from PA programs (Petursdottir et al., 2010). In the current study, a previously unreported pattern emerged which may explain how OA and comorbidity impedes PA participation. Across the interviews, the way participants problematized PA was through a three-level process; an initial barrier to PA was identified, a solution to the barrier was identified, and a subsequent barrier to the solution was identified. More often, the result was a cyclical process of interruption to perusing PA, that opposed any problem-solving progress or solutions to PA barriers. Therefore, it could be said the participants experienced multi-level barriers to PA. The multi-level barrier process is shown in Figure 6.3.2 accompanied by some common examples of multi-level barriers within the interviews.

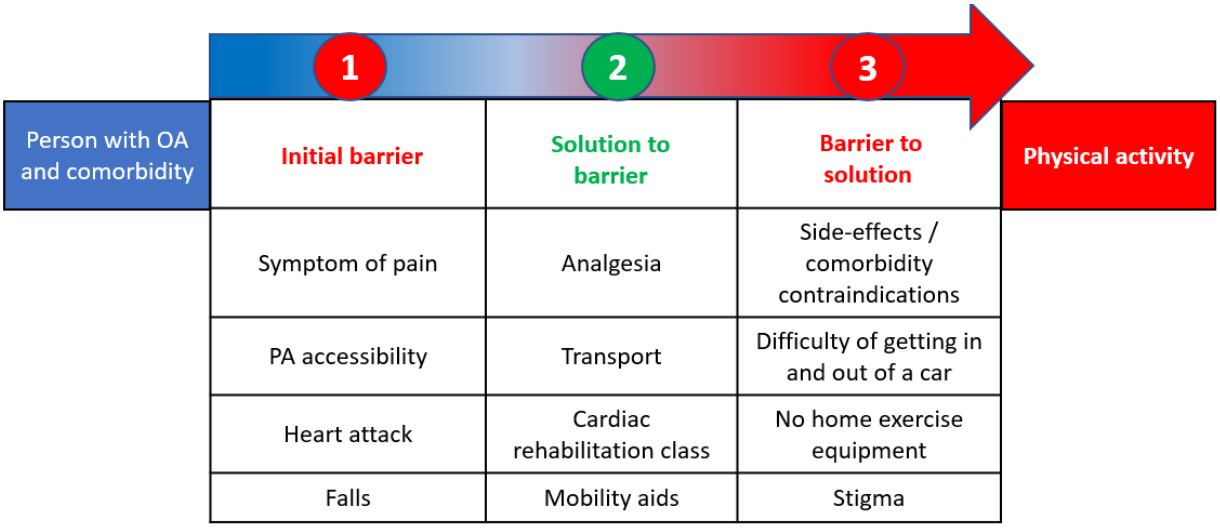


Figure 6.3.2 The multi-level barrier process and common examples of multi-level barriers

This finding draws parallels with patterns of multiplicative and synergistic barriers that have previously been found in multimorbidity patients (Vancampfort et al., 2017). Their quantitative analysis identified a vicious cycle between pain, mobility, sleep problems and subsequent depressive feelings, acting individually and accumulatively as barriers to PA (Vancampfort et al., 2017).

In the current study, a novel finding was the participant experience of barriers to PA, was often a dynamic, multi-level process, whereby in attempting PA*, intending* to participate, they found solutions to barriers, but additional barriers only became evident following a solution (Figure 6.3.3). The Attitude, Social influence and self-efficacy model (ASE) (De Vries et al., 1988) demonstrates how a participant's intention (attitude, social norm and self-efficacy), linked with barriers, can explain PA behaviour. This finding implies that patients and HCPs may need to go beyond discussing initial barriers, and together problem-solve additional barriers that might arise. The HOC framework (Coulter et al., 2016), recommends consultations with a holistic view of the whole patient. However, the multi-level barriers were only evident after threading together disjointed experiences from the participant interviews, as they lacked a holistic view of OA and comorbidity together, as a combined concept impacting their PA. Therefore, a gap remains between the HOC framework for holistic care for people with OA and comorbidity, and how HCPs can address all of the barriers in a consultation, to implement PA behaviour change**.**

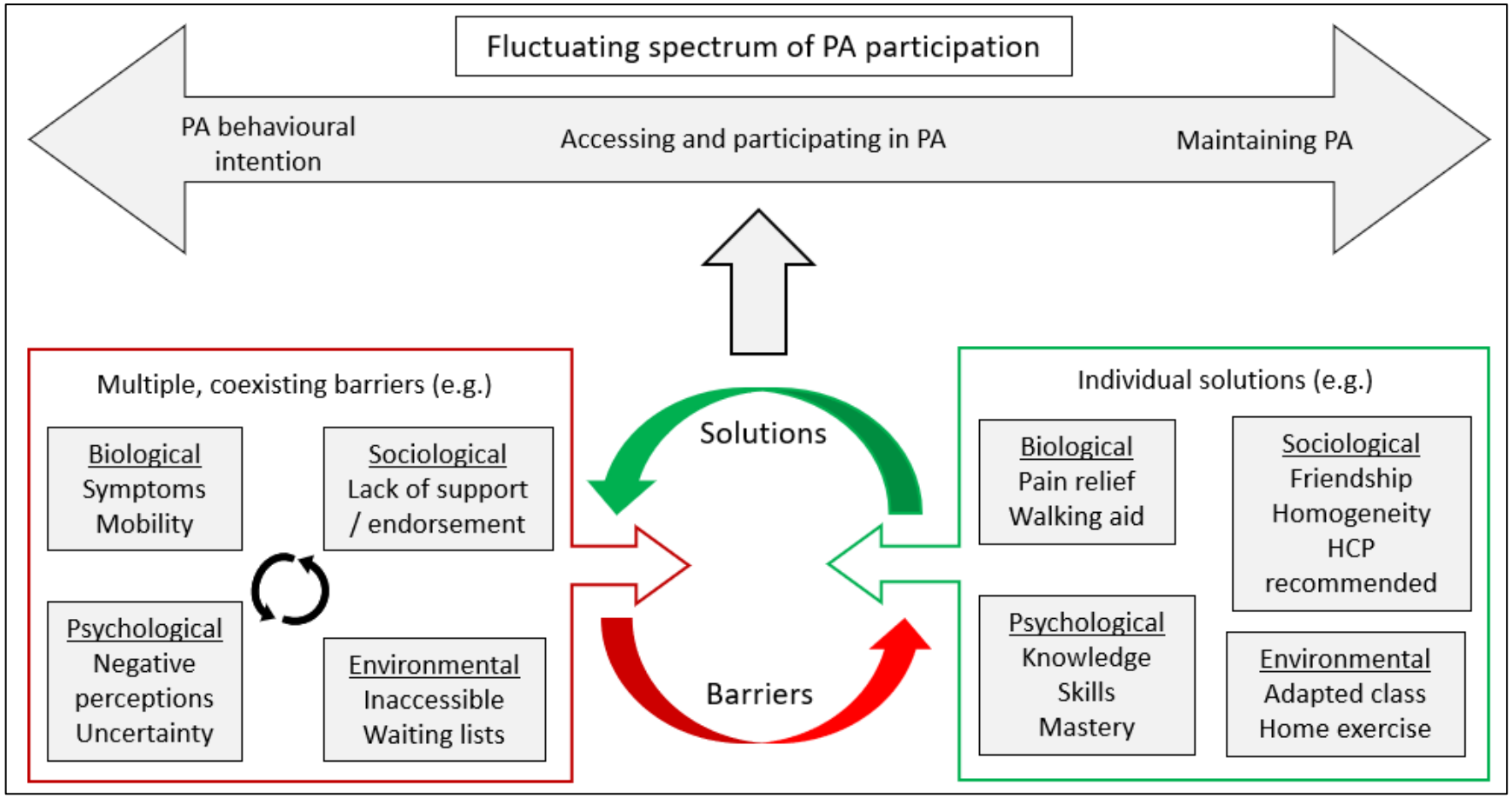


Figure 6.3.3 The existence of multiple, multi-level barriers, and solutions in PA participation

PA=Physical Activity; e.g.=example; HCP=Healthcare Professional.

To summarise the experience of barriers, people with OA and comorbidity are not currently able to reach the goal of regular PA participation. The participants were lacking conceptualisation of their conditions, lacking knowledge of their LTCs and PA, experiencing uncertainty in managing their conditions and the effectiveness of PA, had negative perceptions about the appropriateness of PA for someone of their health, and overall, did not experience barriers to PA in isolation, but in a dynamic and iterative way. The existence of multi-level barriers could imply that PA guidance and interventions need to go beyond identifying initial barriers, fully explore available solutions, and anticipate the barriers to the solutions, to facilitate PA.

6.3.6 Facilitators for physical activity in osteoarthritis and comorbidity

The following section discusses the second theme of results; key facilitators of PA participation in OA and comorbidity. Previous research has reported several facilitators of PA for people with arthritis and OA (Wilcox et al., 2006; Beckwee et al., 2015; Bennell et al., 2014) including social support, organised PA opportunities, professional delivery and knowledge, PA partners, familiarity and positive outcome expectations. In the current study, having social and HCP support, and tailoring and adapting the PA mode and type to fit their life with LTCs facilitated PA, and could offer ways that their barriers and the phenomenon of multi-level barriers could be approached.

6.3.6.1 Social support

Rather than PA being promoted solely based on improving health, participants in the current study were interested in PA that they viewed as being intrinsically enjoyable to them, through social interactions. Social interactions have been reported as a key facilitator in many previous studies (Devereux-Fitzgerald et al., 2016; Farrance et al., 2016; Williams et al., 2018) and in OA, those who perceive that they have good PA support, are more likely to be active (Hendry et al., 2006; Holden et al., 2012). Previous qualitative research following a walking trial found that the support from having a walking partner promoted behaviour, possibly due to the mutual support, enabled discussion, and

companionship (Victor et al., 2016). In contrast, those who believe they do not have support or would have to do PA alone, are likely to see this as a barrier to PA (Holden et al., 2012).

The participants in the current study often referred to 'like conditioned' individuals and people they could empathise with. Other studies (without comorbidity reported) have found the social dimension of PA to be important, as it facilitates enjoyment, positive experiences and therefore provides a "sense of belonging" (Hunt and Papathomas, 2019). By making an activity more enjoyable it can enhance motivation and positive experience and make it more sustainable (Hunt and Papathomas, 2019). This "sense of belonging" could be an explanation for social support as a theme for facilitating PA in the current study. Unlike in situations where people have one condition, in OA and comorbidity, with different healthcare appointments, treatments, experiences, disruptions and difficulties in daily life, the participants could be left not engaging in, or maintaining social activities and becoming more isolated (Gettings, 2010). For some participants, this isolation, accompanied by uncertainty about their conditions and PA, could be an additional factor explaining why there was a desire to carry out PA with 'like-conditioned' individuals and have others empathise with them.

The participants also indicated the value of being referred to a programme by someone relatable (a peer) with OA and comorbidity, who had the first-hand experience, but that this was lacking. Hearing of opportunities and successes, and being recommended by relatable people, could instil confidence in performing the activity (Kaptein et al., 2013). Demographic homogeneity is a term that has been used previously in studies as a sense of community and connectedness amongst groups of shared language, religion, gender and ages (Farrance et al., 2016). Furthermore, previous research has found participants would benefit from meeting in a group by it facilitating normative information about others' behaviour (Normansell et al., 2014). It could be suggested from the findings that people OA and comorbidity place more value on the social interaction in PA, as they are by nature, more likely to experience social isolation from both OA and the complicated and unique nature of comorbidity. Therefore, in people with OA and comorbidity, to make PA more appealing, a sense of belongingness

and new identity through demographic homogeneity (through similar conditions or experiences) could facilitate PA participation. Also, the reciprocal nature of having a homogeneous group could mean that PA would be more targeted toward a specific group of individuals, who could endorse it to the appropriate peer group, to learn and share condition-appropriate information. Furthermore, this could also make the intervention easier to develop and deliver for HCPs, with more self-management abilities, patient activation and shared responsibility.

6.3.6.2 Healthcare professional support

In the current study, participants spoke of how they valued professional support, to aid them in attaining their PA endeavours, such as providing tailored instruction or trusted advice to instil confidence in their abilities, but often, this was lacking. Previous research has shown how HCPs need knowledge about the patient conditions, and the relevant PA, and skill to adapt treatment guidelines to suit the individual patient (de Rooij et al., 2020). Also, continued contact with a physiotherapist has shown a positive connection with PA (Campbell et al., 2001) and previous research has found HCPs must treat patients regularly to properly transfer the knowledge and skills and integrate the strategy into daily practice (de Rooij et al., 2020).

In the current study, patients needed consistent and positive communication, such as shared conversations about PA benefits, between the patient and the HCP, and more PA endorsement from HCPs, to realign patient uncertainty and hesitancy (Paskins et al, 2014). Furthermore, in the interview results, the HCPs play a role as trusted experts in the prescription and delivery of PA. Collaborative HCP-patient communication is important to establish mutual treatment goals, with direction and common purpose (Mair and May, 2014). Forming a partnership by which the appropriate advice and support are delivered, would build patient knowledge and confidence in living with their conditions (Mair and May, 2014). Furthermore, engagement in patient-centred and mutually formed care would better embed treatment into patients' lives, with shared responsibility and minimise patient-burden (Shippee et al., 2012).

In the current study, several findings were related to the participants' experience and ability to manage OA and comorbidity, before relating these experiences to PA. It could be necessary to form beliefs, attitudes and experiences that positively reinforce the participants capacity to self-manage their LTCs (Hendry et al., 2006), before overcoming PA negative perceptions and changing PA behaviour. In an observational study by Olsson et al. (2018), of participants with lower limb OA, the lowest self-efficacy was in people with low education, walking difficulties, low PA level and comorbidity. Therefore, self-efficacy of the participants to confidently manage and cope with their conditions (symptoms, medication, healthcare usage, daily life capacity) could be important as a first step. OA and comorbidity self-efficacy may be especially noteworthy, as managing LTCs and facing challenges associated with them in everyday life could strongly influence whether they are then able to progress to PA engagement.

PA self-efficacy was also found in the participant responses, as they indicated that their need for PA support was to instil confidence in their ability to do PA. As the participants in the study trusted their HCPs, the HCPs could target instilling patient confidence about the safety and effectiveness of PA. Hammer et al. (2016) found in people with hip OA, experiences including inspiration by other participants, encouragement from the HCPs and altered interpretation of PA side-effects contributed to an improved self-efficacy and therefore PA participation. This study also found that self-efficacy was key for the maintenance of PA and a key factor was the disease-specific, individualised support in people with OA (Hammer et al., 2016). Therefore, successful HCP and social support could facilitate positive PA experiences, and stronger self-efficacy for PA (Warner et al., 2014; Marks, 2012).

The study findings suggest that HCP and social support are key influences in both (1) OA and comorbidity self-efficacy and (2) PA self-efficacy, as shown in Figure 6.3.4 below. These constructs are important in facilitating PA in people with OA and comorbidity, and also have relevance to health policy, as they align to the notion of patient activation. Patient activation refers to the knowledge and confidence people have to engage in self-managing their healthcare (Hibbard, 2004; NHS, 2019).

Therefore, both knowledge and beliefs about OA and comorbidity management, and self-efficacy for OA and comorbidity management, are key components of patient activation. This is central to the HOC framework and current policy on LTC management (Coulter et al., 2016). In line with the HOC model, it could be proposed that improving patient OA and comorbidity self-efficacy, and improving PA self-efficacy, could contribute to patient activation and ability to self-manage PA and overcome multi-level barriers to PA (section 6.3.5 above).

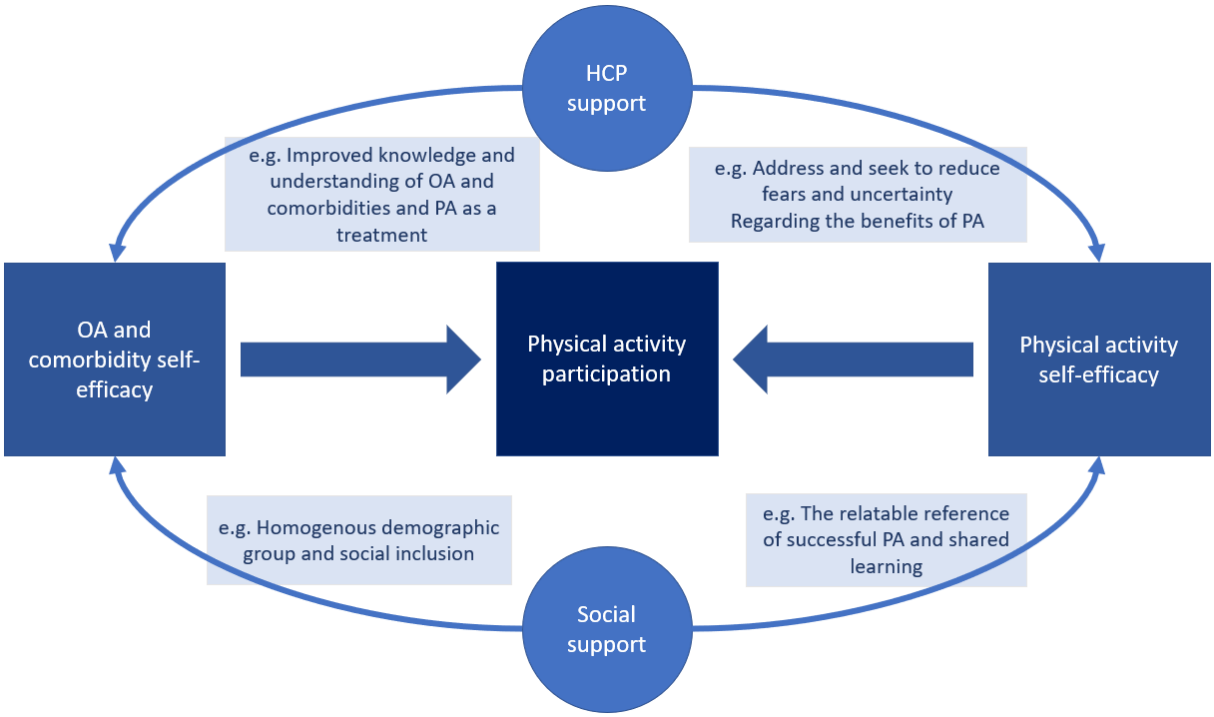


Figure 6.3.4 The relationship between support (HCP and social) and self-efficacy (OA and comorbidity, and PA) in improving PA in people with OA and comorbidity

Middle boxes: the person with OA and comorbidity; circles: external support

Therefore, self-efficacy has been recognised in LTC health policy, and this study provides evidence that this is the case for the population of people with OA and comorbidity. However, in achieving this collaborative process between HCPs and patients, this study has identified how gaps remain, highlighted in the stages below;

1. A HCP-patient discussion about their LTCs, including if OA is the condition priority.

2. Enhancing knowledge and ability to self-manage their conditions (OA and comorbidity self-efficacy).
3. Enhancing knowledge and ability to self-manage PA (PA self-efficacy).
4. A discussion about PA treatment in light of OA, followed by the addition of their comorbidities. However, how HCPs can do this, is unknown.
5. Address the PA barriers at multiple levels.
6. Offer supported self-management and help the patient become more activated, which would mean developing the knowledge and confidence surrounding both their conditions and PA, to increase PA participation.

6.3.6.3 Physical activity mode and type

Adapting the PA mode and type to fit individuals' capabilities and daily routines were identified as facilitating PA in the current study. Programme design, including the mode and type of PA, can include the location, accessibility and affordability of an opportunity (Farrance et al*.,* 2016) but also expand to the structure and content of the PA being relevant and tailored to each individual (Dunlop and Beauchamp, 2013). Many studies have investigated the type and mode of PA intervention in people with OA, but as seen in the systematic review chapter (see chapter 4), few studies have reported interventions for OA and comorbidity, and those that exist, are extremely heterogeneous. Whilst a one size fits all-approach to PA for people with OA and comorbidity does not exist, the following recommendations can be made from this study: PA that is accessible and can be incorporated in daily life, adaptable PA that can be tailored to the individual, an enjoyable experience, with the tailored HCP and social support that can help build self-efficacy for LTCs and PA.

The interviews suggest that adapted forms of familiar PA, appeals to participants, but these opportunities are lacking. Furthermore, participants indicated an intermittent mode, with shorter bouts of PA to fit into daily life was more practical, but currently, they were self-improvising these PA techniques. Previous research found factors that influence non-adherence with physiotherapy include

that the symptoms targeted need to interfere with life enough to deem treatment necessary (priority) and that the treatment needs to be effective and applicable for incorporation into everyday life (Campbell et al., 2001). Activity pacing is a strategy that has been used to modify PA among other LTCs such as patients with chronic pain (Torrance et al., 2011), which considers the balance of improving outcomes whilst reducing the likelihood of exacerbating symptoms (Antcliff et al., 2018). In OA and comorbidity, adopting activity pacing as part of PA management, with planning, prioritising, and adapting activities, could therefore reduce cyclical fluctuations of high and low levels of PA and gradually increase PA level (Antcliff et al., 2018). Above all, the participants were interested in PA they would enjoy, whether it reminisced on previous activities, emphasised interests, skill development and, most prominently, socialisation, which could foster a positive PA experience.

Other interventions to change PA behaviour have previously adopted the self-efficacy theory (Bandura, 1997), and components of self-efficacy theory have been used successfully in interventions to enhance PA level in people in the community (Marks, 2014) and OA populations (Hughes et al., 2004). A feasibility RCT of 26 people with OA and obesity combined PA with self-efficacy counselling strategies (Schlenk et al., 2011) which found it was feasible and could improve PA and physical function (Schlenk et al., 2011). However, this study combined many different PA and non-PA intervention components that make it hard to determine which aspects were effective. Further, the reciprocal is true; a systematic review by Marks (2014) found several interventions using PA benefited arthritis self-efficacy and subsequent symptoms favourably, which included interventions using; aquatic exercise, PA and dietary weight loss, PA and education, tai-chi and Yoga. Those with higher self-efficacy exhibit greater efforts to attain and master behaviour change and are more persistent in the face of obstacles such as barriers to PA (Shin et al., 2006; Van Do et al., 2015).

Therefore, the results of this study could suggest that including components to enhance self-efficacy for condition management and self-efficacy for PA (e.g. motivational counselling) as part of an intervention that could be integrated into their daily life, could be equally important to consider in the

design, rather than solely focusing on the PA type. By combining the above-described strategies for enhancing self-efficacy, such as strengthening condition and PA self-efficacy, particularly focusing on the perceived barriers, PA treatment could be more effective and more sustainable for people with OA and comorbidity.

6.3.7 Strengths

To my best knowledge, this is the first interview study to specifically explore the attitudes towards, and beliefs about, PA in people specifically with OA and comorbidity. This study has several strengths in the choice of design and analysis; the criterion purposive sampling strategy used ensured that a range of individual demographics were included in the interviews, such as diversity of comorbidities (both physical and psychological), and variation in the frequency of comorbidities, which makes the results more transferrable (applicable to populations beyond this sample). The involvement of the PPIE group in the design of the research process ensured that important issues to people specifically with OA and comorbidity were addressed and prompted through the co-designed topic guide. The interview guide was piloted and underwent a rigorous process of discussing the pilot interview findings, making it more trustworthy and credible. The use of the flexible framework approach enabled a deep insight into the experience of living with additional comorbidity alongside the primary condition, OA. The input from the supervisory team (CJ, JQ, EH) throughout the process of interviewing, analysing and interpreting the data helped to ensure that the codes, themes and results were reflective of the participant views. After attending a training course for NVivo, the choice to manually code the data by Word and hand was mostly owing to the closer engagement with the data. Although this choice lacks the sophistication of NVivo software, this method felt more engaged and methodical, with an emphasis on a more flexible process, to focus on depth and meaning in the data. Furthermore, the addition of other analysis strategies, such as a code book, memo recording and drawing diagrams assisted in the interpretation of the data.

6.3.8 Limitations

The sample was selected from a small region in North Staffordshire; therefore, this population may be different from other areas within the UK. The interviewees were purposefully selected to represent individuals with a range of personal, namely comorbidity characteristics, though may differ in their attitudes and beliefs to those who did not volunteer themselves for an interview study. The participants were all Caucasian, mostly female and of an older age in the desired age bracket of 45 and over which may limit the generalisability to other patient groups. It is acknowledged that my presence as an interviewer may have influenced the participant responses and produced socially desirable responses. For example, participants may report higher levels of PA if this is perceived to be socially desirable. Also, despite the benefits of having a flexible interview guide to enhance depth in the interview, participants could steer the discussion toward topics that they were particularly interested or focused on. Thus, with a complex research topic and several aspects contributing to the research themes, it was difficult to maintain focus on the experiences and topic of PA whilst remaining in the context of OA *and* comorbidity. Conceptually, participants tended to focus on one condition in isolation, which reiterates the need to review the branding and conceptualisation of terminology surrounding multimorbidity, complexity and comorbidity. The use of manual analysis is perhaps less transparent than the use of NVivo data management tool, which was considered as a means to store, code and report the data. NVivo has several strengths including a huge range of analysis functions and methods, with clearly labelled and structured coding that allow for the transparent tracking and re-tracing of steps, which makes it well suited to collaborative analysis, but was not used in this study.

6.3.9 Clinical implications

There is a need for more clarity in the concept of comorbidity, for both patients and HCPs. NICE OA (2014) guidelines recommend holistic assessment of a person with OA including a discussion of the risks and benefits of treatment options, which take account of comorbidities. However, the findings of this study show that people with OA and comorbidity perceive a lack of understanding from both HCPs

and themselves about how to manage LTCs but also about PA as a treatment option. HCPs may benefit from more guidance regarding how to support people with OA and comorbidity with tailored PA. Patients with OA and comorbidity may require additional time together with HCPs developing plans to achieve tailored PA including time to develop problem-solving skills to overcome future multi-level barriers to PA. One way this could be achieved would be through consultations that take a more patient-centred approach, looking at the whole patient, rather than diseases in isolation, to encourage active patient engagement. Furthermore, knowledgeable HCPs need to apply techniques that foster improved self-efficacy for patients to self-manage their conditions and foster PA behaviour. Similarities in the participant experiences and PA preferences could direct future treatment approaches, to be tailored toward a homogeneous group with similar priorities and disruptions to their lives, with relatable social support and shared learning experiences. Finally, from the results, it could be suggested that HCPs could first target the condition self-efficacy, by increasing knowledge about OA (e.g. risk and causes), knowledge of their comorbidities, negative perceptions about OA, LTCs and ageing, and the uncertainties about managing OA and LTCs, before offering strategies to improve PA self-efficacy, to enable patient activation in PA treatment.

6.3.10 Research implications

The key findings from this study can be used to add to the understanding of PA in the context of OA and comorbidity. The results suggest that more research is required to investigate how to talk about the issues of living with more than on LTC and how to make PA a viable option as part of core care for people in this group. They also support recent research and opinion (Chew-Graham et al., 2019) that makes the case for rebranding the terminology used to capture the experience of multiple co-existing health conditions. Furthermore, research exploring the reasons for the perceived discordance between the clinical guidelines (NICE, 2014) and the care received by patients with OA and comorbidity (e.g. a lack of understanding of the benefits of PA) could provide understanding as to why there is deviation from the guidelines. Further qualitative research with HCPs could help understand their attitudes towards, and beliefs about, PA in people with OA and comorbidity, including what they

perceive as barriers and opportunities for recommending PA and increasing self-efficacy for PA. More research is indicated of how to deal with the complex nature of problem-solving barriers to PA and the multi-step process that occurs, and how supported self-management can embed PA barrier problem-solving in consultations. As the two key facilitating factors for increasing PA were social support and HCP support, future research is needed to develop combined approaches that include these components to facilitate both condition self-efficacy and PA self-efficacy, and thus, better equip people with OA and comorbidity to deal with multi-level barriers and improve PA participation.

6.3.11 Conclusion

In conclusion, there are key outcomes to highlight from this qualitative study. Patients seem to lack conceptualisation of comorbidity and so it was hard to discuss PA in this context. There remains uncertainty about the relevance of PA as a treatment in people with OA and comorbidity. The concept of 'multi-level' barriers to PA in OA and comorbidity has emerged, which gives a new lens to view the way barriers to PA are problematized.

Also, with a lack of comorbidity conceptualisation, participants prioritised their conditions based on the disruption to their lives, namely what impeded their social functioning ability. There is still a need to focus on OA as a starting point in consultation, as there is a lot of uncertainty about the role of PA for OA in this group. Therefore, it is important to ensure PA treatment is appropriate and effectively tailored for people with OA, before then adapted and tailored taking account of their comorbidities. Further, participants did not respond well to a prescriptive, non-holistic approach to PA, as it was instead perceived an additional burden. Participants strived for belonging and demographic homogeneity (people who were 'like-conditioned'), which could instil confidence in both their condition self-efficacy and PA self-efficacy. In applying aspects of self-efficacy theory in PA interventions, HCPs and social support mechanisms could better support participants to anticipate and overcome multi-level barriers and increase PA participation.

6.3.12 Chapter summary

This chapter described a qualitative study to investigate the attitudes towards, and beliefs about, PA in people with OA and comorbidity, to understand their experiences and seek ways to improve their PA participation. There was a good balance between breadth and depth of participant characteristics through 17 interviews with people with OA and a range of comorbidity frequencies, types and PA endeavours. Although the population was mostly Caucasian females. Comorbidity as a concept in qualitative research was complicated to hold as the main topic throughout the interviews, as participants found it a challenge to relate their experiences in the comorbidity context. This qualitative study highlights that barriers to PA are more complicated and dynamic than previously reported in people with OA and can be multi-level. Currently, the management of LTCs in the HOC model emphasises collaborations between HCPs and patients to encourage self-management (Coulter et al., 2016). However, the patient responses in the current study indicate that this is not currently happening. It suggests an opportunity to improve PA levels through targeted interventions to increase self-efficacy for OA and comorbidity management first, before targeting the same features in self-efficacy for PA, through a model of self-efficacy and support.

The results from the three thesis studies have now been presented and discussed; (1) the systematic review, (2) the secondary data analysis study and (3) the qualitative investigation. The next chapter of this thesis (chapter 7) will bring together the findings of these three studies, in context of the whole thesis picture, to make recommendations about how to improve PA in people with OA and comorbidity.

Chapter 7

Thesis synthesis

Chapter 7. Synthesis of findings and discussion

7.1 Introduction

This chapter summarises and synthesises the key findings from each of the three thesis studies. The findings are discussed in relation to future research and clinical practice to make recommendations for future interventions, to better support people with OA and comorbidity to successfully self-manage and increase PA. The strengths and limitations of the thesis are discussed, before making overall thesis conclusions.

7.2 Thesis rationale revisited

In the UK, approximately a third of all adults aged 45 and over have OA (ARUK, 2015) and this prevalence is likely to increase because of obesity rates and the ageing population (ARUK, 2017; NICE, 2014). People with OA are more likely to have comorbidity than those without the condition (Smith et al*.,* 2016; ARUK, 2015); the proportion of people with OA reporting various comorbidities ranges from 68 to 85% (Zambon et al., 2016), which is linked to greater disability, functional limitations and reduced QOL (Van Dijk et al*.,* 2009; Kriegsman et al*.,* 2004; ARUK, 2017; Dhalwani et al*.,* 2016).

Despite clinical guidelines recommending PA in the form of therapeutic exercise for people with OA (NICE, 2014; OARSI, 2014; EULAR, 2013), and the well-associated health benefits, such as reduced pain, improved function and increased QOL in people with OA generally (Fransen et al*.*, 2015; Felson et al*.,* 2000; Kanavaki et al*.,* 2017; Dallosso et al*.,* 2018; Uthman et al*.,* 2013), the effectiveness of PA on clinical outcomes for people with OA who specifically also have comorbidity, is unknown. To my knowledge, this thesis is the first time that RCT evidence regarding the effectiveness of PA interventions for OA and comorbidity has been systematically reviewed.

In addition, PA levels in people with OA are lower than PA guideline recommendations (Holden et al*.*, 2015; Wallis et al*.*, 2013; Bennell and Hinman, 2011; Dekker et al., 2009) and comorbidity has previously been suggested as a barrier to the successful prescription, uptake and maintenance of PA

in people with OA (Theis et al*.,* 2016; Loza et al*.,* 2009; Schoenberg et al*.,* 2009; de Rooij et al*.,* 2014). However, the relationship between comorbidity presence, frequency and type as the independent variable, and PA level in people with OA had not been investigated in detail.

Furthermore, despite comorbidity emerging as a theme in OA and PA qualitative research (Paskins et al., 2014; Hurley et al*.,* 2010; Marks, 2012), it had not been investigated as the key topic in qualitative interviews, and therefore it was not fully understood why or how comorbidity impacts on PA levels in people with OA. By addressing these research questions this thesis sought to contribute to a new understanding of how people with OA and comorbidity could be better supported to self-manage and increase PA levels in primary care.

7.3 Thesis aim and research questions revisited

The thesis aimed to investigate the impact of comorbidity on PA and clinical outcomes in those with OA in primary care. To fulfil this research aim, the following research questions were raised;

1. What is the effectiveness of PA interventions for people with OA and comorbidity?
2. Is comorbidity associated with PA levels in people with OA?
3. How do people with OA experience PA in the context of comorbidity?

7.4 Thesis key findings

This multi-method thesis used quantitative and qualitative approaches in a multi-phase manner (described in chapter 3) with each study conducted and concluded, independently of each other; (1) a systematic review, (2) secondary data analysis and, (3) a qualitative investigation. Key findings from each independent study are highlighted and summarised in Table 7.1. Following this, a joint display (Table 7.2) outlines quantitative and qualitative findings data side-by-side with further meta-findings. Integrated findings are reported with accompanying statistics, themes and example excerpts, before integrated meta-inferences and insights are made (see chapter 3, section 3.5.4) These two tables of results are then narratively described, as a unified whole (Guetterman et al., 2015).

Table 7.1 Thesis key findings

Study 1. ***What is the effectiveness of PA based interventions for people with OA and comorbidity?***
• 14 RCTs (n= 4224 participants) were identified that specifically included samples of people with OA and comorbidity • Most evidence related to people with knee OA and obesity • In people with knee OA, PA interventions lead to mixed trends of small, mostly non-significant improvements in clinical outcomes in people who also have; obesity (pain, function (significant result for 6MWT) and QOL), T2DM (pain and function) and depression (QOL) • PA interventions tailored to people with knee OA and multimorbidity, improved pain and function with statistical significance as measured by the WOMAC and 6MWT, but not the SF-36 function measure • The studies identified were heterogeneous, making it hard to determine optimal PA interventions for people with OA and comorbidity
Study 2. ***Is comorbidity associated with PA levels in people with OA?***
• Comorbidity presence was associated with lower PA level in people with knee OA • A potential dose-response relationship exists with PA levels decreasing as the number of comorbidities increases in people with OA • Distinct comorbidity types had different magnitudes of association with PA level in people with OA. CVD was consistently significantly associated with a reduction in PA level across both datasets • The impact of comorbidity on PA levels appears to be influenced by how comorbidity is measured
Study 3. ***How do people with OA experience PA in the context of comorbidity?***
• OA is the main concern for participants with LTCs due to the disruption it causes to daily life, social functioning and QOL • People with OA and comorbidity discussed PA in the context of isolated conditions, rather than in the context of having OA and comorbidity. There was a lack of "comorbidity" conceptualisation • Multiple barriers to PA include uncertainty regarding the management of LTCs and the clinical effectiveness of PA and negative perceptions including low self-efficacy for both managing OA and comorbidity and PA • PA barriers co-existed in every participant and impacted them in more than one way. Participants problematised their experience of barriers in a multi-level process identifying initial barriers, solutions to barriers, and barriers to solutions • Support mechanisms were identified as facilitators to help improve PA levels in people with OA and comorbidity. First, a PA peer group that provided demographic homogeneity and shared learning, and second, supervision and tailored advice from informed HCPs, to instil confidence, help re-align uncertainty and negative beliefs regarding (1) OA and comorbidity, and (2) PA

OA=Osteoarthritis; PA=Physical Activity; HCP=Healthcare Professional; RCT=Randomised Controlled Trial; n=number; QOL=Quality Of Life; PASE=Physical Activity Scale for the Elderly; T2DM=Type Two Diabetes Mellitus; CVD=Cardiovascular Disease; 6MWT=6-Minute Walking Test; WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index; SF-36= Short Form health survey

Table 7.2 A side-by-side joint display of findings and meta-findings

Topic	Systematic review	Secondary data analysis	Qualitative interviews	Integration	Meta-inferences and insight
Meta-finding 1: Research and treatment using PA for OA needs to be inclusive of comorbidity					
Comorbidity is common and impacts PA, but often disregarded. Comorbidity types such as CVD require further investigation	Only 14 RCTs identified investigating PA interventions for OA and comorbidity 10 out of 14 included RCTs were focused on OA and obesity	Comorbidity presence: 66%; 52% (B; M) Comorbidity associated with PA level: e.g. −32.25 (−48.57, −15.93) (B) CVD associated with PA level: β= -27.15 (-53.25, -1.05) (B) β= -30.84 (-51.89, -9.80) (M)	N/A	Divergent	Research in this population is lacking despite comorbidity being highly prevalent in OA and associated with lower PA level. Need for research explicitly investigating the effectiveness of PA tailored for OA and comorbidities other than obesity.
PA may be clinically effective, but results are mixed and uncertain	PA interventions may improve clinical outcomes of pain, function and QOL, but current evidence is inconclusive	N/A	HCP preference for pharmacological treatments; *'They put me on the morphine tablets, and nobody has ever recommended anything else for it' (Jackie)* Theme: lack of comorbidity concept Theme: multi-level barriers	Expanded	PA may improve clinical outcomes in people with OA and comorbidity, but the results in the SR are mixed and thus, uncertain. Further, PA is not consistently being endorsed by HCPs in clinical practice. This could be, in part, due to the lack of conceptualisation of comorbidity and interventions not currently including strategies toward dealing with multi-level barriers or how they are problematised.
Comorbidity frequency could be important to consider	N/A	Two comorbidities significantly associated with a decrease in PA level β= -34.76 (-56.05, -13.48)(B)	Theme: Multiple, multi-level barriers existed to PA, beyond those reported in OA only research, potentially due to the existence of multiple comorbidities	Convergent	The evidence indicates that the frequency of comorbidities alongside OA could be an important consideration for future research. There may be a relationship between additional comorbidity and multi-level barriers to PA, but this is unknown.

		β= -26.84 (-49.30, -4.38)(M), greater than one comorbidity e.g. β=-24.4 (-42.5, -6.4)(B)			
Comorbidity influences the experience of OA	People with comorbidity had worse baseline pain than OA only	N/A	Pain key barrier which impacted in multiple ways; *'That level of pain and that level of will power is quite tiring' (Dave)* *'I can't do anything you know, and it hurts too much' (Vera)*	Expanded	Comorbidity could influence OA symptoms and PA behaviour. There is a need for HCPs to take this into account in supporting people with OA and comorbidity.
Meta-finding 2: Function and quality of life are important patient-prioritised outcome targets					
Functional disruptions are prioritised and can be reduced with PA	6MWT significant improvement: 0.29(95% CI 0.13, 0.46; obesity), 34.2 (95% CI 17.7, 50.6), 12.2% (95% CI 6.9, 17.5) (multimorbidity n=2); WOMAC: -7.4 (95% CI -9.9, -4.9)(multimorbid)	N/A	Priorities due to disruption on functioning and social ability; *'I'm quite frustrated now because of my hip, I can't get up and go' (Kate)*	Convergent	Function is prioritised in people with OA and comorbidity, and this outcome is often improved with PA interventions. Therefore, should be endorsed as a key outcome / incentive for PA participation.
Current outcome measures may be suboptimal for OA *and* comorbidity	Differences in outcome measures: e.g. WOMAC & 6MWT significantly improve but SF-36 did not QOL not routinely measured in RCTs (n=5)	N/A	QOL focus; *'it's because it's going to impact on my life, as to how much I can get about…meet friends and do the things I want to do' (Kate)*	Divergent	Function results in RCTs varied between outcome measurement. QOL was not routinely measured. These outcomes are important to patients. However, it could be complicated for an outcome measure to adequately accommodate all factors related to OA *and* comorbidity QOL.
Meta-finding 3: PA in people with OA and comorbidity may be facilitated by increasing self-efficacy for (1) OA and comorbidity and (2) PA					
HCP support is needed to increase patient knowledge	Increased supervision (Messier et al., 2004), teaching and encouragement (Somers et al., 2012)	N/A	HCP support *'helps you think about it, helps you embed it' (Alice)*	Expanded	Foster improved self-efficacy for patients to understand their conditions and self-efficacy to self-manage using PA, through gained knowledge and HCP support.

about their LTCs and PA					
Social support can increase patient knowledge about LTCs and encourage PA	PA interventions identified were mostly conducted in a group setting	N/A	Social support; *'exercise with people with the same complaint' (Tim)* *'people with a like condition' (Kate)*	Convergent	Foster improved self-efficacy for patients to understand their conditions and self-efficacy for PA, through meaningful group interactions to provide homogeneity and improve learning opportunities from a relevant peer group.
Uncertainty remains regarding the safety of PA for people with OA and comorbidity	Adverse events not generally reported in RCTs (only reported in n=3 studies) Adverse events were all falls	N/A	Negative PA outcome expectancies; *'If I went on one of these physical things…it'd probably do more harm than good' (John)* Fears of PA and fear of falling; *I am frightened, I'm very frightened of falling over again' (Jane)*	Expanded	People with OA and comorbidity may be at risk of falls and have fears of falling. Negative PA perceptions remain. Patients need confidence and reassurance in PA treatment and safety of PA. Negative perceptions need re-aligning.
Focus for PA interventions to tailor and integrate PA into daily life	Heterogeneous PA interventions (type, mode, delivery) with uncertain results	People with comorbidity have a lower PA level than those without comorbidity e.g. β= −32.25 (−48.57, −15.93) (B)	PA integrated into daily life; *'I set out errands each day to make me do it'(Alice)* Intermittent PA mode; *'do it, ten minutes and then rest'(Karen*) Adapted conventional PA; *'she adapted…it makes a big difference' (Debbie)*	Expanded	Diverse PA interventions were used for people with OA and comorbidity, with mixed and uncertain results. A likely key PA intervention component is how best to integrate PA into the daily life of patients, to enhance their self-efficacy for PA with their conditions and increase PA levels.

OA=Osteoarthritis; PA=Physical Activity; B=BEEP (Benefits of Effective Exercise for knee Pain); M=MOSAICS (Management of Osteoarthritis In Consultations Study); HCP=Healthcare Professional; RCT=Randomised Controlled Trial; e.g.=example; CVD=Cardiovascular Disease; PASE=Physical Activity Scale for the Elderly; QOL=Quality Of Life; n=number; CI=Confidence Interval; β=Beta coefficient; 6MWT=6-Minute Walking Test; WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index; SF-36= Short Form health survey; N/A=Not Applicable.

7.5 Narrative interpretation of the whole thesis findings.

7.5.1 Research and treatment using physical activity for osteoarthritis needs to be inclusive of comorbidity

The first meta-finding in the thesis relates to the lack of research, consistent evidence and guidance for HCPs to support PA in people with OA and comorbidity. The secondary data analysis demonstrated the high prevalence of comorbidity in OA, and the systematic review identified that despite a dearth of, and heterogeneous study findings, overall, trends suggest PA may improve clinical outcomes in people with OA and comorbidity.

The secondary data analysis found that the levels of PA in people with comorbidity are lower than those without comorbidity and the systematic review results were mixed and uncertain about the clinical effectiveness of PA for people with OA and comorbidity. This could, in part, be explained by the qualitative finding if a lack of conceptualisation of OA and comorbidity in HCPs and patients, which is a consequence of a gap in clear guidance for HCPs to support and tailor PA treatment in light of OA and comorbidity. Perhaps, it is then not surprising that HCPs do not confidently endorse PA, and PA levels are low, and RCTs do not successfully target OA and comorbidity, nor target the situation of multiple barriers and how they are problematised, to provide comparable information about the effectiveness of PA for OA inclusive of comorbidity.

CVD comorbidity was most consistently significantly associated with reduced PA level. However, to date, no RCT has focussed on the effectiveness of PA interventions in people with OA and CVD, who may be at high risk of negative health consequences associated with low levels of PA. This could be for several reasons, such as people with CVD comorbidity having worse symptoms and more barriers to PA participation than those with OA alone, or other comorbidity types, and this OA and comorbidity group likely have a higher frequency of comorbidities (Van Den Oever et al*.,* 2014; Jeong et al*.,* 2019). Therefore, future PA interventions could consider prioritising the subgroup of OA and CVD.

Furthermore, having a greater number of comorbidities was associated with lower levels of PA. Perhaps, a higher frequency of comorbidity could explain an increase in the likelihood of having multi-level barriers, as demonstrated in the participant experiences in the qualitative sample. Also, comorbidity presence could influence OA symptoms, such as the heightened perception of pain. Therefore, there is a need to focus on OA management first and to truly have a collaborative understanding of this condition between HCPs and patients, but then for HCPs to go beyond OA management considering comorbidities. Better understanding and knowledge of OA and comorbidity as a concept could provide knowledge of symptoms could improve condition self-efficacy.

7.5.2 Function and quality of life are important patient-prioritised outcome targets

The integrated findings suggest that outcomes and conditions, such as function and OA, which impact QOL most, are prioritised in people with OA and comorbidity. This converges with the function outcome improving with PA interventions in the systematic review. Contrasting this, function results varied between outcome measurements in the systematic review, and QOL was not routinely measured in RCTs.

Instead of PA treatment targeting disease-specific outcomes (Reuben and Tinetti, 2012; Muth et al*.,* 2014), the findings of the thesis confirm those of previous research suggesting that the impact on disability, mobility, daily life and QOL (Muth et al*.,* 2014; Young et al*.,* 2016), have higher patient value and priority. Furthermore, the qualitative finding; a lack of concept of OA and comorbidity, showed how patients either spoke of conditions in isolation or the whole impact on their QOL. These findings corroborate well with the recent report from the Taskforce on Multiple Conditions (2018) which emphasised how people with several co-existing LTCs don't conceptualise them in terms of their individual diagnoses, but instead as the compound impact they have on their lives. Future interventions could tailor PA toward the patient-reported disturbance to their QOL and functional deficits. Not only could this approach target outcomes that are both clinically important and have the greatest patient impact, but also activate patients in their care.

Furthermore, alongside the focus of QOL disruption, the qualitative investigation revealed uncertainty about how to manage LTCs and about the effectiveness of PA, leading to negative perceptions first surrounding OA and comorbidity management, and then PA. A recent systematic review and meta-ethnography emphasised how PA treatment in older adults focuses largely on the health benefits but instead could emphasise how PA contributes to a purposeful and fulfilling life (Morgan et al*.,* 2019). PA was proposed as a method to reject stereotypes of ageing, regain self-control and provide routine, roles and structure at a time when autonomy and independence are lacking (Morgan et al*.,* 2019). Therefore, PA could offer a similar opportunity to combat the barriers and biographical disruption that people with OA and comorbidity experience, boost self-esteem, provide structure, improve self-identity and purpose, thus improving overall QOL (Morgan et al*.,* 2019).

7.5.3 Physical activity in people with osteoarthritis and comorbidity may be facilitated by increasing self-efficacy for (1) osteoarthritis and comorbidity and (2) physical activity

Due to the dearth and heterogeneity in evidence regarding the effectiveness of PA for people with OA and comorbidity, it is unclear what PA type or mode would be optimal in an intervention. Despite this, it is possible to cautiously recommend intervention components by integrating the thesis findings. Patients experienced multi-level barriers to PA, but also underlying key barriers; a lack in comorbidity conceptualisation, uncertainty in managing their conditions and uncertainty of PA effectiveness, and negative perceptions surrounding their conditions (e.g. normalising ageing) and PA (e.g. fear of exacerbating conditions). These challenges encountered, could, therefore, reduce both (1) OA and comorbidity self-efficacy and (2) PA self-efficacy and create challenges for people with OA and comorbidity to self-manage their conditions with PA.

The relationship between self-efficacy for conditions and LTC management has been found elsewhere; condition self-efficacy and PA self-efficacy are significantly associated with the management of arthritis (Baruth et al., 2013; Marcum et al., 2014; Van Liew et al., 2013), and mediates the relationship between disease, pain and function in people with knee OA (Somers et al., 2009). Moreover, condition

self-efficacy has shown a significant positive association with QOL in OA (Van Liew et al., 2013). A significant relationship also exists between increased comorbidity frequency and decreased self-care management, since condition self-efficacy influences self-care, affecting how people prioritise and cope with multiple, competing condition treatments (Dickson et al*.,* 2013). Therefore, comorbidity could decrease a person's ability to self-manage through mechanisms of condition self-efficacy.

Succeeding this, targeting PA self-efficacy could be important in improving patient ability to self-manage PA, and autonomously integrate it into their life. Patient attitudes, beliefs and perceptions about OA and symptoms are linked with motivation levels and negative outcome expectancies of treatment and PA (Hurley et al., 2018). Further, a consistent link between self-efficacy, arthritis pain and disability, and adherence to recommended treatment strategies have previously been established (Somers et al*.,* 2009; Dekker et al*.,* 2009). Low PA self-efficacy is associated with lower PA levels in people with other LTCs including diabetes (Thomas et al*.,* 2004) and heart failure (Klompstra et al*.,* 2015), and health-related QOL is associated with PA self-efficacy in people with cancer (Perkins et al., 2009). Improving OA and comorbidity self-efficacy could, therefore, be an important precursor to activating patients to self-manage their LTCs in daily life, before targeting PA self-efficacy, to increase self-management of PA behaviour.

7.5.3.1 Fostering improved self-efficacy through healthcare professional and social support

Although a detailed review of self-efficacy enhancing methods are beyond the scope of the thesis, previous research has indicated the importance of assessing and intervening to maximize self-efficacy beliefs, as they are likely to impact outcomes including function and PA participation (Marks, 2014; Jackson, 2020; Hammer et al., 2016). Bandura (1997; 1994) suggests self-efficacy can be improved through mastery, vicarious experiences, verbal persuasion and affective states, to influence people's cognitive, motivational, affective and selective processes. In the thesis systematic review and qualitative investigation, both support from HCPs and social groups played a role in PA participation. More so, the qualitative study went further to say why it was important to have support. Fostering

regular communication with both the HCP and other patients could enhance both OA and comorbidity self-efficacy and PA self-efficacy. Both support mechanisms could alleviate concerns of safety, provide awareness of PA benefits, help experience and visualise the positive outcomes, and realign negative OA and comorbidity interpretations and PA experiences (Bandura, 1997; ACSM, 2018). For example, by having a knowledgeable HCP, delivering tailored PA, patients could be taught skills, gain confidence in their ability, and subsequent empowerment in their health condition self-management and PA treatment (Hurley et al*.,* 2018). Additionally, proactive communication with a HCP and a group, whereby patients experience feelings of a partnership, involvement and accountability, could encourage self-management and ongoing PA engagement (Hurley et al*.,* 2018).

Experiences including HCP encouragement, group inspiration and improved knowledge of PA side-effects have been found to contribute to greater self-efficacy and subsequent PA participation in OA (Hammer et al., 2016). Enhancing patient PA self-efficacy is key for the maintenance of PA, through the HCP providing disease-specific, individualised support, positively perceived PA, and nurtured positive vicarious experience (Hammer et al*.*, 2016; Warner et al*.*, 2014; Marks, 2012). A recent RCT by Wada et al*.* (2019) tested a self-efficacy targeted PA program and found that instruction by PTs, which considered a person's ability and increased awareness of PA benefits, contributed to increased PA self-efficacy and resulted in behaviour change, compared to PA instruction alone (Wada et al*.,* 2019). Therefore, HCP support could be a key vehicle to increase patients' skills to enhance their OA and comorbidity self-efficacy and PA self-efficacy and enable them to self-manage their conditions via PA.

Social support provided by meaningful others is an important factor in predicting PA in older adults (Warner et al*.,* 2011; Bandura 1997). Previous PA programmes for people with OA found that the opportunity to be in a group, meet new people, share stories and gain peer support benefited the participants (Hendry et al*.,* 2006). Having meaningful relationships such as friends can contribute to a support network that can assist both practically and emotionally in PA (Taskforce, 2018). Furthermore, Bandura (1997) suggested self-efficacy could moderate the effects of social support on PA, whereby

individuals with higher self-efficacy are more likely to translate support into productive PA outcomes. More so, a study by Warner et al. (2011) found that in older adults with multiple morbidities, social support predicted PA, which increased with higher self-efficacy (Warner et al., 2011).

Sharing experiences and peer support are more likely to make PA fun and enjoyable experience, which could replace feelings of isolation, due to the experience of comorbidity, or the perception of PA as an additional burden or a chore (Moody et al., 2012). Morgan et al. (2019) found a link between a sense of togetherness and belonging and the development of positive health behaviours. Therefore, relevant social support is needed to improve self-efficacy for (1) OA and comorbidity and (2) PA, by providing demographic homogeneity and belonging which may enhance social learning, contribute to better QOL, and foster long-term PA behaviour change.

7.6 Findings in the context of healthcare service delivery

The HOC framework provides an approach to managing LTCs adopted by UK health policy (Coulter et al., 2016). People with OA and comorbidity experience gaps in components identified within the HOC framework including having; clear and consistent guidelines for how to self-manage their OA and comorbidity via PA, holistic condition services for each of their comorbidities and associated healthcare interactions, and HCP collaborations to achieve patient-centred care (Epping-Jordan et al., 2004; Wagner, 1998; Coulter et al., 2016).

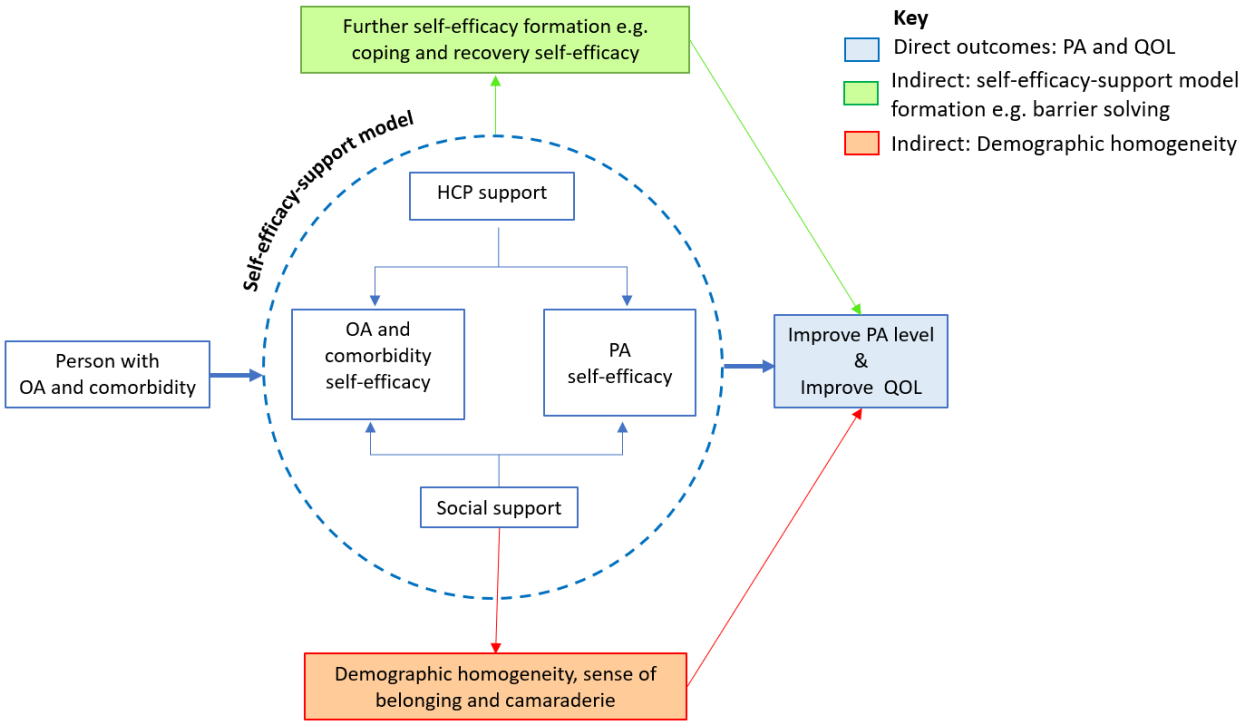
There is still a requirement for a holistic, proactive and collaborative model (Coulter et al., 2016) which houses productive interactions between well-resourced and informed HCPs and activated patients (Wagner, 1998) who can confidently self-manage 1) OA and comorbidity and 2) PA treatment, at the core. The following section outlines potential pathways to progress toward this HOC approach.

7.6.1 Self-efficacy-support model

It is clear from the findings that the commonality in the patient's experiences, of low condition self-efficacy, low PA self-efficacy and the disruption to QOL could be targeted. To achieve this, patients

need to be activated and develop their ability to self-manage disruptions to their QOL and PA. Therefore, I propose the 'self-efficacy-support model' for future research and clinical practice to consider (Figure 7.1), which encourages the collaboration of a relatable group of patients to enhance shared learning, with knowledgeable HCPs to teach skills, to foster self-efficacy for both their conditions and PA, to attain PA participation. The primary outcomes would be improved PA level and QOL (blue box). Also, being within a group of relatable patients could offer demographic homogeneity, a sense of belonging and camaraderie, which would further enhance QOL (and thus PA level) (orange box).

Furthermore, if an effective model of PA and condition self-efficacy-support is established, then this could expand to other self-efficacy components. For example, coping self-efficacy, to promote the ability of patients to deal with multi-level barriers, and thus continued PA participation (green box). Finally, if the model is successfully tested and implemented, it would be a proactive and holistic approach to care that cultivates a collaborative system for HCPs in partnership with people with OA and comorbidity (Coulter et al., 2013).



OA=Osteoarthritis; PA=Physical Activity; QOL=Quality Of Life

Figure 7.1 A self-efficacy-support model to improve PA levels and QOL in people with OA and comorbidity through HCP and social support

7.6.1.1 Continued self-efficacy-support

As described in the qualitative chapter, in a sample of people with OA and comorbidity, multi-level barriers to PA existed, which could be why in the secondary data analysis, the presence of comorbidity negatively influenced PA level, and why in the systematic review, current PA interventions results are mixed and uncertain. A potential solution for HCPs in supporting people with OA and comorbidity to increase their PA levels is to collaborate in anticipating and planning to overcome the multi-level barriers, as protection from relapse in PA participation. By establishing an efficient self-efficacy-support model, continued self-efficacy development could be a result. Participants being activated, knowing how to adapt and develop strategies to cope and tailor PA to suit them, they could regain some control over their health status, daily lives, PA participation and PA barriers (Taskforce, 2018). A similar theory was described by Schwarzer et al. (2011), who describe their Health Action Process Approach (HAPA) to address the discordance between intention and behaviour, by an additional level of self-efficacy in handling barriers (Schwarzer et al., 2011). To prevent relapse in PA behaviour, the self-efficacy-support model also highlights how to foster 'coping self-efficacy' for improved action and coping planning, and even 'recovery self-efficacy' to resume behaviour after set-backs (Schwarzer et al., 2011).

A patient-centred, holistic approach requires the prioritisation of planned and proactive practice, rather than reactive, to meet the needs of patients with multiple LTCs (Theis et al., 2016). Therefore, HCPs and patients with OA and comorbidity using the self-efficacy-support model could have a proactive partnership that cultivates self-management and problem-solving for the uptake and maintenance of PA.

7.7 Thesis strengths and limitations

This thesis, by its multi-method nature, had several strengths not mentioned in the three previous studies. By using more than one method; both quantitative and qualitative, results from each of the studies could stand alone, or be interpreted together, to offer further expansion and explanation of findings, more depth and a richer investigation of PA in people with OA and comorbidity.

The critical path of conducting different thesis studies in a multiphase manner meant that each study was completed within its own timeframe and the study results were finalised, before viewing the thesis as a whole. A weakness of multi-methods, compared with a mixed method approach, could have meant the results from one study could have informed the methods for subsequent investigations. For example, knowledge of specific comorbidity associations with PA could have directed the interview guide topics or questions to purposefully expand the thesis findings.

A further limitation was the use of secondary data (both systematic review and secondary data analysis studies), which does not allow control over the variables investigated other than those collected for the original research. For example, previous RCTs did not consistently measure QOL, or use a measurement tool that could capture outcomes in OA and comorbidity (not just OA).

It should be noted that all participants; in the RCTs included in the systematic review, in both the secondary data analysis trials (BEEP and MOSAICS) and those in the qualitative investigation consented to take part in research and may not be representative of the population with OA and comorbidity. For example, the results may not generalise to the oldest or most frail populations, nor those with comorbidities considered to contradict PA. Previous studies such as that by Hurley et al. (2018) noted that volunteer bias might be evident as people may only volunteer for PA related research if they are particularly conscious of PA opportunities. As a result, participants may have a prejudiced enthusiasm toward PA and non-representative opinions about PA, compared with the general population.

The systematic review search was completed in 2017, which may mean other relevant RCTs investigating the effectiveness of PA in OA and comorbidity have been published prior to the thesis completion. For example, a recent RCT (Bennell et al., 2020), would have met inclusion for the systematic review which compared the effectiveness of two exercise programs for people with knee OA and obesity comorbidity. Their study recruited from the community, and the non-weight-bearing and weight-bearing interventions were home-based, measured pain and function but also QOL, and found both interventions improved clinical outcomes, but that weight-bearing functional exercise yielded less adverse events for this patient group. The review will be updated on submission for publication in the near future.

7.8 Clinical recommendations

The novel findings from this thesis can add to the clinical management of PA in people with OA and comorbidity. The systematic review supports existing research and recommendations that PA interventions and PA participation provide benefits for people with LTCs, however, the uncertainty and mixed findings indicate that more work needs to be done in accounting for comorbidity. The secondary data analysis highlighted the importance of targeting people with OA and comorbidity with interventions aimed at increasing PA since this group has lower levels of PA compared to people with OA without comorbidity.

PA interventions for people with OA should be inclusive of their comorbidities, requiring tailored support to help them increase their PA levels to gain the associated health benefits. The qualitative findings highlighted the ways in which this could be achieved. For example, HCPs were identified as having an important and valued role in supporting the uptake of PA. HCPs need to offer patients clear guidance on tailored PA considering the patient's comorbidities. In turn, clinical guidelines need to better support HCPs with recommendations for effective tailoring of PA in the presence of OA and comorbidity. HCPS can support self-management of OA and comorbidity by facilitating discussions that identify and problematise in anticipation of multi-level barriers to PA and understanding what barriers

patients prioritise, to provide tailored PA advice. One approach could be implementing the self-efficacy-support model, instead of HCPs targeting unique, dynamic and heterogeneous patient barriers to PA, the intervention should target ways in which a patient can be better equipped to self-manage and cope with the barriers themselves. A shift of viewpoint to a holistic, proactive, and activated patient approach, combined with the additional comorbidity tailoring, could improve self-efficacy skills and better self-management of conditions and PA, and foster planning and coping with inevitable multi-level barriers to PA.

Finally, in using a patient-centred model, treatment could identify patients with similarities in their comorbidity experiences, suitable to be grouped in PA treatment. This could facilitate relevant social support from peer groups (e.g. social learning, confidence and belonging), and provide HCPs with direction for their treatment approach (e.g. appropriate PA tailoring, providing knowledge, re-aligning negative perceptions and re-assurance). Furthermore, PA treatment encompassing HCP and social support could increase PA level both indirectly by targeting (1) OA and comorbidity self-efficacy and directly through (2) PA self-efficacy.

Recently, NICE published their draft guidance for the management of chronic pain (NICE clinical guideline GID-NG10069; 2020). The findings of this thesis complement the guideline recommendations, stressing the need for person-centred models of care. The guideline suggests that in order to match the heterogeneous, complex, and distressing nature of chronic pain (of which OA is considered a condition of chronic pain), people need involvement in discussions and decisions about their care (NICE, 2020). Specifically, emphasis is placed on; knowing the patient as an individual, how pain affects their life, patient activation, communication, information, and shared decision making, alongside fostering a collaborative, supportive relationship (NICE, 2020). The guideline suggests supervised group PA as non-pharmacological management, provided it is developed with the patient, accounting for their specific needs, preferences, and abilities, to ensure they attain long-term health benefits (NICE, 2020).

7.9 Research recommendations

Several research implications and recommendations were described in each of the three thesis studies. This section highlights the other key recommendations for future research areas which could help to improve PA in people with OA and comorbidity. First, the main body of the discussion has summarised targeting improving PA and QOL through a self-efficacy-support model. Future trials in people with OA and comorbidity are needed to test whether PA can be combined with the self-efficacy-support model, using both HCP and social support, to improve self-efficacy and subsequently PA and QOL. An example of how this intervention could be designed is presented in Figure 7.2.

<table>
<tr><th>Population</th><th>Setting</th></tr>
<tr><td>Adults with OA and comorbidity that have clinical guidelines recommending PA</td><td>UK NHS primary care</td></tr>
<tr><th>Intervention and control groups</th><th>Outcomes of interest</th></tr>
<tr><td>1. PA and self-efficacy-support intervention
2. Usual UK NHS care for OA</td><td>1. PA level, pain, function, QOL, Self-efficacy
2. Long-term follow-up of outcomes, self-management and adherence</td></tr>
<tr><th colspan="2">Intervention procedure</th></tr>
<tr><td colspan="2">1. Identify the population: group based on their demographic homogeneity: comorbidities, symptoms, disruptions or shared barriers to PA
2. Discussions with the patient group and clinical reasoning: to determine what aspects are important to the individuals to shape the intervention
3. Deliver PA and self-efficacy-support strategies in line with UK guidance
4. Monitor progress (outcomes) and follow-up</td></tr>
<tr><th colspan="2">Example self-efficacy components through HCP and social support*</th></tr>
<tr><td>OA and comorbidity self-efficacy
• Increase disease knowledge
• Improve symptom management
• Problem-solving and decision-making skills
• Re-align negative perceptions and beliefs
• Combat uncertainty and fears
• Encourage self-monitoring</td><td>PA self-efficacy
• Increase PA knowledge
• Re-align negative PA perceptions and beliefs
• Foster mastery and skills training
• Enable modelling and exposure to PA
• Provide verbal persuasion and feedback
• Increase encouragement and referral/endorsement
• Activate to set goals and problem-solve</td></tr>
<tr><th colspan="2">Potential mechanisms of intervention effects**</th></tr>
<tr><td>OA and comorbidity self-efficacy
• Emotional support
• Self-management skills
• Sense of control
• Coping skills
• Problem-solving ability
• Positive expectations
• Structure to life</td><td>PA self-efficacy
• Alleviate concerns, such as safety
• Importance and belief in the effect
• Develop personal motivations
• Physiological feedback reinterpretation
• Barrier anticipation and planning
• Adherence</td></tr>
<tr><th colspan="2">Anticipated benefits for a person with OA and comorbidity</th></tr>
</table>

- Improve PA level, pain, function and QOL
- Increase self-efficacy for OA and comorbidity management
- Improve the self-efficacy of patients to self-manage their OA and comorbidity via PA
- Reduce the impact of multi-level barriers and improve coping abilities and planning
- Improve social functioning: combat isolation, sense of identity and belonging
- Prioritising PA as a less burdensome, relevant, manageable and enjoyable long-term behaviour

Figure 7.2 An intervention using PA and self-efficacy-support to increase PA and QOL in people with OA and comorbidity

*OA: osteoarthritis; PA: physical activity; UK: United Kingdom; NHS: national health service; QOL: quality of life; HCP: healthcare professional.*Bandura (1997) suggests improving self-efficacy requires; mastery experiences, vicarious experience, verbal persuasion and physiological and affective states. **Bandura (1994) suggests improving self-efficacy can positively influence four human processes; cognitive, motivational, affective and selective processes.*

7.9.1 More research on osteoarthritis inclusive of comorbidity

Several gaps in the literature exploring the effectiveness of PA in people with OA and comorbidity are evident. For example, research into the effectiveness of PA in OA and comorbidity outside of knee OA, including hip OA, other sites and multisite OA is needed. Also, other specific comorbidities to OA that are highly prevalent and common in OA other than obesity, such as depression, CVD, T2DM and common comorbidity clusters require further investigation.

The results of the secondary data analysis suggest a potential dose-response relationship with comorbidity increasing and PA levels decreasing. However, it is unknown and could be important to know whether the accumulation of common clusters of comorbidities to OA or specific combinations of comorbidities to OA are most prevalent and disruptive to PA level. Future research could take the associations in the current study a step further and consider patterns and clusters of conditions existing alongside OA to investigate the impact and association with PA level. The growing literature on this concept has highlighted that treating diseases in isolation creates complication (Guthrie et al., 2012) and that services need to reconfigure from individual systems (e.g. haematology or gastroenterology) to recognise clusters of disease in one person (Whitty et al., 2020). For example, investigating disease patterns existing in electronic medical records (Whitty and Watt, 2020) could determine whether specific comorbidity combinations (e.g. OA, obesity and diabetes), have important combined influences on PA.

7.9.2 Future physical activity interventions for osteoarthritis and comorbidity

Future research is needed to establish how to best deliver PA interventions for people with OA and comorbidity in primary care, which enable people to adopt an active self-management approach with regards to PA treatment.

There is still a need to determine the optimal dose, mode, intensity, duration and frequency of PA for OA and different types and frequencies of comorbidity. In the systematic review, most interventions had multiple components and methods, making the comparison of interventions difficult. Secondary data analysis from RCTs and individual participant data investigating subgrouping and targeted PA for people with OA are currently being carried out (Legha et al., 2020; Quicke et al., 2020; Holden et al., 2017). These methods could increase the power to identify what patients benefit most from PA and may produce more clinically relevant results, by allowing direct derivation of desired data (e.g. specific comorbidities) from original publications.

The qualitative findings suggested that people with OA and comorbidity are more likely to participate in PA if they find it enjoyable, however, whether enjoyment focussed PA produces similar effects on clinical outcomes, is unclear. Future research should consider evaluating the effectiveness of alternative PA modes, such as exergaming and adapted versions of conventional PA types. These types of interventions could be important to consider as they are suggested as more enjoyable or sustainable types, which also may support long-term adherence. It is important to ascertain what PA interventions are effective long-term in improving clinical outcomes, but also are maintainable, for people with OA and comorbidity, as thesis findings suggest long-term follow up is not currently well documented in current RCTs. Furthermore, although some combinations of PA with other intervention components were identified (e.g. counselling), future combination trials could test self-efficacy-support strategies alongside PA.

7.9.3 Outcomes to better measure the effectiveness of physical activity in osteoarthritis and comorbidity

The systematic review identified several different outcome measures being employed in different OA RCTs. There is a gap in establishing the most critical clinical outcomes, outcome measures and reporting styles, for RCTs investigating PA in people with OA and comorbidity. There are existing international recommendations for outcome measures (e.g. OMERACT OARSI criteria (Smith et al., 2019)) to be used in trials of people with OA but not specifically OA and comorbidity. Recent research has established health-related outcome measures that apply to people with a range of different LTCs (including OA) (Smith et al., 2018). The use of existing, consensus recommended, core outcomes sets for people with OA, combined with those for people with multiple LTCs could be used in future research to investigate the effectiveness of PA in people with OA and comorbidity. Furthermore, the potential importance of QOL to people with OA and comorbidity, and the lack of reporting of QOL in the systematic review, could make a case for its increased use as an outcome measure in future RCTs for people with OA and comorbidity.

The qualitative self-efficacy findings should be further investigated using quantitative methods to establish associations between self-efficacy, PA, and OA and comorbidity. Also, the relationship between comorbidity and PA level in people with OA in this thesis was based on self-report measures. Given the limitations of self-report PA measures, future associations between OA and comorbidity with PA level using objective PA measures could offer external validation.

7.9.4 Multi-method research on physical activity in osteoarthritis and comorbidity

There is an unquestionable dearth of research unpicking OA and comorbidity and PA to explore the *how* and *why* questions. Therefore, future multi-method research could be a useful way to understand how and why comorbidity impacts on PA level in people with OA. Further, how PA interventions could be better tailored, and what components are most effective and helpful for both HCPs and people with OA and comorbidity to enable them to better support the self-management of PA and increase PA

levels, still needs work. Future trials of PA interventions for people with OA and comorbidity could embed qualitative methods to help and understand this.

Chapter 8. Conclusion

This multi-method thesis has made a novel and useful contribution to the field of PA for adults with OA and comorbidity. The systematic review was the first to specifically investigate the effectiveness of PA interventions on clinical outcomes for people with OA and comorbidity. The secondary data analysis offers additional and new insights into the relationship between comorbidity presence, frequency and type and PA in people with OA. The qualitative study is the first to explicitly explore how people with OA experience PA in the context of comorbidity.

The thesis findings have shown that there is a lack of consistent evidence regarding the effectiveness of, and optimal specification for, PA interventions for people with OA and comorbidity. Whilst trends in the systematic review findings suggest small clinical benefits, the findings of individual studies are mixed and most of the existing studies relate to people with knee OA and obesity. It has shown that comorbidity is associated with lower PA levels in people with OA and that this relationship grows in magnitude with increased comorbidity frequency. Investigating the patient perspective gave insight as to how multiple, multi-level barriers were encountered by people with OA and comorbidity, limiting their ability to carry out and maintain PA. Potential mechanisms to facilitate PA in this group were also identified including support mechanisms (such as HCP and social support) and targeting both OA and comorbidity self-efficacy and PA self-efficacy, to activate patients to better self-manage their PA treatment.

This thesis has important implications for treatment recommendations, HCP delivery of PA, and for the people with OA and comorbidity themselves. The NHS vision (NHS, 2019) emphasised patient-centred partnerships between HCPs and patients, that enable patients to have a voice in their care. The findings of this thesis support this vision, that people with OA and comorbidity need to be empowered to have a voice, to talk *their* talk, reflective of their lived experience. HCPs then have an important role in working with patients with OA and comorbidity, to support them to develop the skills to problem-solve and overcome barriers and increase their PA levels.

References

Aiden, H. (2018). Multimorbidity. Understanding the Challenge. The Richmond Group of Charities. London. https://richmondgroupofcharities.org.uk/sites/default/files/multimorbidity_-_understanding_the_challenge.

Ajzen, I., Andreason, A. R., & Bandura, A. (1985). “From Intentions to Actions: A Theory of Planned Behavior,” in KJ Beckman, and J. Beckman, eds, Action Control: From Cognition to Behavior, Berlin: Springer, 11–39.

Alami, S., Boutron, I., Desjeux, D., Hirschhorn, M., Meric, G., Rannou, F., & Poiraudeau, S. (2011). Patients' and practitioners' views of knee osteoarthritis and its management: A qualitative interview study. PLoS One, 6(5), e19634.

Alkatan, M., Machin, D. R., Baker, J. R., Akkari, A. S., Park, W., & Tanaka, H. (2016). Effects of swimming and cycling exercise intervention on vascular function in patients with osteoarthritis. The American Journal of Cardiology, 117(1), 141-145.

Altman, R., Alarcon, G., Appelrouth, D., Bloch, D., Borenstein, D., Brandt, K., . . . Feldman, D. (1991). The American college of rheumatology criteria for the classification and reporting of osteoarthritis of the hip. Arthritis & Rheumatology, 34(5), 505-514.

American College of Sports Medicine (ACSM) Chodzko-Zajko, W. J., Proctor, D. N., Singh, M. A. F., Minson, C. T., Nigg, C. R., Salem, G. J., & Skinner, J. S. (2009). Exercise and physical activity for older adults. Medicine & Science in Sports & Exercise, 41(7), 1510-1530.

American College of Sports Medicine (ACSM) Riebe, D., Ehrman, J. K., Liguori, G., Magal, M., & (Eds.). (2018). ACSM's guidelines for exercise testing and prescription. Wolters Kluwer.

American College of Sports Medicine (ACSM) Thompson, P. D., Franklin, B. A., Balady, G. J., Blair, S. N., Corrado, D., ... & Link, M. S. (2007). Exercise and acute cardiovascular events: placing the risks into perspective: a scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism and the Council on Clinical Cardiology. Circulation, 115(17), 2358-2368.

American College of Sports Medicine (ACSM). (2014). ACSM's guidelines for exercise testing and prescription. Lippincott Williams & Wilkins.

Anguera, M. T., Blanco-Villaseñor, A., Losada, J. L., Sánchez-Algarra, P., & Onwuegbuzie, A. J. (2018). Revisiting the difference between mixed methods and multimethods: Is it all in the name? Quality & Quantity, 52(6), 2757-2770.

Antcliff, D., Keeley, P., Campbell, M., Woby, S., Keenan, A. M., & McGowan, L. (2018). Activity pacing: moving beyond taking breaks and slowing down. Quality of Life Research, 27(7), 1933-1935.

Arthritis Research (ARUK) UK. (2015). The musculoskeletal calculator. Online at www.arthritisresearchuk.org/ mskcalculator.

Arthritis Research UK (ARUK) Duffield, S. J., Ellis, B. M., Goodson, N., Walker-Bone, K., Conaghan, P. G., Margham, T., & Loftis, T. (2017). The contribution of musculoskeletal disorders in multimorbidity: Implications for practice and policy. Best Practice & Research Clinical Rheumatology, 31(2), 129-144.

Arthritis Research UK (ARUK). (2013). Osteoarthritis in General Practice-Data and Perspectives. Arthritis Research, 222, 253-258.

Arthritis Research UK (ARUK). (2017). Musculoskeletal conditions and multimorbidity. https://www.versusarthritis.org/media/2078/msk-conditions-and-multimorbidity-report.

Arthritis Research UK (ARUK). (2019). The Musculoskeletal Calculator (prevalence data tool). https://www.versusarthritis.org/policy/resources-for-policy-makers/musculoskeletal-calculator/.

Austin, P. C., & Steyerberg, E. W. (2015). The number of subjects per variable required in linear regression analyses. Journal of Clinical Epidemiology, 68(6), 627-636.

Babyak, M. A. (2004). What you see may not be what you get: a brief, nontechnical introduction to overfitting in regression-type models. Psychosomatic Medicine, 66(3), 411-421.

Ball, K., Crawford, D., & Owen, N. (2000). Obesity as a barrier to physical activity. Australian and New Zealand Journal of Public Health, 24(3), 331-333.

Bandura, A. (1986). Social foundations of thought and action. Englewood Cliffs, NJ, 1986.

Bandura, A. (1994). Social cognitive theory and exercise of control over HIV infection. In Preventing AIDS (pp. 25-59). Springer, Boston, MA.

Bandura, A. (1997). Self-efficacy: The exercise of control. W.H. Freeman and Company, New York.

Bandura, A. (2006). Toward a psychology of human agency. Perspectives on Psychological Science, 1(2), 164-180.

Barber, J., Muller, S., Whitehurst, T., & Hay, E. (2009). Measuring morbidity: self-report or health care records? Family Practice, 27(1), 25-30.

Barnett, K., Mercer, S. W., Norbury, M., Watt, G., Wyke, S., & Guthrie, B. (2012). Epidemiology of multimorbidity and implications for health care, research, and medical education: A cross-sectional study. The Lancet, 380(9836), 37-43.

Barnett, L. A., Jordan, K. P., Edwards, J. J., & van der Windt, D. A. (2017). Does metformin protect against osteoarthritis? An electronic health record cohort study. Primary Health care Research & Development, 18(6), 623-628.

Barnett, L. A., Bailey, J., Bondesson, E., Campbell, P., Chew-Graham, C. A., Edwards, J. J., Hayward, R. A., Jöud, A., Schelin, M., Sumathipala, Wynne-Jones, G., Jordan, K. P. (TBP). Consultation

prevalence of mental health problems: a cross-national electronic health record database study.

Barney, L. J., Griffiths, K. M., Jorm, A. F., & Christensen, H. (2006). Stigma about depression and its impact on help-seeking intentions. Australian & New Zealand Journal of Psychiatry, 40(1), 51-54.

Bartels, E. M., Juhl, C. B., Christensen, R., Hagen, K. B., Danneskiold-Samsøe, B., Dagfinrud, H., & Lund, H. (2016). Aquatic exercise for the treatment of knee and hip osteoarthritis. Cochrane Database of Systematic Reviews, (3), 1465-1858.

Baruth, M., Wilcox, S., Schoffman, D. E., & Becofsky, K. (2013). Factors associated with disability in a sample of adults with arthritis. Disability and Health Journal, 6(4), 377-384.

Bauman, A. E., Reis, R. S., Sallis, J. F., Wells, J. C., Loos, R. J., Martin, B. W., & Lancet Physical Activity Series Working Group. (2012). Correlates of physical activity: why are some people physically active and others not? The Lancet, 380(9838), 258-271.

Bazeley, P. (2018). Integrating analyses in mixed methods research. Thousand Oaks, CA: Sage.

Becker, M. H., & Maiman, L. A. (1975). Sociobehavioral determinants of compliance with health and medical care recommendations. Medical Care, 10-24.

Beckwée, D., Bautmans, I., Scheerlinck, T., & Vaes, P. (2015). Exercise in knee osteoarthritis–preliminary findings: Exercise-induced pain and health status differs between dropouts and retainers. Experimental Gerontology, 72, 29-37.

Bedson, J., & Croft, P. R. (2008). The discordance between clinical and radiographic knee osteoarthritis: a systematic search and summary of the literature. BMC Musculoskeletal Disorders, 9(1), 116.

Bellamy, N., Buchanan, W. W., Goldsmith, C. H., Campbell, J., & Stitt, L. W. (1988). Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. The Journal of Rheumatology, 15(12), 1833-1840.

Bennell, K. L., Dobson, F., & Hinman, R. S. (2014). Exercise in osteoarthritis: Moving from prescription to adherence. Best Practice & Research Clinical Rheumatology, 28(1), 93-117.

Bennell, K. L., Dobson, F., Roos, E. M., Skou, S. T., Hodges, P., Wrigley, T. V., ... & Hinman, R. S. (2015). Influence of biomechanical characteristics on pain and function outcomes from exercise in medial knee osteoarthritis and varus malalignment: exploratory analyses from a randomized controlled trial. Arthritis Care & Research, 67(9), 1281-1288.

Bennell, K. L., Hall, M., & Hinman, R. S. (2016). Osteoarthritis year in review 2015: rehabilitation and outcomes. Osteoarthritis and Cartilage, 24(1), 58-70.

Bennell, K. L., Nelligan, R. K., Kimp, A. J., Schwartz, S., Kasza, J., Wrigley, T. V., ... & Hinman, R. S. (2020). What type of exercise is most effective for people with knee osteoarthritis and co-morbid

obesity?: The TARGET randomized controlled trial. Osteoarthritis and Cartilage, 28(6), 755-765.

Bennell, K., & Hinman, R. (2013). Exercise prescription for people with hip or knee osteoarthritis: accounting for co-morbidities. Physical Therapy Reviews, 18(3), 221-222.

Berry, A., McCabe, C. S., Halls, S., Muir, S., & Walsh, N. (2020). Beliefs, motives and gains associated with physical activity in people with osteoarthritis. Musculoskeletal Care. 1-7.

Bilbao, A., Martín-Fernández, J., Arenaza, J. C., García, I., Tomás-García, N., Trujillo-Martín, E., & García-Perez, L. (2017). Validation of the EQ-5D-5L in patients with hip or knee osteoarthritis. Value in Health, 20(9), A760.

Blackburn, S., Higginbottom, A., Taylor, R., Bird, J., Østerås, N., Hagen, K. B., ... & Dziedzic, K. (2016). Patient-reported quality indicators for osteoarthritis: a patient and public generated self-report measure for primary care. Research Involvement and Engagement, 2(1), 5.

Blair, S. N. (2009). Physical inactivity: the biggest public health problem of the 21st century. British Journal of Sports Medicine, 43(1), 1-2.

Borkan, J. M. (2004). Mixed methods studies: a foundation for primary care research. The Annals of Family Medicine, 2(1), 4-6.

Braun, V., & Clarke, V. (2006). Using thematic analysis in psychology. Qualitative Research in Psychology, 3(2), 77-101.

Bricca, A., Juhl, C. B., Steultjens, M., Wirth, W., & Roos, E. M. (2019). Impact of exercise on articular cartilage in people at risk of, or with established, knee osteoarthritis: a systematic review of randomised controlled trials. British Journal of Sports Medicine, *53*(15), 940-947.

Bruce, B., Fries, J. F., & Hubert, H. (2008). Regular vigorous physical activity and disability development in healthy overweight and normal-weight seniors: a 13-year study. American Journal of Public Health, 98(7), 1294-1299.

Bryman, A. (2006). Integrating quantitative and qualitative research: how is it done? Qualitative Research, 6(1), 97-113.

Buffel du Vaure, C., Ravaud, P., Baron, G., Barnes, C., Gilberg, S., & Boutron, I. (2016). Potential workload in applying clinical practice guidelines for patients with chronic conditions and multimorbidity: a systematic analysis. BMJ Open, 6(3), 6:e010119.

Bury, M. (1982). Chronic illness as biographical disruption. Sociology of Health & Illness, 4(2), 167-182.

Campbell, R., Evans, M., Tucker, M., Quilty, B., Dieppe, P., & Donovan, J. L. (2001). Why don't patients do their exercises? Understanding non-compliance with physiotherapy in patients with osteoarthritis of the knee. Journal of Epidemiology & Community Health, 55(2), 132-138.

Caporali, R., Cimmino, M. A., Sarzi-Puttini, P., Scarpa, R., Parazzini, F., Zaninelli, A., ... & Montecucco, C. (2005). Comorbid conditions in the AMICA study patients: effects on the quality of life and drug prescriptions by general practitioners and specialists. Seminars in Arthritis and Rheumatism, 35(1), 31-37.

Casilda-López, J., Valenza, M. C., Cabrera-Martos, I., Díaz-Pelegrina, A., Moreno-Ramírez, M. P., & Valenza-Demet, G. (2017). Effects of a dance-based aquatic exercise program in obese postmenopausal women with knee osteoarthritis: a randomized controlled trial. Menopause, 24(7), 768-773.

Caspersen, C. J., Powell, K. E., & Christenson, G. M. (1985). Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. Public Health Reports, 100(2), 126.

Centre for Policy and Ageing (CPA) Lievesley, N., Hayes, R., Jones, K., Clark, A., & Crosby, G. (2009). Ageism and age discrimination in mental health care in the United Kingdom. A review from the literature. United Kingdom: Centre for Policy and Ageing. http://www.cpa.org.uk/information/reviews/CPA.

Chad, K. E., Reeder, B. A., Harrison, E. L., Ashworth, N. L., Sheppard, S. M., Schultz, S. L., ... & Lawson, J. A. (2005). Profile of physical activity levels in community-dwelling older adults. Medicine & Science in Sports & Exercise, 37(10), 1774-1784.

Charmaz, K. (2006). Constructing grounded theory: A practical guide through qualitative analysis. Sage. London.

Chen, A. G. C. M., Gupte, C., Akhtar, K., Smith, P., & Cobb, J. (2012). The global economic cost of osteoarthritis: how the UK compares. Arthritis.

Chen, Y. W., Hunt, M. A., Campbell, K. L., Peill, K., & Reid, W. D. (2016). The effect of Tai Chi on four chronic conditions—cancer, osteoarthritis, heart failure and chronic obstructive pulmonary disease: a systematic review and meta-analyses. British Journal of Sports Med, 50(7), 397-407.

Chen, Y., Hayward, R. A., Chew-Graham, C. A., Hubbard, R., Croft, P., Sims, K., Jordan, K. P. (2020). Prognostic value of first-recorded breathlessness for future chronic respiratory and heart disease a cohort study using a UK national primary care database. British Journal of General Practice. (E-pub ahead of print).

Cheraghi-Sohi, S., Bower, P., Kennedy, A., Morden, A., Rogers, A., Richardson, J., . . . Ong, B. N. (2013). Patient priorities in osteoarthritis and comorbid conditions: A secondary analysis of qualitative data. Arthritis Care & Research, 65(6), 920-927.

Chew-Graham, C., O'Toole, L., Taylor, J., & Salisbury, C. (2019). 'Multimorbidity': an acceptable term for patients or time for a rebrand? British Journal of General Practice, 69 (685), 372-373.

Christensen, R., Henriksen, M., Leeds, A. R., Gudbergsen, H., Christensen, P., Sørensen, T. J., . . . Frederiksen, R. (2015). Effect of weight maintenance on symptoms of knee osteoarthritis in

obese patients: A Twelve-Month randomized controlled trial. Arthritis Care & Research, 67(5), 640-650.

Christiansen, M. B., White, D. K., Christian, J., Waugh, E., Gakhal, N., King, L., ... & Webster, F. (2020). "It... doesn't always make it [to] the top of the list": Primary care physicians' experiences with prescribing exercise for knee osteoarthritis. Canadian Family Physician, 66(1), 14-20.

Cochrane Group. (2016). Communication Review Group. 'Cochrane Consumers and Communication Review Group Reviews: How to Consider Equity Issues'. CCCG http://cccrg.cochrane.org/author-resources. La Trobe University, Melbourne.

Cohen, L., Manion, L., & Morrison, K. (2013). Research methods in education. Routledge.

Collins, H. (2010). Creative research: The theory and practice of research for the creative industries. Bloomsbury Publishing.

CONSORT statement. (2010). Checklist of information to include when reporting a randomised trial. 2010. Available from: www.Consort-Statement. Org / Index.

Cook, M. J., Bellou, E., Bowes, J., Sergeant, J. C., O'Neill, T. W., Barton, A., & Verstappen, S. M. (2018). The prevalence of co-morbidities and their impact on physical activity in people with inflammatory rheumatic diseases compared with the general population: results from the UK Biobank. Rheumatology, 57(12), 2172-2182.

Coulter, A., Kramer, G., Warren, T., & Salisbury, C. (2016). Building the House of Care for people with long-term conditions: the foundation of the House of Care framework. British Journal of General Practice, 66(645), 288-290.

Coulter, A., Roberts, S., & Dixon, A. (2013). Delivering better services for people with long-term conditions. Building the house of care. London: The King's Fund, 1-28.

Coventry, P. A., Fisher, L., Kenning, C., Bee, P., & Bower, P. (2014). Capacity, responsibility, and motivation: a critical qualitative evaluation of patient and practitioner views about barriers to self-management in people with multimorbidity. BMC Health Services Research, 14(1), 536.

Coventry, P. A., Hays, R., Dickens, C., Bundy, C., Garrett, C., Cherrington, A., & Chew-Graham, C. (2011). Talking about depression: a qualitative study of barriers to managing depression in people with long term conditions in primary care. BMC Family Practice, 12(1), 10.

Creswell, J. W. (2009). Research design: Qualitative, quantitative, and mixed methods approaches. Los Angeles: Sage (3rd ed.).

Creswell, J. W., & Clark, V. L. P. (2017). Designing and conducting mixed methods research. Sage Publications.

Cuperus, N., Smink, A. J., Bierma-Zeinstra, S. M., Dekker, J., Schers, H. J., de Boer, F., . . . Vlieland, T. P. V. (2013). Patient reported barriers and facilitators to using a self-management booklet for hip

and knee osteoarthritis in primary care: Results of a qualitative interview study. BMC Family Practice, 14(1), 181.

Dallosso, H., Yates, T., Mani, H., Gray, L. J., Dhalwani, N., Baldry, E., ... & Khunti, K. (2018). Movement through Active Personalised engagement (MAP)—a self-management programme designed to promote physical activity in people with multimorbidity: study protocol for a randomised controlled trial. Trials, 19(1), 576.

Damman, W., Liu, R., & Kloppenburg, M. (2016). Comorbidity in hand osteoarthritis: its impact on hand pain and function. Osteoarthritis and Cartilage, 24, S446-S447.

Davis, G. C., Hiemenz, M. L., & White, T. L. (2002). Barriers to managing chronic pain of older adults with arthritis. Journal of Nursing Scholarship, 34(2), 121-126.

De Groot, I. B., Bussmann, J. B., Stam, H. J., & Verhaar, J. A. N. (2008). Actual everyday physical activity in patients with end-stage hip or knee osteoarthritis compared with healthy controls. Osteoarthritis and Cartilage, 16(4), 436-442.

de Rooij, M., van der Leeden, M., Avezaat, E., Häkkinen, A., Klaver, R., Maas, T., ... & Dekker, J. (2014). Development of comorbidity-adapted exercise protocols for patients with knee osteoarthritis. Clinical Interventions in Aging, 9, 829.

de Rooij, M., van der Leeden, M., Cheung, J., van der Esch, M., Häkkinen, A., Haverkamp, D., ... & Dekker, J. (2016). Effectiveness of tailored exercise therapy in patients with knee osteoarthritis and comorbidity: a randomized controlled trial. Osteoarthritis and Cartilage, 24, S466-S467.

de Rooij, M., van der Leeden, M., Cheung, J., van der Esch, M., Häkkinen, A., Haverkamp, D., . . . Lems, W. F. (2017). Efficacy of tailored exercise therapy on physical functioning in patients with knee osteoarthritis and comorbidity: A randomized controlled trial. Arthritis Care & Research, 69(6), 807-816.

de Rooij, M., van Der Leeden, M., Heymans, M. W., Holla, J. F., Häkkinen, A., Lems, W. F., ... & Dekker, J. (2016). Course and predictors of pain and physical functioning in patients with hip osteoarthritis: Systematic review and meta-analysis. Journal of Rehabilitation Medicine, 48(3), 245-252.

de Rooij, M., van der Leeden, M., Heymans, M. W., Holla, J. F., Häkkinen, A., Lems, W. F., ... & Dekker, J. (2016). Prognosis of pain and physical functioning in patients with knee osteoarthritis: a systematic review and meta-analysis. Arthritis Care & Research, 68(4), 481-492.

de Rooij, M., van der Leeden, M., van der Esch, M., Lems, W. F., Meesters, J. J., Peter, W. F., ... & Dekker, J. (2020). Evaluation of an educational course for primary care physiotherapists on comorbidity-adapted exercise therapy in knee osteoarthritis: an observational study. Musculoskeletal Care, 18(2), 122-133.

de Souto Barreto, P. (2017). Exercise for Multimorbid Patients in Primary Care: One Prescription for All? Sports Medicine, 47(11), 2143-2153.

de Vries, H., Dijkstra, M., & Kuhlman, P. (1988). Self-efficacy: the third factor besides attitude and subjective norm as a predictor of behavioural intentions. Health Education Research, 3(3), 273-282.

Deci, E. L., & Ryan, R. M. (1985). Cognitive evaluation theory. In Intrinsic motivation and self-determination in human behavior. Springer, Boston, MA, 43-85

Dekker, J., Buurman, B. M., & van der Leeden, M. (2019). Exercise in people with comorbidity or multimorbidity. Health Psychology, 38(9), 822.

Dekker, J., de Rooij, M., & van der Leeden, M. (2016). Exercise and comorbidity: the i3-S strategy for developing comorbidity-related adaptations to exercise therapy. Disability and Rehabilitation, 38(9), 905-909.

Dekker, J., van Dijk, G. M., & Veenhof, C. (2009). Risk factors for functional decline in osteoarthritis of the hip or knee. Current Opinion in Rheumatology, 21(5), 520-524.

Denoeud, L., Mazieres, B., Payen-Champenois, C., & Ravaud, P. (2005). First line treatment of knee osteoarthritis in outpatients in France: adherence to the EULAR 2000 recommendations and factors influencing adherence. Annals of the Rheumatic Diseases, 64(1), 70-74.

Department of Health & Social Care (DOH). (2019) UK Chief Medical Officers' Physical Activity Guidelines. Available at: https://assets.publishing.service.gov.uk/government/uploads /system/uploads/attachment_data/file/832868/ukchief-medical-officers-physical-activity-guidelines.

Department of Health (DOH) Davies, S. C. (2012). Annual Report of the Chief Medical Officer, Volume One, 2011, On the State of the Public's Health. London: Department of Health, 11.

Department of Health (DOH) Davies, S. C., Fowler, T., & McKee, M. (2012). On the state of public health in England. The Lancet, 380(9856), 1793-1795.

Department of Health (DOH). (2009). Research governance framework for health and social care. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_ data/file/139565/dh_4122427.

Department of Health (DOH). (2011). Start active, Stay Active. A Report on Physical Activity for Health from the Four Home Countries' Chief Medical Officers Get active, stay active: report on physical activity in the UK. London, UK: Department of Health.

Department of Health (DOH). (2012). Long-term conditions compendium of information: third edition. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_ data/file/216528/dh_134486.

Der Ananian, C., Wilcox, S., Saunders, R., Watkins, K., & Evans, A. (2006). Factors That Influence Exercise Among Adults With Arthritis in Three Activity Levels. Preventing Chronic Disease, 3(3). A81.

Devereux-Fitzgerald, A., Powell, R., Dewhurst, A., & French, D. P. (2016). The acceptability of physical activity interventions to older adults: A systematic review and meta-synthesis. Social Science & Medicine, 158, 14-23.

Dhalwani, N. N., O'Donovan, G., Zaccardi, F., Hamer, M., Yates, T., Davies, M., & Khunti, K. (2016). Long terms trends of multimorbidity and association with physical activity in older English population. International Journal of Behavioral Nutrition and Physical Activity, 13(1), 8.

Dickson, V. V., Buck, H., & Riegel, B. (2013). Multiple comorbid conditions challenge heart failure self-care by decreasing self-efficacy. Nursing Research, 62(1), 2-9.

Dixon, K. E., Keefe, F. J., Scipio, C. D., Perri, L. M., & Abernethy, A. P. (2007). Psychological interventions for arthritis pain management in adults: a meta-analysis. Health Psychology, 26(3), 241.

Dobson, F., Bennell, K. L., French, S. D., Nicolson, P. J., Klaasman, R. N., Holden, M. A., ... & Hinman, R. S. (2016). Barriers and facilitators to exercise participation in people with hip and/or knee osteoarthritis: synthesis of the literature using behavior change theory. American Journal of Physical Medicine & Rehabilitation, 95(5), 372-389.

Dörenkamp, S., Mesters, I., Vos, R., Schepers, J., Akker, M. V. D., Teijink, J., & de Bie, R. (2016). Synergistic effects of six chronic disease pairs on decreased physical activity: the SMILE Cohort Study. BioMed Research International.

du Vaure, C. B., Ravaud, P., Baron, G., Barnes, C., Gilberg, S., & Boutron, I. (2016). Potential workload in applying clinical practice guidelines for patients with chronic conditions and multimorbidity: a systematic analysis. BMJ Open, 6(3), e010119.

Duguay, C., Gallagher, F., & Fortin, M. (2014). The experience of adults with multimorbidity: a qualitative study. Journal of Comorbidity, 4(1), 11-21.

Dunlop, D. D., Song, J., Semanik, P. A., Chang, R. W., Sharma, L., Bathon, J. M., ... & Mysiw, W. J. (2011). Objective physical activity measurement in the osteoarthritis initiative: are guidelines being met? Arthritis & Rheumatism, 63(11), 3372-3382.

Dunlop, D. D., Song, J., Semanik, P. A., Sharma, L., & Chang, R. W. (2011). Physical activity levels and functional performance in the osteoarthritis initiative: a graded relationship. Arthritis & Rheumatism, 63(1), 127-136.

Dunlop, W. L., & Beauchamp, M. R. (2013). Birds of a feather stay active together: a case study of an all-male older adult exercise program. Journal of Aging and Physical Activity, 21(2), 222-232.

Dziedzic, K. S., Healey, E. L., Porcheret, M., Ong, B. N., Main, C. J., Jordan, K. P., ... & McHugh, G. A. (2014). Implementing the NICE osteoarthritis guidelines: a mixed methods study and cluster randomised trial of a model osteoarthritis consultation in primary care-the Management of OsteoArthritis In Consultations (MOSAICS) study protocol. Implementation Science, 9(1), 95.

Edwards, J. J., Khanna, M., Jordan, K. P., Jordan, J. L., Bedson, J., & Dziedzic, K. S. (2015). Quality indicators for the primary care of osteoarthritis: a systematic review. Annals of the Rheumatic Diseases, 74(3), 490-498.

Egerton, T., Diamond, L. E., Buchbinder, R., Bennell, K. L., & Slade, S. C. (2017). A systematic review and evidence synthesis of qualitative studies to identify primary care clinicians' barriers and enablers to the management of osteoarthritis. Osteoarthritis and Cartilage, 25(5), 625-638.

Epping-Jordan, J. E., Pruitt, S. D., Bengoa, R., & Wagner, E. H. (2004). Improving the quality of health care for chronic conditions. BMJ Quality & Safety, 13(4), 299-305.

Ernstgård, A., PirouziFard, M., & Thorstensson, C. A. (2017). Health enhancing physical activity in patients with hip or knee osteoarthritis-an observational intervention study. BMC Musculoskeletal Disorders, 18(1), 42.

Ettinger, W. H., Burns, R., Messier, S. P., Applegate, W., Rejeski, W. J., Morgan, T., ... & Craven, T. (1997). A randomized trial comparing aerobic exercise and resistance exercise with a health education program in older adults with knee osteoarthritis: the Fitness Arthritis and Seniors Trial (FAST). Jama, 277(1), 25-31.

Ettinger, W. H., Davis, M. A., Neuhaus, J. M., & Mallon, K. P. (1994). Long-term physical functioning in persons with knee osteoarthritis from NHANES I: effects of comorbid medical conditions. Journal of Clinical Epidemiology, 47(7), 809-815.

European League Against Rheumatism (EULAR) Fernandes, L., Hagen, K. B., Bijlsma, J. W., Andreassen, O., Christensen, P., Conaghan, P. G., ... & Lohmander, L. S. (2013). EULAR recommendations for the non-pharmacological core management of hip and knee osteoarthritis. Annals of the Rheumatic Diseases, 72(7), 1125-1135.

European League Against Rheumatism (EULAR) Osthoff, A. K. R., Niedermann, K., Braun, J., Adams, J., Brodin, N., Dagfinrud, H., ... & Juhl, C. B. (2018). 2018 EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis. Annals of the Rheumatic Diseases, 77(9), 1251-1260.

EUROQOL group (1990). EuroQol-a new facility for the measurement of health-related quality of life. Health Policy, 16(3), 199-208.

Farrance, C., Tsofliou, F., & Clark, C. (2016). Adherence to community based group exercise interventions for older people: A mixed-methods systematic review. Preventive Medicine, 87, 155-166.

Feinstein, A. (1970). The pre-therapeutic classification of co-morbidity in chronic disease. Journal of Chronic Disease, 23, 455–468.

Felson, D. T., Lawrence, R. C., Dieppe, P. A., Hirsch, R., Helmick, C. G., Jordan, J. M., ... & Sowers, M. (2000). Osteoarthritis: new insights. Part 1: the disease and its risk factors. Annals of Internal Medicine, 133(8), 635-646.

Fetters, M. D., Curry, L. A., & Creswell, J. W. (2013). Achieving integration in mixed methods designs—principles and practices. Health Services Research, 48(6pt2), 2134-2156.

Field, A. (2013). Discovering statistics using IBM SPSS statistics. Sage.

Finney, A., Dziedzic, K. S., Lewis, M., & Healey, E. (2017). Multisite peripheral joint pain: a cross-sectional study of prevalence and impact on general health, quality of life, pain intensity and consultation behaviour. BMC Musculoskeletal Disorders, 18(1), 535.

Fishman, E. I., Steeves, J. A., Zipunnikov, V., Koster, A., Berrigan, D., Harris, T. A., & Murphy, R. (2016). Association between objectively measured physical activity and mortality in NHANES. Medicine and Science in Sports and Exercise, 48(7), 1303.

Fleury, J., Lee, S. M., Matteson, B., & Belyea, M. (2004). Barriers to physical activity maintenance after cardiac rehabilitation. Journal of Cardiopulmonary Rehabilitation and Prevention, 24(5), 296-305.

Focht, B. C., Gauvin, L., & Rejeski, W. J. (2005). The contribution of daily experiences and acute exercise to fluctuations in daily feeling states among older, obese adults with knee osteoarthritis. Journal of Behavioral Medicine, 27(2), 101-121.

Ford, J. C., & Ford, J. A. (2018). Multimorbidity: will it stand the test of time? Age and Ageing, 47(1), 6-8.

Foster, N. E., Healey, E. L., Holden, M. A., Nicholls, E., Whitehurst, D. G., Jowett, S., ... & Hay, E. M. (2014). A multicentre, pragmatic, parallel group, randomised controlled trial to compare the clinical and cost-effectiveness of three physiotherapy-led exercise interventions for knee osteoarthritis in older adults: the BEEP trial protocol (ISRCTN: 93634563). BMC musculoskeletal disorders, 15(1), 254.

Foy, C. G., Lewis, C. E., Hairston, K. G., Miller, G. D., Lang, W., Jakicic, J. M., ... & Look AHEAD Research Group. (2011). Intensive lifestyle intervention improves physical function among obese adults with knee pain: findings from the Look AHEAD trial. Obesity, 19(1), 83-93.

Fransen, M., & McConnell, S. (2015). Exercise for osteoarthritis of the knee. Cochrane Database of Systematic Reviews (1).

Fransen, M., McConnell, S., Hernandez-Molina, G., & Reichenbach, S. (2015). Exercise for osteoarthritis of the hip. Cochrane Database of Systematic Reviews, (4).

Freeling, P., Rao, B. M., Paykel, E. S., Sireling, L. I., & Burton, R. H. (1985). Unrecognized depression in general practice. Br Med J (Clin Res Ed), 290(6485), 1880-1883.

Fries, J. F. (1996). Physical activity, the compression of morbidity, and the health of the elderly. Journal of the Royal Society of Medicine, 89(2), 64-68.

Gale, N. K., Heath, G., Cameron, E., Rashid, S., & Redwood, S. (2013). Using the framework method for the analysis of qualitative data in multi-disciplinary health research. BMC Medical Research Methodology, 13(1), 117.

Garber, C. E., Blissmer, B., Deschenes, M. R., Franklin, B. A., Lamonte, M. J., Lee, I. M., ... & Swain, D. P. (2011). Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. Medicine and Science in Sports and Exercise, 43(7) 1334-1359.

Gay, C., Chabaud, A., Guilley, E., & Coudeyre, E. (2016). Educating patients about the benefits of physical activity and exercise for their hip and knee osteoarthritis. Systematic literature review. Annals of Physical and Rehabilitation Medicine, 59(3), 174-183.

Geneen, L. J., Moore, R. A., Clarke, C., Martin, D., Colvin, L. A., & Smith, B. H. (2017). Physical activity and exercise for chronic pain in adults: an overview of Cochrane Reviews. Cochrane Database of Systematic Reviews, (4).

Gettings, L. (2010). Psychological well-being in rheumatoid arthritis: a review of the literature. Musculoskeletal Care, 8(2), 99-106.

Gibson-Moore, H. (2019). UK Chief Medical Officers' physical activity guidelines 2019: What's new and how can we get people more active? Nutrition Bulletin, 44(4), 320-328.

Gill, P., Stewart, K., Treasure, E., & Chadwick, B. (2008). Methods of data collection in qualitative research: interviews and focus groups. British Dental Journal, 204(6), 291.

Glaser, B. G. (1978). Strauss (1967): The Discovery of Grounded Theory: Strategies for Qualitative Research. London: Wiedenfeld and Nicholson, 81, 86.

Gleicher, Y., Croxford, R., Hochman, J., & Hawker, G. (2011). A prospective study of mental health care for comorbid depressed mood in older adults with painful osteoarthritis. BMC Psychiatry, 11(1), 147.

Goh, S. L., Persson, M. S., Stocks, J., Hou, Y., Lin, J., Hall, M. C., ... & Zhang, W. (2019). Efficacy and potential determinants of exercise therapy in knee and hip osteoarthritis: A systematic review and meta-analysis. Annals of Physical and Rehabilitation Medicine, 62(5), 356.

Goodwin, N., Curry, N., Naylor, C., Ross, S., & Duldig, W. (2010). Managing people with long-term conditions. London: The Kings Fund. https://www.kingsfund.org.uk/sites/default/files/field/field_document/managing-people-long-term-conditions-gp-inquiry-research-paper-mar11.

Greene, J. C., Caracelli, V. J., & Graham, W. F. (1989). Toward a conceptual framework for mixed-method evaluation designs. Educational Evaluation and Policy Analysis, 11(3), 255-274.

Greenhalgh, T., Howick, J., & Maskrey, N. (2014). Evidence based medicine: a movement in crisis? BMJ, 348, 3725.

Guba, E. G., & Lincoln, Y. S. (1994). Competing paradigms in qualitative research. Handbook of Qualitative Research, 2(163-194), 105.

Guccione, A. A., Felson, D. T., Anderson, J. J., Anthony, J. M., Zhang, Y., Wilson, P. W., ... & Kannel, W. B. (1994). The effects of specific medical conditions on the functional limitations of elders in the Framingham Study. American Journal of Public Health, 84(3), 351-358.

Guetterman, T. C., Fetters, M. D., & Creswell, J. W. (2015). Integrating quantitative and qualitative results in health science mixed methods research through joint displays. The Annals of Family Medicine, 13(6), 554-561.

Guthrie, B., Payne, K., Alderson, P., McMurdo, M. E., & Mercer, S. W. (2012). Adapting clinical guidelines to take account of multimorbidity. BMJ, 345, e6341.

Hall, R. (2012). Mixed methods: In search of a paradigm. Vortrag. https://www.researchgate.net/profile/Ralph_Hall/publication/259045135_Mixed_Methods_In_search_of_a_paradigm/links/0a85e533910ff933b1000000/Mixed-Methods-In-search-of-a-paradigm.

Hall, A. J., Stubbs, B., Mamas, M. A., Myint, P. K., & Smith, T. O. (2016). Association between osteoarthritis and cardiovascular disease: systematic review and meta-analysis. European Journal of Preventive Cardiology, 23(9), 938-946.

Hammer, N. M., Bieler, T., Beyer, N., & Midtgaard, J. (2016). The impact of self-efficacy on physical activity maintenance in patients with hip osteoarthritis–a mixed methods study. Disability and Rehabilitation, 38(17), 1691-1704.

Harrell Jr, F. E. (2015). Regression modeling strategies: with applications to linear models, logistic and ordinal regression, and survival analysis. Springer.

Harris, T. J., Owen, C. G., Victor, C. R., Adams, R., Ekelund, U., & Cook, D. G. (2009). A Comparison of Questionnaire, Accelerometer, and Pedometer. Medicine & Science in Sports & Exercise, 41(7), 1392–1402.

Haseler, C., Crooke, R., & Haseler, T. (2019). Promoting physical activity to patients. BMJ, 366, l5230.

Hawker, G. A., Croxford, R., Bierman, A. S., Harvey, P. J., Ravi, B., Stanaitis, I., & Lipscombe, L. L. (2014). All-cause mortality and serious cardiovascular events in people with hip and knee osteoarthritis: a population based cohort study. PloS One, 9(3), e91286.

Hawker, G. A., Davis, A. M., French, M. R., Cibere, J., Jordan, J. M., March, L., ... & Dieppe, P. (2008). Development and preliminary psychometric testing of a new OA pain measure–an OARSI/OMERACT initiative. Osteoarthritis and Cartilage, 16(4), 409-414.

Hawker, G. A., Stewart, L., French, M. R., Cibere, J., Jordan, J. M., March, L., ... & Gooberman-Hill, R. (2008). Understanding the pain experience in hip and knee osteoarthritis–an OARSI/OMERACT initiative. Osteoarthritis and Cartilage, 16(4), 415-422.

Hay, E. M., Dziedzic, K. S., Foster, N. E., Peat, G., van der Windt, D. A., Bartlam, B., ... & Hughes, R. (2018). Optimal primary care management of clinical osteoarthritis and joint pain in older people: a mixed-methods programme of systematic reviews, observational and qualitative studies, and randomised controlled trials. Programme Grants for Applied Research, 6(4), 1-260.

Heale, R., & Forbes, D. (2013). Understanding triangulation in research. Evidence-Based Nursing, 16(4), 98-98.

Healey, E. L., Afolabi, E. K., Lewis, M., Edwards, J. J., Jordan, K. P., Finney, A., ... & Dziedzic, K. S. (2018). Uptake of the NICE osteoarthritis guidelines in primary care: a survey of older adults with joint pain. BMC Musculoskeletal Disorders, 19(1), 295.

Healey, E. L., Jinks, C., Tan, V. A., Chew-Graham, C. A., Lawton, S. A., Nicholls, E., ... & Dziedzic, K. S. (2015). Improving the care of people with long-term conditions in primary care: protocol for the ENHANCE pilot trial. Journal of Comorbidity, 5(1), 135-149.

Hendry, M., Williams, N. H., Markland, D., Wilkinson, C., & Maddison, P. (2006). Why should we exercise when our knees hurt? A qualitative study of primary care patients with osteoarthritis of the knee. Family Practice, 23(5), 558-567.

Henriksen, M., Hansen, J. B., Klokker, L., Bliddal, H., & Christensen, R. (2016). Comparable effects of exercise and analgesics for pain secondary to knee osteoarthritis: a meta-analysis of trials included in Cochrane systematic reviews. Journal of Comparative Effectiveness Research, 5(4), 417-431.

Herbolsheimer, F., Schaap, L. A., Edwards, M. H., Maggi, S., Otero, Á., Timmermans, E. J., ... & Dennison, E. M. (2016). Physical activity patterns among older adults with and without knee osteoarthritis in six European countries. Arthritis Care & Research, 68(2), 228-236.

Hibbard, J. H., Stockard, J., Mahoney, E. R., & Tusler, M. (2004). Development of the Patient Activation Measure (PAM): conceptualizing and measuring activation in patients and consumers. Health Services Research, 39(4p1), 1005-1026.

Higgins, J. P., Altman, D. G., Sterne, J. A. (2017). Chapter 8: Assessing risk of bias in included studies. In Cochrane Handbook for Systematic Reviews of Interventions version 5.2.0. Cochrane, Available from: www.training.cochrane.org/handbook.

Higgins, J. P., & Green, S. (2011). Cochrane handbook for systematic reviews of interventions. John Wiley & Sons. 2nd Edition. Chichester UK.

Higgins, J. P., Thomas, J., Chandler, J., Cumpston, M., Li, T., Page, M. J., & Welch, V. A. (Eds.). (2019). *Cochrane handbook for systematic reviews of interventions*. John Wiley & Sons.

Hoffmann, T. C., Glasziou, P. P., Boutron, I., Milne, R., Perera, R., Moher, D., ... & Lamb, S. E. (2016). Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. Gesundheitswesen (Bundesverband der Arzte des Offentlichen Gesundheitsdienstes (Germany)), *78*(3), 175.

Holden, M. A., Burke, D. L., Runhaar, J., van Der Windt, D., Riley, R. D., Dziedzic, K., ... & Brown, J. (2017). Subgrouping and TargetEd Exercise pRogrammes for knee and hip OsteoArthritis (STEER OA): a systematic review update and individual participant data meta-analysis protocol. BMJ open, 7(12), e018971.

Holden, M. A., Nicholls, E. E., Young, J., Hay, E. M., & Foster, N. E. (2012). Role of exercise for knee pain: what do older adults in the community think? Arthritis Care & Research, 64(10), 1554-1564.

Holden, M. A., Nicholls, E. E., Young, J., Hay, E. M., & Foster, N. E. (2009). UK-based physical therapists' attitudes and beliefs regarding exercise and knee osteoarthritis: Findings from a mixed-methods study. Arthritis Care & Research: Official Journal of the American College of Rheumatology, 61(11), 1511-1521.

Holden, M. A., Nicholls, E. E., Young, J., Hay, E. M., & Foster, N. E. (2014). Exercise and physical activity in older adults with knee pain: a mixed methods study. Rheumatology, 54(3), 413-423.

Holden, M. A., Waterfield, J., Whittle, R., Bennell, K., Quicke, J. G., Chesterton, L., & Mallen, C. D. (2019). How do UK physiotherapists address weight loss among individuals with hip osteoarthritis? A mixed-methods study. Musculoskeletal Care, 17(1), 133-144.

Holla, J. F., van der Leeden, M., Knol, D. L., Roorda, L. D., van der Esch, M., Voorneman, R. E., ... & Dekker, J. (2013). The association of body-mass index and depressed mood with knee pain and activity limitations in knee osteoarthritis: results from the Amsterdam osteoarthritis cohort. BMC Musculoskeletal Disorders, 14(1), 296.

Hoogeboom, T. J., den Broeder, A. A., Swierstra, B. A., de Bie, R. A., & van den Ende, C. H. (2012). Joint-pain comorbidity, health status, and medication use in hip and knee osteoarthritis: A cross-sectional study. Arthritis Care & Research, 64(1), 54-58.

Hootman, J. M., Helmick, C. G., Barbour, K. E., Theis, K. A., & Boring, M. A. (2016). Updated projected prevalence of self-reported doctor-diagnosed arthritis and arthritis-attributable activity limitation among US adults, 2015–2040. Arthritis & Rheumatology, 68(7), 1582-1587.

Hughes, S. L., Seymour, R. B., Campbell, R., Pollak, N., Huber, G., & Sharma, L. (2004). Impact of the fit and strong intervention on older adults with osteoarthritis. The Gerontologist, 44(2), 217-228.

Hunt, E. R., & Papathomas, A. (2019). Being physically active through chronic illness: life experiences of people with arthritis. Qualitative Research in Sport, Exercise and Health, 12(2), 1-14.

Hurley, M. V., Walsh, N., Bhavnani, V., Britten, N., & Stevenson, F. (2010). Health beliefs before and after participation on an exercised-based rehabilitation programme for chronic knee pain: Doing is believing. BMC Musculoskeletal Disorders, 11(1), 31.

Hurley, M., Dickson, K., Hallett, R., Grant, R., Hauari, H., Walsh, N., ... & Oliver, S. (2018). Exercise interventions and patient beliefs for people with hip, knee or hip and knee osteoarthritis: a mixed methods review. Cochrane Database of Systematic Reviews, (4).

Iijima, H., Aoyama, T., Fukutani, N., Isho, T., Yamamoto, Y., Hiraoka, M., ... & Matsuda, S. (2018). Psychological health is associated with knee pain and physical function in patients with knee osteoarthritis: an exploratory cross-sectional study. BMC Psychology, 6(1), 19.

INVOLVE. (2018) National Standards for Public Involvement in Research V1 March 2018. National Institute for Health Research. https://www.invo.org.uk/wp-content/uploads/2019/02/71110_A4_Public_Involvement_Standards_v4_WEB.

Iserson, K. V. (2012). Improvised Medicine Providing Care in Extreme Environments. McGraw Hill Medical. New York.

Jack, K., McLean, S. M., Moffett, J. K., & Gardiner, E. (2010). Barriers to treatment adherence in physiotherapy outpatient clinics: a systematic review. Manual Therapy, 15(3), 220-228.

Jackson, S. E., & Steptoe, A. (2017). Association between perceived weight discrimination and physical activity: a population-based study among English middle-aged and older adults. BMJ Open, 7(3), e014592.

Jackson, T., Xu, T., & Jia, X. (2020). Arthritis self-efficacy beliefs and functioning among osteoarthritis and rheumatoid arthritis patients: a meta-analytic review. Rheumatology, 59(5), 948-958.

Jadad, A. R., To, M. J., Emara, M., & Jones, J. (2011). Consideration of multiple chronic diseases in randomized controlled trials. Jama, 306(24), 2670-2672.

Janz, N. K., & Becker, M. H. (1984). The health belief model: A decade later. Health Education Quarterly, 11(1), 1-47.

Jenkinson, C. M., Doherty, M., Avery, A. J., Read, A., Taylor, M. A., Sach, T. H., ... & Muir, K. R. (2009). Effects of dietary intervention and quadriceps strengthening exercises on pain and function in overweight people with knee pain: randomised controlled trial. BMJ, 339, b3170.

Jeong, S. W., Kim, S. H., Kang, S. H., Kim, H. J., Yoon, C. H., Youn, T. J., & Chae, I. H. (2019). Mortality reduction with physical activity in patients with and without cardiovascular disease. European Heart Journal, 40(43), 3547-3555.

Johnson, R. B., & Onwuegbuzie, A. J. (2004). Mixed methods research: A research paradigm whose time has come. Educational Researcher, 33(7), 14-26.

Johnson, R. B., Onwuegbuzie, A. J., & Turner, L. A. (2007). Toward a definition of mixed methods research. Journal of Mixed Methods Research, 1(2), 112-133.

Johnson, T. P. (2014). Snowball sampling: introduction. Wiley StatsRef: Statistics Reference Online. (eds N. Balakrishnan, T. Colton, B. Everitt, W. Piegorsch, F. Ruggeri and J.L. Teugels). https://onlinelibrary.wiley.com/doi/abs/10.1002/9781118445112.stat05720.

Joling, K. J., van Marwijk, H. W., Piek, E., van der Horst, H. E., Penninx, B. W., Verhaak, P., & van Hout, H. P. (2011). Do GPs' medical records demonstrate a good recognition of depression? A new perspective on case extraction. Journal of Affective Disorders, 133(3), 522-527.

Juhakoski, R., Malmivaara, A., Lakka, T. A., Tenhonen, S., Hannila, M. L., & Arokoski, J. P. (2013). Determinants of pain and functioning in hip osteoarthritis–a two-year prospective study. Clinical Rehabilitation, 27(3), 281-287.

Juhl, C., Christensen, R., Roos, E. M., Zhang, W., & Lund, H. (2014). Impact of exercise type and dose on pain and disability in knee osteoarthritis: a systematic review and meta-regression analysis of randomized controlled trials. Arthritis & Rheumatology, 66(3), 622-636.

Kadam, U. T., Jordan, K., & Croft, P. R. (2004). Clinical comorbidity in patients with osteoarthritis: a case-control study of general practice consulters in England and Wales. Annals of the Rheumatic Diseases, 63(4), 408-414.

Kanavaki, A. M., Rushton, A., Efstathiou, N., Alrushud, A., Klocke, R., Abhishek, A., & Duda, J. L. (2017). Barriers and facilitators of physical activity in knee and hip osteoarthritis: a systematic review of qualitative evidence. BMJ Open, 7(12), e017042.

Kaptein, S. A., Backman, C. L., Badley, E. M., Lacaille, D., Beaton, D. E., Hofstetter, C., & Gignac, M. A. (2013). Choosing where to put your energy: a qualitative analysis of the role of physical activity in the lives of working adults with arthritis. Arthritis Care & Research, 65(7), 1070-1076.

Karlsson, P., & Bergmark, A. (2015). Compared with what? An analysis of control-group types in Cochrane and Campbell reviews of psychosocial treatment efficacy with substance use disorders. Addiction, 110(3), 420-428.

Katz, M. H. (2003). Multivariable analysis: a primer for readers of medical research. Annals of Internal Medicine, 138(8), 644-650.

Kearns, B., Ara, R., Young, T., & Relton, C. (2013). Association between body mass index and health-related quality of life, and the impact of self-reported long-term conditions–cross-sectional study from the south Yorkshire cohort dataset. BMC Public Health, 13(1), 1009.

Keats, M. R., Cui, Y., DeClercq, V., Dummer, T. J., Forbes, C., Grandy, S. A., ... & Parker, L. (2017). Multimorbidity in Atlantic Canada and association with low levels of physical activity. Preventive Medicine, 105, 326-331.

Kerr, E. A., Heisler, M., Krein, S. L., Kabeto, M., Langa, K. M., Weir, D., & Piette, J. D. (2007). Beyond comorbidity counts: how do comorbidity type and severity influence diabetes patients' treatment priorities and self-management? Journal of General Internal Medicine, 22(12), 1635-1640.

King, L. K., Marshall, D. A., Faris, P., Woodhouse, L., Jones, C. A., Noseworthy, T., ... & Hawker, G. A. (2019). Use of recommended non-surgical knee osteoarthritis management in patients prior to total knee arthroplasty: a cross-sectional study. The Journal of Rheumatology, 47(8), 1253-1260.

Kingston, A., Robinson, L., Booth, H., Knapp, M., Jagger, C., & MODEM project. (2018). Projections of multi-morbidity in the older population in England to 2035: estimates from the Population Ageing and Care Simulation (PACSim) model. Age and Ageing, 47(3), 374-380.

Kittelson, A. J., George, S. Z., Maluf, K. S., & Stevens-Lapsley, J. E. (2014). Future directions in painful knee osteoarthritis: harnessing complexity in a heterogeneous population. Physical Therapy, 94(3), 422-432.

Klompstra, L., Jaarsma, T., & Strömberg, A. (2015). Physical activity in patients with heart failure: barriers and motivations with special focus on sex differences. Patient Preference and Adherence, 9, 1603.

Kraus, I., Mueller, G., Haupt, G., Steinhilber, B., Janssen, P., Jentner, N., & Martus, P. (2016). Effectiveness and efficiency of an 11-week exercise intervention for patients with hip or knee osteoarthritis: a protocol for a controlled study in the context of health services research. BMC Public Health, 16(1), 367.

Kraus, V. B., Sprow, K., Powell, K. E., Buchner, D., Bloodgood, B., Piercy, K., ... & Kraus, W. E. (2019). Effects of physical activity in knee and hip osteoarthritis: a systematic umbrella review. Medicine & Science in Sports & Exercise, 51(6), 1324-1339.

Kriegsman, D. M., Deeg, D. J., & Stalman, W. A. (2004). Comorbidity of somatic chronic diseases and decline in physical functioning: The longitudinal aging study Amsterdam. Journal of Clinical Epidemiology, 57(1), 55-65.

Kvale, S. (1983). The qualitative research interview: A phenomenological and a hermeneutical mode of understanding. Journal of Phenomenological Psychology, 14(2), 171.

Kyu, H. H., Bachman, V. F., Alexander, L. T., Mumford, J. E., Afshin, A., Estep, K., ... & Cercy, K. (2016). Physical activity and risk of breast cancer, colon cancer, diabetes, ischemic heart disease, and ischemic stroke events: systematic review and dose-response meta-analysis for the Global Burden of Disease Study 2013. BMJ, 354, i3857.

Legha, A., Burke, D. L., Foster, N. E., van der Windt, D. A., Quicke, J. G., Healey, E. L., ... & Holden, M. A. (2020). Do comorbidities predict pain and function in knee osteoarthritis following an exercise intervention, and do they moderate the effect of exercise? Analyses of data from three randomized controlled trials. Musculoskeletal Care, 18(1), 3-11.

Leite, A. A., Costa, A. J. G., Lima, B. D. A. M. D., Padilha, A. V. L., Albuquerque, E. C. D., & Marques, C. D. L. (2011). Comorbidities in patients with osteoarthritis: frequency and impact on pain and physical function. Revista Brasileira de Reumatologia, 51(2), 118-123.

Liao, S. Y., Benzo, R., Ries, A. L., & Soler, X. (2014). Physical activity monitoring in patients with chronic obstructive pulmonary disease. Chronic Obstructive Pulmonary Diseases, 1(2), 155.

Lim, J. Y., Tchai, E., & Jang, S. N. (2010). Effectiveness of aquatic exercise for obese patients with knee osteoarthritis: a randomized controlled trial. Physical Medicine and Rehabilitation, 2(8), 723-731.

Lin, E. H., Katon, W., Von Korff, M., Tang, L., Williams Jr, J. W., Kroenke, K., ... & Hoffing, M. (2003). Effect of improving depression care on pain and functional outcomes among older adults with arthritis: a randomized controlled trial. Jama, 290(18), 2428-2429.

Lincoln, YS. & Guba, EG. (1985). Naturalistic Inquiry. Newbury Park, CA: Sage Publications.

Litwic, A., Edwards, M. H., Dennison, E. M., & Cooper, C. (2013). Epidemiology and burden of osteoarthritis. British Medical Bulletin, 105(1), 185-199.

Loeb, D. F., Binswanger, I. A., Candrian, C., & Bayliss, E. A. (2015). Primary care physician insights into a typology of the complex patient in primary care. The Annals of Family Medicine, 13(5), 451-455.

Louati, K., & Berenbaum, F. (2019). Comorbidities that impact management of osteoarthritis. Available from: https://www.uptodate.com/contents/comorbidities-that-impact-management-of-osteoarthritis.

Louati, K., Vidal, C., Berenbaum, F., & Sellam, J. (2015). Association between diabetes mellitus and osteoarthritis: systematic literature review and meta-analysis. RMD Open, 1(1), e000077.

Loza, E., Jover, J. A., Rodriguez, L., Carmona, L., & EPISER Study Group. (2009). Multimorbidity: prevalence, effect on quality of life and daily functioning, and variation of this effect when one condition is a rheumatic disease. In Seminars in Arthritis and Rheumatism, 38(4), 312-319.

Mackichan, F., Adamson, J., & Gooberman-Hill, R. (2013). 'Living within your limits': activity restriction in older people experiencing chronic pain. Age and Ageing, 42(6), 702-708.

MacMahon, S. (2018). Multimorbidity: a priority for global health research. The Academy of Medical Sciences: London, UK. https://acmedsci.ac.uk/file-download/82222577.

Mair, F. S., & May, C. R. (2014). Thinking about the burden of treatment. BMJ Clinical Research, 349, g6680.

Malterud, K. (2001). Qualitative research: standards, challenges, and guidelines. The Lancet, 358(9280), 483-488.

Manaf, H. (2013). Barriers to participation in physical activity and exercise among middle-aged and elderly individuals. Singapore Med J, 54(10), 581-586.

Mancuso, C. A., Sayles, W., Robbins, L., Phillips, E. G., Ravenell, K., Duffy, C., ... & Charlson, M. E. (2006). Barriers and facilitators to healthy physical activity in asthma patients. Journal of Asthma, 43(2), 137-143.

Mangani, I., Cesari, M., Kritchevsky, S. B., Maraldi, C., Carter, C. S., Atkinson, H. H., . . . Pahor, M. (2006). Physical exercise and comorbidity. results from the fitness and arthritis in seniors trial (FAST). Aging Clinical and Experimental Research, 18(5), 374-380.

Manning, E., & Gagnon, M. (2017). The complex patient: A concept clarification. Nursing & Health Sciences, 19(1), 13-21.

Marcum, Z. A., Zhan, H. L., Perera, S., Moore, C. G., Fitzgerald, G. K., & Weiner, D. K. (2014). Correlates of gait speed in advanced knee osteoarthritis. Pain Medicine, 15(8), 1334-1342.

Marill, K. A. (2004). Advanced statistics: linear regression, part I: simple linear regression. Academic Emergency Medicine, 11(1), 87-93.

Marks, R. (2012). Knee osteoarthritis and exercise adherence: A review. Current Aging Science, 5(1), 72-83.

Marks, R. (2014). Self-efficacy and arthritis disability: An updated synthesis of the evidence base and its relevance to optimal patient care. Health Psychology Open, 1(1).

Martin, K. A., Rejeski, W. J., Miller, M. E., James, M. K., Walter H Ettinger, J. R., & Messier, S. P. (1999). Validation of the PASE in older adults with knee pain and physical disability. Medicine & Science in Sports & Exercise, 31(5), 627-633.

Mason, J. (2006). Six strategies for mixing methods and linking data in social science research. National Centre for Research Methods. Economic and Social Research Council. Manchester. http://eprints.ncrm.ac.uk/482/1/0406_six%2520strategies%2520for%2520mixing%2520methods.

Maxwell, J. A. (2011). Paradigms or toolkits? Philosophical and methodological positions as heuristics for mixed methods research. Mid-Western Educational Researcher, 24(2), 27-30.

McAlindon, T. E., Wilson, P. W., Aliabadi, P., Weissman, B., & Felson, D. T. (1999). Level of physical activity and the risk of radiographic and symptomatic knee osteoarthritis in the elderly: the Framingham study. The American Journal of Medicine, 106(2), 151-157.

McKenna, K., Leykum, L. K., & McDaniel Jr, R. R. (2013). The role of improvising in patient care. Health Care Management Review, 38(1), 1-8.

McNamara, C. (1999). General guidelines for conducting interviews. Minnesota.

Melendez-Torres, G., O'Mara-Eves, A., Thomas, J., Brunton, G., Caird, J., & Petticrew, M. (2016). Interpretive analysis of 85 systematic reviews suggests that narrative syntheses and meta-analyses are incommensurate in argumentation. Research Synthesis Methods, 8(1), 109-118.

Messier, S. P., Gutekunst, D. J., Davis, C., & DeVita, P. (2005). Weight loss reduces knee-joint loads in overweight and obese older adults with knee osteoarthritis. Arthritis & Rheumatism, 52(7), 2026-2032.

Messier, S. P., Loeser, R. F., Miller, G. D., Morgan, T. M., Rejeski, W. J., Sevick, M. A., . . . Williamson, J. D. (2004). Exercise and dietary weight loss in overweight and obese older adults with knee osteoarthritis: The arthritis, diet, and activity promotion trial. Arthritis & Rheumatology, 50(5), 1501-1510.

Messier, S. P., Mihalko, S. L., Legault, C., Miller, G. D., Nicklas, B. J., DeVita, P., . . . Eckstein, F. (2013). Effects of intensive diet and exercise on knee joint loads, inflammation, and clinical outcomes among overweight and obese adults with knee osteoarthritis: The IDEA randomized clinical trial. Jama, 310(12), 1263-1273.

Michie, S., Johnston, M., Abraham, C., Lawton, R., Parker, D., Walker, A. et al. (2005) Making psychological theory useful for implementing evidence based practice: a consensus approach. Quality and Safety in Health Care, 14(1), 26-33.

Michie, S., Van Stralen, M. M., & West, R. (2011). The behaviour change wheel: a new method for characterising and designing behaviour change interventions. Implementation Science, 6(1), 42.

Miller, G. D., Nicklas, B. J., Davis, C., Loeser, R. F., Lenchik, L., & Messier, S. P. (2006). Intensive weight loss program improves physical function in older obese adults with knee osteoarthritis. Obesity, 14(7), 1219-1230.

Miller, G. D., Rejeski, W. J., Williamson, J. D., Morgan, T., Sevick, M. A., Loeser, R. F., ... & Messier, S. P. (2003). The Arthritis, Diet and Activity Promotion Trial (ADAPT): design, rationale, and baseline results. Controlled Clinical Trials, 24(4), 462-480.

Mitchell, A. J., Rao, S., & Vaze, A. (2011). Can general practitioners identify people with distress and mild depression? A meta-analysis of clinical accuracy. Journal of Affective Disorders, 130(1-2), 26-36.

Moher, D., Jadad, A. R., Nichol, G., Penman, M., Tugwell, P., & Walsh, S. (1995). Assessing the quality of randomized controlled trials: An annotated bibliography of scales and checklists. Controlled Clinical Trials, 16(1), 62-73.

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & PRISMA Group. (2010). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. International Journal of Surgery, 8(5), 336-341.

Mold, J. W., Blake, G. H., & Becker, L. A. (1991). Goal-oriented medical care. Fam Med, 23(1), 46-51.

Møller, A., Willadsen, T. G., Jönsson, A. B. R., & Reventlow, S. (2018). 3 Definition of multimorbidity and risk of overdiagnosis. British Medical Journal, 23(2), 1-2.

Moody, J., Hale, L., & Waters, D. (2012). Perceptions of a water-based exercise programme to improve physical function and falls risk in older adults with lower extremity osteoarthritis: barriers, motivators and sustainability. New Zealand Journal of Physiotherapy, 40(2), 64-70.

Morgan, G. S., Willmott, M., Ben-Shlomo, Y., Haase, A. M., & Campbell, R. M. (2019). A life fulfilled: positively influencing physical activity in older adults–a systematic review and meta-ethnography. BMC Public Health, 19(1), 362.

Morris, R. L., Sanders, C., Kennedy, A. P., & Rogers, A. (2011). Shifting priorities in multimorbidity: A longitudinal qualitative study of patient's prioritization of multiple conditions. Chronic Illness, 7(2), 147-161.

Morse, J. M. (1991). Approaches to qualitative-quantitative methodological triangulation. Nursing Research, 40(2), 120-123.

Muckelt, P. E., Roos, E. M., Stokes, M., McDonough, S., Grønne, D. T., Ewings, S., & Skou, S. T. (2020). Comorbidities and their link with individual health status: A cross-sectional analysis of 23,892 people with knee and hip osteoarthritis from primary care. Journal of Comorbidity, 10, 1-11.

Mulrow, C. D. (1994). Rationale for systematic reviews. BMJ (Clinical Research Ed.), 309(6954), 597-599.

Murphy, L. B., Hootman, J. M., Boring, M. A., Carlson, S. A., Qin, J., Barbour, K. E., ... & Helmick, C. G. (2017). Leisure Time Physical Activity Among US Adults With Arthritis, 2008− 2015. American Journal of Preventive Medicine, 53(3), 345-354.

Muth, C., van den Akker, M., Blom, J. W., Mallen, C. D., Rochon, J., Schellevis, F. G., ... & Perera, R. (2014). The Ariadne principles: how to handle multimorbidity in primary care consultations. BMC Medicine, 12(1), 223.

Nardi, R. and Scanelli, G. (2007). In response to: Fortin, M., Soubhi, H., Hudon, C., Bayliss, E. A., & Van den Akker, M. (2007). Multimorbidity's many challenges. BMJ, 334(7602), 1016–1017.

Nardi, R., Scanelli, G., Corrao, S., Iori, I., Mathieu, G., & Amatrian, R. C. (2007). Co-morbidity does not reflect complexity in internal medicine patients. European Journal of Internal Medicine, 18(5), 359-368.

National Health Service (NHS) Alderwick, H., & Dixon, J. (2019). The NHS long term plan. https://www.longtermplan.nhs.uk/wp-content/uploads/2019/08/nhs-long-term-plan-version-1.2.

National Health Service (NHS) Digital. (2016). Health Survey for England, 2016: https:// digital.nhs.uk/data-and-information/publications/statistical/health-survey-forengland/health-survey-for-england-2016.

National Health Service (NHS) Lifestyles Team, Digital. (2019) 'Statistics on Obesity, Physical Activity and Diet – England, 2019'. Health and Social Care Information Centre. https://digital.nhs.uk/data-and-information/publications/statistical/statistics-on-obesity-physical-activity-and-diet/statistics-on-obesity-physical-activity-and-diet-england-2019.

National Health Service (NHS). (2014) NHS Five Year Forward View. England NHS. https://www.england.nhs.uk/wp-content/uploads/2014/10/5yfv-web.

National Health Service (NHS). (2015) Our Declaration: Person centered care for long term conditions. NHS England. https://www.england.nhs.uk/wp-content/uploads/2015/09/ltc-our-declaration.

National Health Service (NHS). (2019) The NHS Long Term Plan. NHS England. https://www.longtermplan.nhs.uk/wp-content/uploads/2019/08/nhs-long-term-plan-version-1.2.

National Health Service (NHS). (2019). House of Care–a framework for long term condition care. https://www.england.nhs.uk/ourwork/clinical-policy/ltc/house-of-care/.

National Institute for health and Care Excellence (NICE) Brown, T. J. (2006). Obesity: guidance on the prevention, identification, assessment and management of overweight and obesity in adults and children. NICE Clinical Guideline 43. National Institute for Health and Clinical Excellence. https://www.nice.org.uk/guidance/cg189.

National Institute for health and Care Excellence (2020). Chronic pain in over 16s: assessment and management. Draft for consultation, In development. GID-NG10069.

National Institute for health and Care Excellence (NICE) Farmer, C., Fenu, E., O'Flynn, N., & Guthrie, B. (2016). Clinical assessment and management of multimorbidity: summary of NICE guidance. BMJ, 354, g4843.

National Institute for health and Care Excellence (NICE) McGuire, H., Longson, D., Adler, A., Farmer, A., & Lewin, I. (2016). Management of type 2 diabetes in adults: summary of updated NICE guidance. BMJ, 353, g1575.

National Institute for health and Care Excellence (2012). Patient experience in adult NHS services: improving the experience of care for people using adult NHS services. National Institute for Health and Care Excellence. CG138.

National Institute for health and Care Excellence (NICE) Rabar, S., Harker, M., O'Flynn, N., & Wierzbicki, A. S. (2014). Lipid modification and cardiovascular risk assessment for the primary and secondary prevention of cardiovascular disease: summary of updated NICE guidance. BMJ, 349, g4356.

National Institute for health and Care Excellence (NICE) Stegenga, H., Haines, A., Jones, K., & Wilding, J. (2014). Identification, assessment, and management of overweight and obesity: summary of updated NICE guidance. BMJ, 349, g6608.

National Institute for health and Care Excellence (NICE). (2009). Depression in adults: Recognition and management. Clinical guideline [CG90]. https://www.nice.org.uk/guidance/cg90.

National Institute for health and Care Excellence (NICE). (2014). Osteoarthritis: care and management. Clinical guideline [CG177]. www.nice.org.uk/guidance/cg177.

National Institute for health and Care Excellence (NICE). (2013). Physical activity: brief advice for adults in primary care. Public Health guideline [PH44]. https://www.nice.org.uk/guidance/PH44/chapter/recommendations-2#brief-advice.

National Institute for health and Care Excellence (NICE). (2016) Multimorbidity: clinical assessment and Multimorbidity: clinical assessment and management. NICE guideline [CG56]. nice.org.uk/guidance/ng56.

National Institute for Health and Care Excellence (NICE). (2016). Type 2 diabetes in adults: management: NICE guideline [NG28]. https://www.nice.org.uk/guidance/ng28.

National Institute for Health and Care Excellence (NICE). (2018). Chronic obstructive pulmonary disease in over 16s: diagnosis and management. NICE guideline [NG115]. https://www.nice.org.uk/guidance/ng115.

National Institute for Health and Care Excellence (NICE). (2014). Behaviour change: individual approaches. Public Health Guideline (PH49). https://www.nice.org.uk/guidance/ph49.

National Institute for Health and Care Excellence (NICE). (2007). Behaviour change: general approaches. Public Health Guideline (PH6). https://www.nice.org.uk/guidance/ph6.

National Joint Registry. (2018). National Joint Registry for England, Wales, Northern Ireland and the Isle of Man: 15th annual report, 2017. National Joint Registry Centre. https://www.hqip.org.uk/resource/national-joint-registry-15th-annual-report-2018/#.X1tTpmhKg2w.

Nicholls, E., Thomas, E., van der Windt, D. A., Croft, P. R., & Peat, G. (2014). Pain trajectory groups in persons with, or at high risk of, knee osteoarthritis: findings from the Knee Clinical Assessment Study and the Osteoarthritis Initiative. Osteoarthritis and Cartilage, 22(12), 2041-2050.

Nicolson, P. J., Bennell, K. L., Dobson, F. L., Van Ginckel, A., Holden, M. A., & Hinman, R. S. (2017). Interventions to increase adherence to therapeutic exercise in older adults with low back pain and/or hip/knee osteoarthritis: a systematic review and meta-analysis. British Journal of Sports Medicine, 51(10), 791-799.

Nicolson, P. J., Lee, H., Sanchez-Santos, M., Williamson, E., & Lamb, S. (2020). Synergistic effects of hip and knee osteoarthritis and comorbidities among older adults: analysis of the oxford pain, activity and lifestyle cohort study. Osteoarthritis and Cartilage, 28, S42-S43.

Nimon, K. F., & Oswald, F. L. (2013). Understanding the results of multiple linear regression: Beyond standardized regression coefficients. Organizational Research Methods, 16(4), 650-674.

Noble, N., Paul, C., Walsh, J., Wyndham, K., Wilson, S., & Stewart, J. (2019). Concordance between self-report and medical records of preventive healthcare delivery among a sample of disadvantaged patients from four aboriginal community controlled health services. BMC Health Services Research, 19(1), 111.

Normansell, R., Smith, J., Victor, C., Cook, D. G., Kerry, S., Iliffe, S., ... & Harris, T. (2014). Numbers are not the whole story: a qualitative exploration of barriers and facilitators to increased physical activity in a primary care based walking intervention. BMC Public Health, 14(1), 1272.

Nüesch, E., Dieppe, P., Reichenbach, S., Williams, S., Iff, S., & Jüni, P. (2011). All cause and disease specific mortality in patients with knee or hip osteoarthritis: population based cohort study. BMJ, 342, d1165.

O'Brien, K. K., Bayoumi, A. M., Strike, C., Young, N. L., & Davis, A. M. (2008). Exploring disability from the perspective of adults living with HIV/AIDS: development of a conceptual framework. Health and Quality of Life Outcomes, 6(1), 76.

O'Cathain, A., Murphy, E., & Nicholl, J. (2007). Why, and how, mixed methods research is undertaken in health services research in England: a mixed methods study. BMC Health Services Research, 7(1), 85.

Olsson, C. B., Ekelund, J., Degerstedt, Å., & Thorstensson, C. A. (2018). Change in self-efficacy after participation in a supported self-management program for osteoarthritis–an observational study of 11 906 patients. Disability and Rehabilitation, 42(15), 1-8.

Ong, K. Y., Lee, P. S. S., & Lee, E. S. (2019). Patient-centred and not disease-focused: a review of guidelines and multimorbidity. Singapore Medical Journal. [published online ahead of print, 2019 Sep 6]

Onwuegbuzie, A. J., & Johnson, R. B. (2004). The validity issue in mixed research. Research in the Schools, 13(1), 48-63.

Osteoarthritis Research Society International (OARSI) Lotz, M., Abramson, S., Eckstein, F., Berenbaum, F., Moskowitz, R., Aigner, T., ... & Loeser Jr, R. (2016). Osteoarthritis: A serious Disease. Osteoarthritis Research Society International. https://bit.ly/2I8sAfN.

Osteoarthritis Research Society International (OARSI) McAlindon, T. E., Bannuru, R., Sullivan, M. C., Arden, N. K., Berenbaum, F., Bierma-Zeinstra, S. M., ... & Kwoh, K. (2014). OARSI guidelines for the non-surgical management of knee osteoarthritis. Osteoarthritis and Cartilage, 22(3), 363-388.

Osteoarthritis Research Society International (OARSI) Zhang, W., Nuki, G., Moskowitz, R. W., Abramson, S., Altman, R. D., Arden, N. K., ... & Dougados, M. (2010). OARSI recommendations for the management of hip and knee osteoarthritis: part III: Changes in evidence following systematic cumulative update of research published through January 2009. Osteoarthritis and Cartilage, 18(4), 476-499.

Östlund, U., Kidd, L., Wengström, Y., & Rowa-Dewar, N. (2011). Combining qualitative and quantitative research within mixed method research designs: a methodological review. International Journal of Nursing Studies, 48(3), 369-383.

Paddison, C. A., Saunders, C. L., Abel, G. A., Payne, R. A., Campbell, J. L., & Roland, M. (2015). Why do patients with multimorbidity in England report worse experiences in primary care? Evidence from the General Practice Patient Survey. BMJ Open, 5(3), e006172.

Palazzo, C., Nguyen, C., Lefevre-Colau, M. M., Rannou, F., & Poiraudeau, S. (2016). Risk factors and burden of osteoarthritis. Annals of Physical and Rehabilitation Medicine, 59(3), 134-138.

Palinkas, L. A., Horwitz, S. M., Green, C. A., Wisdom, J. P., Duan, N., & Hoagwood, K. (2015). Purposeful sampling for qualitative data collection and analysis in mixed method implementation research. Administration and Policy in Mental Health and Mental Health Services Research, 42(5), 533-544.

Palys, T. (2008). Purposive sampling. In L. M. Given (Ed.) The Sage Encyclopedia of Qualitative Research Methods. Sage: Los Angeles, 697-8.

Park, J., McCaffrey, R., Newman, D., Liehr, P., & Ouslander, J. G. (2017). A Pilot Randomized Controlled Trial of the Effects of Chair Yoga on Pain and Physical Function Among Community-Dwelling Older Adults With Lower Extremity Osteoarthritis. Journal of the American Geriatrics Society, 65(3), 592-597.

Parkinson, L., Waters, D. L., & Franck, L. (2017). Systematic review of the impact of osteoarthritis on health outcomes for comorbid disease in older people. Osteoarthritis and Cartilage, 25(11), 1751-1770.

Paskins, Z., Sanders, T., & Hassell, A. B. (2014). Comparison of patient experiences of the osteoarthritis consultation with GP attitudes and beliefs to OA: A narrative review. BMC Family Practice, 15(1), 46.

Perkins, H. Y., Baum, G. P., Carmack Taylor, C. L., & Basen-Engquist, K. M. (2009). Effects of treatment factors, comorbidities and health-related quality of life on self-efficacy for physical activity in cancer survivors. Psycho-Oncology: Journal of the Psychological, Social and Behavioral Dimensions of Cancer, 18(4), 405-411.

Petursdottir, U., Arnadottir, S. A., & Halldorsdottir, S. (2010). Facilitators and barriers to exercising among people with osteoarthritis: A phenomenological study. Physical Therapy, 90(7), 1014-1025.

Pierce, C. (1905) 'What pragmatism is', The Monist, Vol. 15(2), 161-181.

Pisters, M. F., Veenhof, C., Van Dijk, G. M., Heymans, M. W., Twisk, J. W. R., & Dekker, J. (2012). The course of limitations in activities over 5 years in patients with knee and hip osteoarthritis with moderate functional limitations: risk factors for future functional decline. Osteoarthritis and Cartilage, 20(6), 503-510.

Popay, J., Roberts, H., Sowden, A., Petticrew, M., Arai, L., Rodgers, M., . . . Duffy, S. (2006). Guidance on the conduct of narrative synthesis in systematic reviews. A Product from the ESRC Methods Programme Version, 1, b92.

Porcheret, M., Jordan, K., Jinks, C., & P. Croft in collaboration with the Primary Care Rheumatology Society. (2007). Primary care treatment of knee pain—a survey in older adults. Rheumatology, 46(11), 1694-1700.

Prince, S. A., Adamo, K. B., Hamel, M. E., Hardt, J., Gorber, S. C., & Tremblay, M. (2008). A comparison of direct versus self-report measures for assessing physical activity in adults: a systematic review. International Journal of Behavioral Nutrition and Physical Activity, 5(1), 56.

Prior, J. A., Jordan, K. P., & Kadam, U. T. (2014). Associations between cardiovascular disease severity, osteoarthritis co-morbidity and physical health: a population-based study. Rheumatology, 53(10), 1794-1802.

Prior, J. A., Rushton, C. A., Jordan, K. P., & Kadam, U. T. (2012). Comorbidity Cohort (2C) study: cardiovascular disease severity and comorbid osteoarthritis in primary care. BMC Health Services Research, 12(1), 295.

Qin, J., Barbour, K. E., Murphy, L. B., Nelson, A. E., Schwartz, T. A., Helmick, C. G., ... & Jordan, J. M. (2017). Lifetime risk of symptomatic hand osteoarthritis: the Johnston County Osteoarthritis Project. Arthritis & Rheumatology, 69(6), 1204-1212.

Qin, J., Theis, K. A., Barbour, K. E., Helmick, C. G., Baker, N. A., & Brady, T. J. (2015). Impact of arthritis and multiple chronic conditions on selected life domains—United States, 2013. MMWR. Morbidity and Mortality Weekly Report, 64(21), 578.

Quicke, J. G., Foster, N. E., Ogollah, R. O., Croft, P. R., & Holden, M. A. (2017). Relationship between attitudes and beliefs and physical activity in older adults with knee pain: secondary analysis of a randomized controlled trial. Arthritis Care & Research, 69(8), 1192-1200.

Quicke, J. G., Foster, N. E., Thomas, M. J., & Holden, M. A. (2015). Is long-term physical activity safe for older adults with knee pain? a systematic review. Osteoarthritis and Cartilage, 23(9), 1445-1456.

Quicke, J. G., Runhaar, J., van der Windt, D., Healey, E. L., Foster, N. E., & Holden, M. A. (2020). Moderators of the effects of exercise for hip and knee osteoarthritis: a systematic review of subgroup analyses from randomised controlled trials. Osteoarthritis and Cartilage, 28, S161.

Rech, C., Camargo, E., Almeida, M., Bronoski, R., Okuno, N., & Reis, R. (2016). Barriers for physical activity in overweight adults. Revista Brasileira de Atividade Física & Saúde, 21(3), 272-279.

Reeuwijk, K. G., de Rooij, M., van Dijk, G. M., Veenhof, C., Steultjens, M. P., & Dekker, J. (2010). Osteoarthritis of the hip or knee: which coexisting disorders are disabling? Clinical Rheumatology, 29(7), 739-747.

Reges, O., Vilchinsky, N., Leibowitz, M., Khaskia, A., Mosseri, M., & Kark, J. D. (2013). Illness cognition as a predictor of exercise habits and participation in cardiac prevention and rehabilitation programs after acute coronary syndrome. BMC Public Health, 13(1), 956.

Rejeski, W. J., Focht, B. C., Messier, S. P., Morgan, T., Pahor, M., & Penninx, B. (2002). Obese, older adults with knee osteoarthritis: Weight loss, exercise, and quality of life. Health Psychology, 21(5), 419.

Reuben, D. B., & Tinetti, M. E. (2012). Goal-oriented patient care-an alternative health outcomes paradigm. The New England Journal of Medicine, 366(9), 777.

Rewald, S., Mesters, I., Lenssen, A. F., Emans, P. J., Wijnen, W., & de Bie, R. A. (2016). Effect of aqua-cycling on pain and physical functioning compared with usual care in patients with knee osteoarthritis: study protocol of a randomised controlled trial. BMC Musculoskeletal Disorders, 17(1), 88.

Ritchie, J. and Spencer, l. (1994). Qualitative data analysis for applied policy research. Bryman and Burgess (Eds.), Analysing Qualitative Data, 173-194.

Ritchie, J. L., & Lewis, J. J. and Elam, G.(2003). Designing and Selecting Samples. Qualitative research practice. A guide for social science students and researchers, 77-108.

Ritchie, J., & Spencer, L. (2002). Qualitative data analysis for applied policy research. The qualitative researcher's companion, 573, 305-29.

Ritchie, J., Lewis, J., Nicholls, C. M., & Ormston, R. (Eds.). (2013). Qualitative research practice: A guide for social science students and researchers. sage.

Roddy, E., Zhang, W., & Doherty, M. (2005). Aerobic walking or strengthening exercise for osteoarthritis of the knee? A systematic review. Annals of the Rheumatic Diseases, 64(4), 544-548.

Rosemann, T., Grol, R., Herman, K., Wensing, M., & Szecsenyi, J. (2008). Association between obesity, quality of life, physical activity and health service utilization in primary care patients with osteoarthritis. International Journal of Behavioral Nutrition and Physical Activity, 5(1), 4.

Ross, J., Stevenson, F. A., Dack, C., Pal, K., May, C. R., Michie, S., ... & Murray, E. (2019). Health care professionals' views towards self-management and self-management education for people with type 2 diabetes. BMJ Open, 9(7), e029961.

Roubille, C., Coste, J., Sellam, J., Rat, A., Guillemin, F., & Roux, C. (2019). Impact of comorbidities on the progression of knee osteoarthritis and hip osteoarthritis: results of the KHOALA cohort. Osteoarthritis and Cartilage, 27, S225.

Salaffi, F., Leardini, G., Canesi, B., Mannoni, A., Fioravanti, A., Caporali, R. O., ... & Punzi, L. (2003). Reliability and validity of the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index in Italian patients with osteoarthritis of the knee. Osteoarthritis and Cartilage, 11(8), 551-560.

Salisbury, C., Johnson, L., Purdy, S., Valderas, J. M., & Montgomery, A. A. (2011). Epidemiology and impact of multimorbidity in primary care: A retrospective cohort study. The British Journal of General Practice: The Journal of the Royal College of General Practitioners, 61(582), e12-21.

Salisbury, C., Montgomery, A.A., Hollinghurst, S., Hopper, C., Bishop, A., Franchini, A., ... & Foster, N. E. (2013). Effectiveness of PhysioDirect telephone assessment and advice services for patients with musculoskeletal problems: pragmatic randomised controlled trial. British Medical Journal, 346.

Sanchez-Villegas, A., Schlatter, J., Ortuno, F., Lahortiga, F., Pla, J., Benito, S., & Martinez-Gonzalez, M. A. (2008). Validity of a self-reported diagnosis of depression among participants in a cohort study using the Structured Clinical Interview for DSM-IV (SCID-I). BMC Psychiatry, 8(1), 43.

Saunders, B., Sim, J., Kingstone, T., Baker, S., Waterfield, J., Bartlam, B., . . . Jinks, C. (2017). Saturation in qualitative research: Exploring its conceptualization and operationalization. Quality & Quantity, 1-15.

Schlenk, E. A., Lias, J. L., Sereika, S. M., Dunbar-Jacob, J., & Kwoh, C. K. (2011). Improving physical activity and function in overweight and obese older adults with osteoarthritis of the knee: A feasibility study. Rehabilitation Nursing, 36(1), 32-42.

Schmidt, F. L. (1971). The relative efficiency of regression and simple unit predictor weights in applied differential psychology. Educational and Psychological Measurement, 31(3), 699-714.

Schoenberg, N. E., Leach, C., & Edwards, W. (2009). "It's a toss up between my hearing, my heart, and my hip": prioritizing and accommodating multiple morbidities by vulnerable older adults. Journal of Health Care for the Poor and Underserved, 20(1), 134.

Schutzer, K. A., & Graves, B. S. (2004). Barriers and motivations to exercise in older adults. Preventive Medicine, 39(5), 1056-1061.

Schwandt, T. A. (2012). Valuing methodological diversity. Qualitative Social Work, 11(2), 125-129.

Schwarzer, R., Lippke, S., & Luszczynska, A. (2011). Mechanisms of health behavior change in persons with chronic illness or disability: the Health Action Process Approach (HAPA). Rehabilitation Psychology, 56(3), 161.

Sedjo, R. L., Flatt, S. W., Byers, T., Colditz, G. A., Demark-Wahnefried, W., Ganz, P. A., ... & Naughton, M. (2016). Impact of a behavioral weight loss intervention on comorbidities in overweight and obese breast cancer survivors. Supportive Care in Cancer, 24(8), 3285-3293.

Sharfstein, S., & Chrvala, C. A. (1999). Definition of Serious and Complex Medical Conditions. National Academies Press. Washington.

Sharma, A., Kudesia, P., Shi, Q., & Gandhi, R. (2016). Anxiety and depression in patients with osteoarthritis: impact and management challenges. Open access Rheumatology: Research and Reviews, 8, 103–113.

Shin, Y. H., Hur, H. K., Pender, N. J., Jang, H. J., & Kim, M. S. (2006). Exercise self-efficacy, exercise benefits and barriers, and commitment to a plan for exercise among Korean women with osteoporosis and osteoarthritis. International Journal of Nursing Studies, 43(1), 3-10.

Shippee, N. D., Shah, N. D., May, C. R., Mair, F. S., & Montori, V. M. (2012). Cumulative complexity: a functional, patient-centered model of patient complexity can improve research and practice. Journal of Clinical Epidemiology, 65(10), 1041-1051.

Silverwood, V., Blagojevic-Bucknall, M., Jinks, C., Jordan, J. L., Protheroe, J., & Jordan, K. P. (2015). Current evidence on risk factors for knee osteoarthritis in older adults: a systematic review and meta-analysis. Osteoarthritis and Cartilage, 23(4), 507-515.

Simões, D., Araújo, F. A., Severo, M., Monjardino, T., Cruz, I., Carmona, L., & Lucas, R. (2017). Patterns and consequences of multimorbidity in the general population: there is no chronic disease management without rheumatic disease management. Arthritis Care & Research, 69(1), 12-20.

Simonik, A., Vader, K., Ellis, D., Kesbian, D., Leung, P., Jachyra, P., . . . O'Brien, K. K. (2016). Are you ready? exploring readiness to engage in exercise among people living with HIV and multimorbidity in Toronto, Canada: A qualitative study. BMJ Open, 6(3), e010029.

Sinnott, C., Mc Hugh, S., Browne, J., & Bradley, C. (2013). GPs' perspectives on the management of patients with multimorbidity: systematic review and synthesis of qualitative research. BMJ Open, 3(9), e003610.

Skelly, A. C., Dettori, J. R., & Brodt, E. D. (2012). Assessing bias: the importance of considering confounding. Evidence-based Spine-care Journal, 3(01), 9-12.

Skou, S. T., Pedersen, B. K., Abbott, J. H., Patterson, B., & Barton, C. (2018). Physical activity and exercise therapy benefit more than just symptoms and impairments in people with hip and knee osteoarthritis. Journal of Orthopaedic & Sports Physical Therapy, 48(6), 439-447.

Slater, M., Perruccio, A. V., & Badley, E. M. (2011). Musculoskeletal comorbidities in cardiovascular disease, diabetes and respiratory disease: the impact on activity limitations; a representative population-based study. BMC Public Health, 11(1), 77.

Smith SM, Wallace E, Salisbury C, Sasseville M, Bayliss E, Fortin M. (2018). A Core Outcome Set for Multimorbidity Research (COSmm). Ann Fam Med, 16(2), 132-138.

Smith, J., & Firth, J. (2011). Qualitative data analysis: The framework approach. Nurse Researcher, 18(2), 52-62.

Smith, J., Porter, A., Shaw, S., Rosen, R., Blunt, I., & Mays, N. (2013). Commissioning high-quality care for people with long-term conditions. Research Summary. Nuffield Trust. www.nuffieldtrust.org.uk/commissioning-high-quality-care.

Smith, R. D., Dziedzic, K. S., Quicke, J. G., Holden, M. A., McHugh, G. A., & Healey, E. L. (2019). Identification and Evaluation of Self-Report Physical Activity Instruments in Adults with Osteoarthritis: A Systematic Review. Arthritis Care & Research, 71(2), 237-251.

Smith, S. M., Soubhi, H., Fortin, M., Hudon, C. and O'Dowd, T. (2012). Interventions for improving outcomes in patients with multimorbidity in primary care and community settings. Cochrane Database of Systematic Reviews, 18;(4).

Smith, S. M., Wallace, E., O'Dowd, T., & Fortin, M. (2016). Interventions for improving outcomes in patients with multimorbidity in primary care and community settings. Cochrane Database of Systematic Reviews, (3).

Smith, T. O., Hawker, G. A., Hunter, D. J., March, L. M., Boers, M., Shea, B. J., ... & Dodd, S. (2019). The OMERACT-OARSI core domain set for measurement in clinical trials of hip and/or knee osteoarthritis. The Journal of Rheumatology, 46(8), 981-989.

Somers, T. J., Blumenthal, J. A., Guilak, F., Kraus, V. B., Schmitt, D. O., Babyak, M. A., ... & Shelby, R. A. (2012). Pain coping skills training and lifestyle behavioral weight management in patients with knee osteoarthritis: a randomized controlled study. Pain, 153(6), 1199-1209.

Somers, T. J., Keefe, F. J., Pells, J. J., Dixon, K. E., Waters, S. J., Riordan, P. A., ... & Schmitt, D. (2009). Pain catastrophizing and pain-related fear in osteoarthritis patients: relationships to pain and disability. Journal of Pain and Symptom Management, 37(5), 863-872.

Somers, T. J., Wren, A. A., & Shelby, R. A. (2012). The context of pain in arthritis: self-efficacy for managing pain and other symptoms. Current Pain and Headache Reports, 16(6), 502-508.

Sparkes, A. (1992). Research in physical education and sport: Exploring alternative visions. Psychology Press. Routledge.

Sperber, N., Hall, K. S., Allen, K., DeVellis, B. M., Lewis, M., & Callahan, L. F. (2014). The role of symptoms and self-efficacy in predicting physical activity change among older adults with arthritis. Journal of Physical Activity and Health, 11(3), 528-535.

Spitzer, R. L., Kroenke, K., Williams, J. B., & Löwe, B. (2006). A brief measure for assessing generalized anxiety disorder: the GAD-7. Archives of Internal Medicine, 166(10), 1092-1097.

Stafford, M., Steventon, A., Thorlby, R., Fisher, R., Turton, C., & Deeny, S. (2018). Briefing: Understanding the health care needs of people with multiple health conditions. The Health Foundation. London.

Stange, K. C., Zyzanski, S. J. (1989). Integrating qualitative and quantitative research methods. Fam Med, 21, 448–451.

Sterne, J. A., White, I. R., Carlin, J. B., Spratt, M., Royston, P., Kenward, M. G., ... & Carpenter, J. R. (2009). Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. BMJ, 338, b2393.

Stubbs, B., Hurley, M., & Smith, T. (2015). What are the factors that influence physical activity participation in adults with knee and hip osteoarthritis? A systematic review of physical activity correlates. Clinical Rehabilitation, 29(1), 80-94.

Suri, P., Morgenroth, D. C., & Hunter, D. J. (2012). Epidemiology of osteoarthritis and associated comorbidities. Physical Medicine and Rehabilitation, 4, S10-S19.

Svege, I., Kolle, E., & Risberg, M. A. (2012). Reliability and validity of the Physical Activity Scale for the Elderly (PASE) in patients with hip osteoarthritis. BMC Musculoskeletal Disorders, 13(1), 26.

Swain, S., Coupland, C., Mallen, C., Kuo, C. F., Sarmanova, A., Doherty, M., & Zhang, W. (2020). Temporal relationship between osteoarthritis and comorbidities: a combined case control and cohort study in the United Kingdom primary care setting. Osteoarthritis and Cartilage, 28, S72-S73.

Swain, S., Sarmanova, A., Coupland, C., Doherty, M., & Zhang, W. (2019). Comorbidities in Osteoarthritis: A systematic review and meta-analysis of observational studies. Arthritis Care & Research, 72(7), 991-1000.

Szklo, M., & Nieto, F. J. (2014). Epidemiology: beyond the basics. Jones & Bartlett Publishers. Fourth Ed.

Tamari, K. (2010). Baseline comorbidity associated with the short-term effects of exercise intervention on quality of life in the Japanese older population: an observational study. Archives of Physical Medicine and Rehabilitation, 91(9), 1363-1369.

Tariq, S., & Woodman, J. (2013). Using mixed methods in health research. Journal of the Royal Society of Medicine: short reports, 4(6).

Taris, T. W. (2000). A primer in longitudinal data analysis. Sage Publications Ltd.

Taskforce. (2018). 'just one thing after another. Living with multiple conditions. A report from the Taskforce on Multiple Conditions. https://richmondgroupofcharities.org.uk/sites/default/files/final_just_one_thing_after_another_report_-_singles.

Theis, K. A., Brady, T. J., & Helmick, C. G. (2016). No one dies of old age anymore: a coordinated approach to comorbidities and the rheumatic diseases. Arthritis Care & Research, 69(1), 1-4.

Thomas, N., Alder, E., & Leese, G. P. (2004). Barriers to physical activity in patients with diabetes. Postgraduate Medical Journal, 80(1), 287-291.

Torrance, N., Smith, B. H., Elliott, A. M., Campbell, S. E., Chambers, W. A., Hannaford, P. C., & Johnston, M. (2011). Potential pain management programmes in primary care. A UK-wide questionnaire and Delphi survey of experts. Family Practice, 28(1), 41-48.

Tsai, P. F., Chang, J. Y., Beck, C., Kuo, Y. F., & Keefe, F. J. (2013). A pilot cluster-randomized trial of a 20-week Tai Chi program in elders with cognitive impairment and osteoarthritic knee: effects on pain and other health outcomes. Journal of Pain and Symptom Management, 45(4), 660-669.

Tu, Y. K., Kellett, M., Clerehugh, V., & Gilthorpe, M. S. (2005). Problems of correlations between explanatory variables in multiple regression analyses in the dental literature. British Dental Journal, 199(7), 457.

Turkas, N. (2012). Arthritis and Physical Activity in Mid-and Later-Life. Age in Action, 27(4), 1.

Urquhart, D. M., Soufan, C., Teichtahl, A. J., Wluka, A. E., Hanna, F., & Cicuttini, F. M. (2008). Factors that may mediate the relationship between physical activity and the risk for developing knee osteoarthritis. Arthritis Research & Therapy, 10(1), 203.

Uthman, O. A., van der Windt, D. A., Jordan, J. L., Dziedzic, K. S., Healey, E. L., Peat, G. M., & Foster, N. E. (2013). Exercise for lower limb osteoarthritis: systematic review incorporating trial sequential analysis and network meta-analysis. BMJ, 347, f5555.

Valderas, J. M., Mercer, S. W., & Fortin, M. (2011). Research on patients with multiple health conditions: different constructs, different views, one voice. Journal of Comorbidity, 1(1), 1-3.

Valderas, J. M., Starfield, B., Sibbald, B., Salisbury, C., & Roland, M. (2009). Defining comorbidity: implications for understanding health and health services. The Annals of Family Medicine, 7(4), 357-363.

van den Oever, I. A., van der Esch, M., Visman, I., van der Leeden, M., de Rooij, M., Lems, W., ... & Dekker, J. (2014). Cardiovascular diseases, biomechanical factors and activity limitations in patients with knee and/or hip osteoarthritis: results of the ams-oa study. Osteoarthritis and Cartilage, 22, S393-S394.

van Dijk, G. M., Veenhof, C., Lankhorst, G. J., & Dekker, J. (2009). Limitations in activities in patients with osteoarthritis of the hip or knee: the relationship with body functions, comorbidity and cognitive functioning. Disability and Rehabilitation, 31(20), 1685-1691.

van Dijk, G. M., Veenhof, C., Schellevis, F., Hulsmans, H., Bakker, J. P., Arwert, H., ... & Dekker, J. (2008). Comorbidity, limitations in activities and pain in patients with osteoarthritis of the hip or knee. BMC Musculoskeletal Disorders, 9(1), 95.

Van Do, L. Y., Barnason, S., & Tran, H. (2015). Relationships between activation level, knowledge, self-efficacy, and self-management behavior in heart failure patients discharged from rural hospitals. F1000 Research Open Access Publishing Platform. 11(4), 150.

Van Esch, P., & Van Esch, L. (2013). Justification of a qualitative methodology to investigate the emerging concept: The dimensions of religion as underpinning constructs for mass media social marketing campaigns. Journal of Business Theory and Practice, 1(2), 214-243.

Van Gool, C. H., Penninx, B. W., Kempen, G. I., Rejeski, W. J., Miller, G. D., Van Eijk, J. T. M., ... & Messier, S. P. (2005). Effects of exercise adherence on physical function among overweight older adults with knee osteoarthritis. Arthritis Care & Research, 53(1), 24-32.

Van Liew, C., Santoro, M. S., Chalfant, A. K., Gade, S., Casteel, D. L., Tomita, M., & Cronan, T. A. (2013). The good life: assessing the relative importance of physical, psychological, and self-efficacy statuses on quality of well-being in osteoarthritis patients. Arthritis, 1-10.

Vancampfort, D., Koyanagi, A., Ward, P. B., Rosenbaum, S., Schuch, F. B., Mugisha, J., ... & Stubbs, B. (2017). Chronic physical conditions, multimorbidity and physical activity across 46 low-and middle-income countries. International Journal of Behavioral Nutrition and Physical Activity, 14(1), 6.

Veenhof, C., Huisman, P. A., Barten, J. A., Takken, T., & Pisters, M. F. (2012). Factors associated with physical activity in patients with osteoarthritis of the hip or knee: a systematic review. Osteoarthritis and Cartilage, 20(1), 6-12.

Victor, C. R., Rogers, A., Woodcock, A., Beighton, C., Cook, D. G., Kerry, S. M., ... & Harris, T. J. (2016). What factors support older people to increase their physical activity levels? An exploratory analysis of the experiences of PACE-Lift trial participants. Archives of Gerontology and Geriatrics, 67, 1-6.

Vilagut, G., Valderas, J. M., Ferrer, M., Garin, O., López-García, E., & Alonso, J. (2008). Interpretation of SF-36 and SF-12 questionnaires in Spain: physical and mental components. Medicina clinica, 130(19), 726-735.

Vincent, H. K., Heywood, K., Connelly, J., & Hurley, R. W. (2012). Obesity and weight loss in the treatment and prevention of osteoarthritis. Physical Medicine and Rehabilitation, 4(5), S59-S67.

Vitaloni, M., Botto-van Bemden, A., Contreras, R. M. S., Scotton, D., Bibas, M., Quintero, M., ... & Cabot, M. R. (2019). Global management of patients with knee osteoarthritis begins with quality of life assessment: a systematic review. BMC Musculoskeletal Disorders, 20(1), 493.

Vlaeyen, J. W., & Linton, S. J. (2000). Fear-avoidance and its consequences in chronic musculoskeletal pain: a state of the art. Pain, 85(3), 317-332.

Vogels, E. M. H. M., Hendriks, H. J. M., Van Baar, M. E., J., Hopman-Rock, M., Oostendorp, R. A., ... & Verhoef, J. (2001). Clinical practice guidelines for physical therapy in patients with osteoarthritis of the hip or knee. Royal Dutch Society for Physical Therapy. Amersfoort: KNGF. http://www.ipts.org.il/_Uploads/dbsAttachedFiles/osteoarthritis_of_the_hip_and_knee_practice_guidelines_2010.

Vos, T., Flaxman, A. D., Naghavi, M., Lozano, R., Michaud, C., Ezzati, M., ... & Abraham, J. (2012). Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. The Lancet, 380(9859), 2163-2196.

Wada, T., Matsumoto, H., & Hagino, H. (2019). Customized exercise programs implemented by physical therapists improve exercise-related self-efficacy and promote behavioral changes in elderly individuals without regular exercise: a randomized controlled trial. BMC Public Health, 19(1), 917.

Wagner, E. H. (1998). Chronic disease management: what will it take to improve care for chronic illness? Effective Clinical Practice, 1(1), 2.

Wallis, J. A., Taylor, N. F., Bunzli, S., & Shields, N. (2019). Experience of living with knee osteoarthritis: a systematic review of qualitative studies. BMJ Open, 9(9), e030060.

Wallis, J. A., Webster, K. E., Levinger, P., & Taylor, N. F. (2013). What proportion of people with hip and knee osteoarthritis meet physical activity guidelines? A systematic review and meta-analysis. Osteoarthritis and Cartilage, 21(11), 1648-1659.

Walsh, N., Jordan, J. L., Babatunde, O. O., Powell, J., & Healey, E. L. (2016). Community based exercise and physical activity programmes led by exercise professionals for osteoarthritis (protocol). Cochrane Database of Systematic Reviews, 4.

Walsh, R., & Koelsch, L. E. (2012). Building across fault lines in qualitative research. The Humanistic Psychologist, 40(4), 380-390.

Wang, H., Bai, J., He, B., Hu, X., & Liu, D. (2016). Osteoarthritis and the risk of cardiovascular disease: a meta-analysis of observational studies. Scientific Reports, 6, 39672.

Ware Jr, J. E., Kosinski, M., & Keller, S. D. (1996). A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Medical Care, 220-233.

Warner, L. M., Schüz, B., Wolff, J. K., Parschau, L., Wurm, S., & Schwarzer, R. (2014). Sources of self-efficacy for physical activity. Health Psychology, 33(11), 1298.

Warner, L. M., Ziegelmann, J. P., Schüz, B., Wurm, S., & Schwarzer, R. (2011). Synergistic effect of social support and self-efficacy on physical exercise in older adults. Journal of Aging and Physical Activity, 19(3), 249-261.

Washburn, R. A., McAuley, E., Katula, J., Mihalko, S. L., & Boileau, R. A. (1999). The physical activity scale for the elderly (PASE): evidence for validity. Journal of Clinical Epidemiology, 52(7), 643-651.

Washburn, R. A., Smith, K. W., Jette, A. M., & Janney, C. A. (1993). The Physical Activity Scale for the Elderly (PASE): development and evaluation. Journal of Clinical Epidemiology, 46(2), 153-162.

Watt, G. (2017). The subversive challenges of multimorbidity. Br J General Practice, 67(659), 280-281.

Webber, S. C., Ripat, J. D., Pachu, N. S., & Strachan, S. M. (2018). Exploring physical activity and sedentary behaviour: perspectives of individuals with osteoarthritis and knee arthroplasty. Disability and Rehabilitation, 42(14), 1971-1978.

Webster, F., Rice, K., Bhattacharyya, O., Katz, J., Oosenbrug, E., & Upshur, R. (2019). The mismeasurement of complexity: provider narratives of patients with complex needs in primary care settings. International Journal for Equity in Health, 18(1), 107.

Whitty, C. J., & Watt, F. M. (2020). Map clusters of diseases to tackle multimorbidity. Spring Nature Limited, 579, 494-496.

Whitty, C. J., MacEwen, C., Goddard, A., Alderson, D., Marshall, M., Calderwood, C., ... & Reid, W. (2020). Rising to the challenge of multimorbidity. BMJ, 368(6964), 1-2.

Wilcox, S., Der Ananian, C., Abbott, J., Vrazel, J., Ramsey, C., Sharpe, P. A., & Brady, T. (2006). Perceived exercise barriers, enablers, and benefits among exercising and nonexercising adults with arthritis: Results from a qualitative study. Arthritis Care & Research, 55(4), 616-627.

Wilhelm, K. A., Finch, A. W., Davenport, T. A., & Hickie, I. B. (2008). What can alert the general practitioner to people whose common mental health problems are unrecognised? Medical Journal of Australia, 188, S114-S118.

Wilkie, R., Parmar, S. S., Blagojevic-Bucknall, M., Smith, D., Thomas, M. J., Seale, B. J., ... & Peat, G. (2019). Reasons why osteoarthritis predicts mortality: path analysis within a Cox proportional hazards model. BMJ Rheumatic and musculoskeletal Diseases Open, 5(2), 1-9.

Willett, M. J., Greig, C., Rogers, D., Fenton, S., Duda, J., & Rushton, A. (2019). Barriers and facilitators to recommended physical activity in lower-limb osteoarthritis: protocol for a qualitative study

exploring patients and physiotherapist perspectives using the theoretical domains framework and behaviour change taxonomy. BMJ Open, 9(10).

Williams, T. L., Hunt, E. R., Papathomas, A., & Smith, B. (2018). Exercise is medicine? Most of the time for most; but not always for all. Qualitative Research in Sport, Exercise and Health, 10(4), 441-456.

World Health Organization (WHO). (2001). International classification of functioning, disability and health: ICF. Geneva: World Health Organization. https://www.who.int/classifications/icf/en/.

World Health Organization (WHO). (2012). World Health Organization Fact sheet: Depression. World Health Organization. https://www.who.int/news-room/fact-sheets/detail/depression.

World Health Organization (WHO). (2015). Global recommendations on physical activity for health. https://apps.who.int/iris/bitstream/handle/10665/44399/9789245599975_chi.

Wshah, A., Guilcher, S. J., Goldstein, R., & Brooks, D. (2018). Prevalence of osteoarthritis in individuals with COPD: a systematic review. International Journal of Chronic Obstructive Pulmonary Disease, 13, 1207.

Xu, X., Mishra, G. D., & Jones, M. (2017). Evidence on multimorbidity from definition to intervention: an overview of systematic reviews. Ageing Research Reviews, 37, 53-68.

Yeol, S., Kang, J. H., & Jang, J. H. (2013). Clinical feasibility of exercise game for depression treatment in older women with osteoarthritis: A pilot study. Journal of Physical Therapy Science, 25(2), 165-167.

Younas, A., Pedersen, M., & Durante, A. (2020). Characteristics of joint displays illustrating data integration in mixed-methods nursing studies. Journal of Advanced Nursing, 76(2), 676-686.

Young, C. E., Boyle, F. M., & Mutch, A. J. (2016). Are care plans suitable for the management of multiple conditions? Journal of Comorbidity, 6(2), 103-113.

Zambon, S., Siviero, P., Denkinger, M., Limongi, F., Victoria Castell, M., van der Pas, S., ... & Sánchez-Martinez, M. (2016). Role of osteoarthritis, comorbidity, and pain in determining functional limitations in older populations: European project on osteoarthritis. Arthritis Care & Research, 68(6), 801-810.

Zgibor, J. C., Ye, L., Boudreau, R. M., Conroy, M. B., Vander Bilt, J., Rodgers, E. A., . . . Albert, S. M. (2017). Community-based healthy aging interventions for older adults with arthritis and multimorbidity. Journal of Community Health, 42(2), 390-399.

Zhang, Y., & Jordan, J. M. (2010). Epidemiology of osteoarthritis. Clinics in Geriatric Medicine, 26(3), 355-369.

Zullig, L. L., Bosworth, H. B., Jeffreys, A. S., Corsino, L., Coffman, C. J., Oddone, E. Z., ... & Allen, K. D. (2015). The association of comorbid conditions with patient-reported outcomes in Veterans with hip and knee osteoarthritis. Clinical Rheumatology, 34(8), 1435-1441

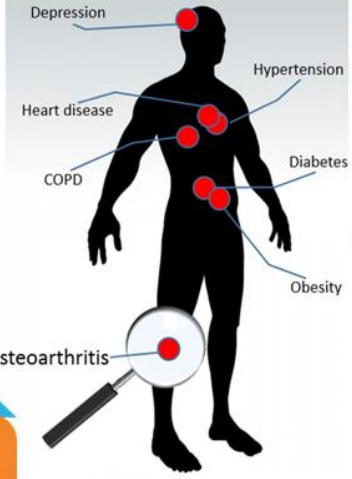
Appendices

Appendix 1. Thesis conceptual map

Osteoarthritis (OA) one of the most common long-term conditions
Leads to pain, reduced function and reduced QOL.

NICE
National Institute for Health and Care Excellence

Clinical guidelines recommend treatments of education, exercise and weight loss.



Up to 85% people with OA report comorbidity

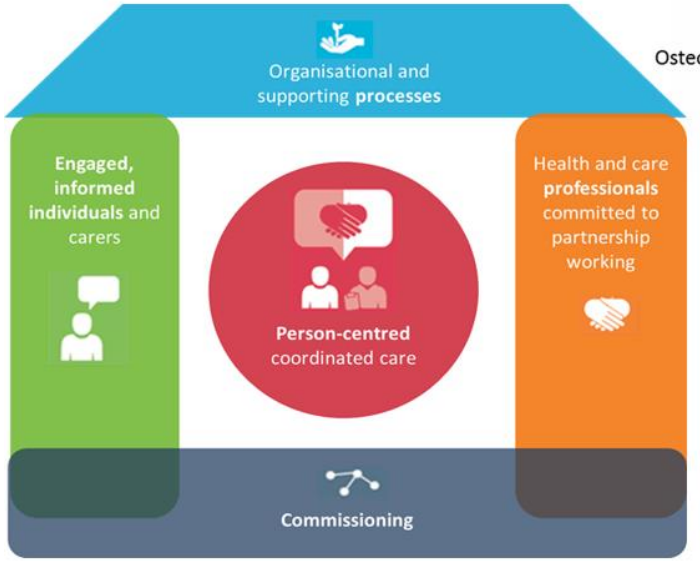
Additional condition alongside primary condition

Increases complexity for patients and carers

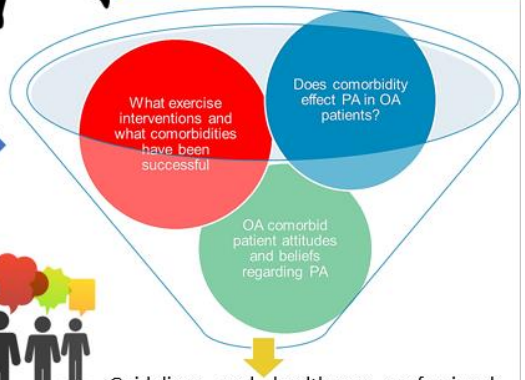
Physical activity (PA) improves pain and function in people with OA

Recommended for both OA and multimorbidity

Currently underused and PA levels are low



Integration and meta-inferences



Guidelines and healthcare professionals tailored to and working with the needs of OA comorbid patients.

Patients informed on PA and activated to self-manage and work with professionals to optimise and improve their PA modifiable condition symptoms and QOL.

A pragmatic stance to methodology involves the mixing and matching design components that **congregate** to offer optimal opportunity to answer **complex** research questions

Multi-methods

Systematic review	•To investigate the effectiveness of PA interventions on clinical outcomes in people with OA and comorbidity
Secondary data analysis	•To determine the PA levels in people with OA with and without comorbidity
Qualitative interviews	•To explore the attitudes towards, and beliefs about, PA in people with OA and comorbidity

Appendix 2. Systematic review: choosing comorbidities

Considerations informing the decision:

- Global burden of disease
- Commonly occurring conditions and frequency / co-existence with Osteoarthritis
- Commonalities in management of conditions
- Physical activity in treatment guidelines
- Quality Outcomes Framework (QOF) primary care
- Conditions that already have management in place (asthma, COPD, respiratory, cardiovascular, diabetes)
- Patient impact

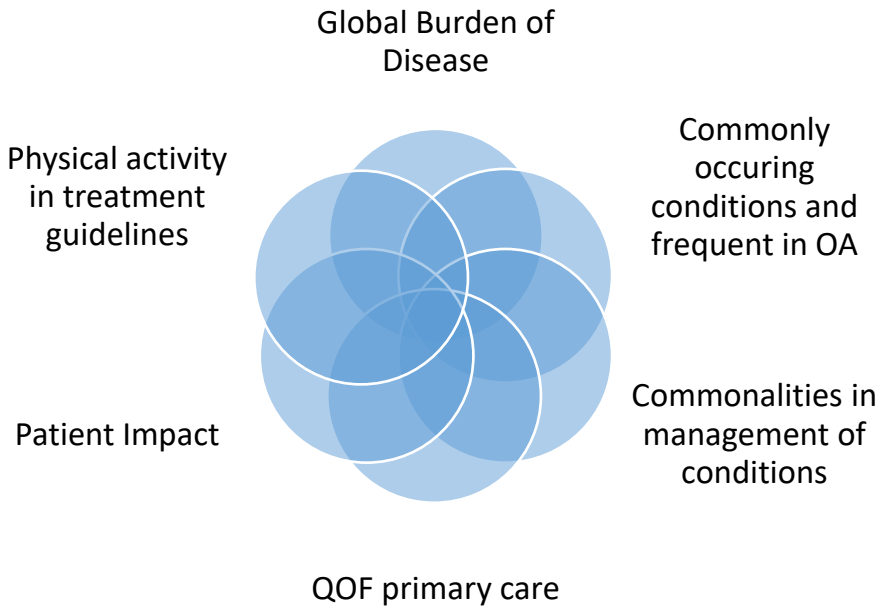


Figure: A2.1 Considerations informing the decision to choose comorbidities

Table: A2.1 Display of the diseases most relevant under different categories within various guidelines for patient care**.**

Factor	Most deaths	Most premature death	Cause most disability	Exercise for Chronic diseases	Advice for Arthritis and comorbidities	NICE exercise guidelines	QOF primary Care
Source	Institution for Health Metrics and health Evaluation profile for the Global Burden of Disease. Results for UK, ENGLAND 2015.	Institution for Health Metrics and health Evaluation profile for the Global Burden of Disease. Results for UK, ENGLAND 2015.	Institution for Health Metrics and health Evaluation profile for the Global Burden of Disease. Results for UK, ENGLAND 2015.	Mayo Clinic; Exercise and Chronic Disease facts.	Arthritis Foundation advice on living with Arthritis and comorbidities	NICE guidelines	Quality and Outcomes Framework
Diseases	Ischemic **Heart Disease** Cerebrovascular disease Alzheimer Disease Lower respiratory Infection **COPD** Cancer	Ischemic **Heart Disease** Cancer Cerebrovascular disease **COPD** Lower respiratory infection Alzheimer disease	Low back and neck pain Sense organ disease **Depressive disorders** Other musculoskeletal Asthma Anxiety	**Heart Disease** **Diabetes** Asthma Back pain Arthritis	**Depression** **Diabetes** **Heart disease** **Obesity**	Myocardial Infarction **Stroke** Chronic **Heart** Failure **COPD** **Depression** Chronic Fatigue Syndrome **Hypertension**	**Diabetes** Asthma **COPD** Kidney Disease **Cardiovascular**

Bold: *Comorbidities of interest; diabetes, chronic obstructive pulmonary disease, hypertension, heart disease (CVD), obesity and depression.*

Source: Institution for Health Metrics and health Evaluation profile for the Global Burden of Disease.

Results for the UK, ENGLAND 2015. (Institute for Health Metrics and Evaluation website: http://www.healthdata.org/united-kingdom-england)

Source: Mayo Clinic: Exercise and Chronic Disease in depth

(Mayo Clinic website: http://www.mayoclinic.org/healthy-lifestyle/fitness/in-depth/exercise-and-chronic-disease/art-20046049)

1. **Heart disease:** Regular exercise can help improve your heart health. Recent studies have shown that interval training is often tolerated well in people with heart disease, and it can produce significant benefits.
2. **Diabetes:** Regular exercise can help insulin more effectively lower your blood sugar level. Physical activity also can help you control your weight and boost your energy.
3. **Asthma:** Often, exercise can help control the frequency and severity of asthma attacks.
4. **Back pain:** Regular low-impact aerobic activities can increase strength and endurance in your back and improve muscle function. Abdominal and back muscle exercises (core-strengthening exercises) may help reduce symptoms by strengthening the muscles around your spine.
5. **Arthritis:** Exercise can reduce pain; help maintain muscle strength in affected joints and reduce joint stiffness.

Source: Arthritis Foundation advice on living with Arthritis and comorbidities

(http://www.arthritis.org/living-with-arthritis/comorbidities/)

The foundation provides advice on four conditions for those living with comorbidities to arthritis;

1. Depression
2. Diabetes
3. Heart Disease
4. Obesity

Source: NICE guidelines

1. Obesity (see NICE clinical guideline 189)
2. Type 2 diabetes (see NICE clinical guideline 28)
3. Hypertension (see NICE clinical guideline 136)
4. Myocardial infarction (see NICE clinical guideline 172 on secondary prevention)
1. Stroke (see NICE clinical guideline 162 on rehabilitation)
2. Chronic heart failure (see NICE clinical guideline 108)
3. Cardiovascular diseases (CVD) (see NICE clinical guideline 181)
4. Chronic obstructive pulmonary disease (COPD) (see NICE clinical guideline 101; 115)
5. Depression (see NICE clinical guideline 90 for adults)
6. Low back pain (see NICE clinical guideline 88)
7. Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (see NICE clinical guideline 53)

Appendix 3. Systematic review search strategy MeSH terms

1) Osteoarthritis AND
2) Physical activity / exercise AND
3) Comorbidity OR COPD OR Heart disease OR Hypertension OR Diabetes OR Depression OR Obesity.

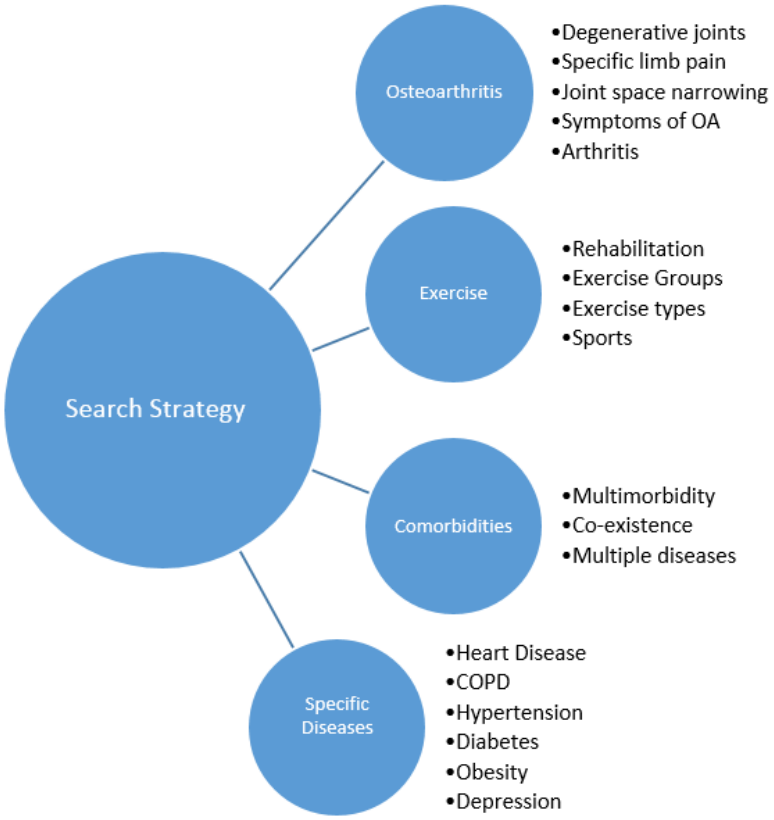


Figure: A3.1 The four-component search strategy

Table: A3.1 The terms, MeSH terms and words used within the search strategy

Component	MeSH term	Words
Osteoarthritis	Osteoarthritis	Osteoarthriti*
		osteo-arthriti*
		osteoarthros*
		osteoarthrotic
		"degenerative joint"
		"joint pain"
		"hand pain"
		"hip pain"
		arthrosis
		"degenerative joint disease"
		"joint space narrowing"
		Osteophyte
		"knee pain"

		"knee osteoarthritis"
		"musculoskeletal pain"
		arthritis
		coxarthrosis
		osteoarthr*
Exercise	Exercise	Exercise
	Rehab exp	aerobic*
		Hydrotherap*
		sports
		movement
		yoga
		walk*
		cycling
		treadmill
		aquatherap*
		swim*
		"tai chi"
		"muscle strength*"
		"range of motion exercise"
		"aerobic exercise prog*"
		"aerobic adj3 train*"
		"Strength train*"
		"exercise train*"
		"exercise movement techniques"
		"Physical activit*"
		"Physical fitness"
		"Physical therap*"
		"exercise therap*"
		"Circuit-Based Exercise"
		"High-Intensity Interval Training"
		"Plyometric Exercise"
		"recreat* activit*"
		physiotherap*
		rehab*
		"resistance train*"
Comorbidity	Comorbidity	Comorbid*
		Co-morbid*
		multimorbid*
		multi-morbid*
		"coexist* diseas*"
		"co-exist* diseas*"
		"co-occur* diseas*"
		"multiple diseas*"
		"concurrent dis*"
		"multiple condition*"

		"charlson comorbidity index"
Heart Diseases	Myocardial Ischemia	"heart diseas*"
		"inflammatory heart disease"
		"Cardiac failure"
		"congestive heart failure"
		"coronary heart disease"
		"ischemic heart disease"
		angina
		coronary
		"cardiac disease"
COPD	Pulmonary disease, chronic obstructive	"pulmonary disease, chronic obstructive"
		COPD
		"chronic bronchitis"
		"pulmonary emphysema"
		"chronic obstructive airway disease"
		"chronic obstructive lung disease"
		"chronic airflow obstruction"
Hypertension	Hypertension	Hypertens*
		"high blood pressure"
		"high systolic"
		"high diastolic"
Diabetes	Diabetes Mellitus	diabetes
		T2DM
		Hyperglycemia
		"glucose intolerance"
		"Diabetes Mellitus, type 2"
Obesity	Obesity	obesity
		overweight
		"morbid* obese"
Depression	Depressive disorder	depression
	depression	depressi*
		"depressive neurosis"
		"depressive syndrome"
		"mood disorder"
		"low mood"
		"dysthymic disorder"

Appendix 4. Systematic review study eligibility form

Study ID:	**Report ID :**	Date form completed:
First author:	Year of study:	Study screener:
Citation:		

1. General Information

Publication type Journal Article ☐ Abstract ☐	
Country of study:	
Funding source of study:	Conflict of interest from funding? Y / N / unclear

2. Study Eligibility

Study Characteristics			**Page**
Type of study	Study type	☐ Randomised Controlled Trial (RCT) ☐ Cluster Randomised Controlled Trial (cluster RCT)	
	Does the study design meet the criteria for inclusion?	**Yes** ☐ **No** ☐ **→Exclude Unclear** ☐	**Y / N / U**
	Description in text:		
Participants	Describe the participants included:		
	Adults mean age ≥45	Yes ☐ No ☐ Unclear ☐	
	Clinical Osteoarthritis (with or without radiographic diagnosis)	Yes ☐ No ☐ Unclear ☐	
	OA at any site AND ≥ comorbidities of interest	Yes ☐ No ☐ Unclear ☐ Details:	
	Do the participants meet the criteria for inclusion?	**Yes** ☐ **No** ☐ **→Exclude Unclear** ☐	**Y / N / U**
Types of intervention	Any exercise intervention (alone or in combination)	Yes ☐ No ☐ Unclear ☐ Details:	

	Control group	Yes ☐ No ☐ Unclear ☐ Details:	
	Does the intervention meet the criteria for inclusion?	**Yes ☐ No ☐ →Exclude Unclear ☐**	**Y / N / U**
Types of outcome measures	Primary Outcome (pain, function, QOL, GH)	Yes ☐ No ☐ Unclear ☐ Details:	
	Secondary / additional outcomes (exercise adherence, adverse events, long-term FU)	Details:	
	Do the outcome measures meet the criteria for inclusion?	**Yes ☐ No ☐ →Exclude Unclear ☐**	**Y / N / U**

3. Summary of Assessment for Inclusion

Include in review ☐ **Exclude from review ☐**	
Independently assessed, and then compared? Yes ☐ No ☐	Differences resolved Yes ☐ No ☐
Request further details? Yes ☐ No ☐	Contact details of authors:
Notes:	

DO NOT PROCEED IF PAPER EXCLUDED FROM REVIEW

Appendix 5. Systematic review data extraction form

Data extraction (Spacing reduced for thesis)

ONLY WHEN PASSED STUDY ELIGIBILITY

- Section 1: General review information
- Section 2: Methods of the study
- Section 3: Risk of bias assessment
- Section 4: Study characteristics - participants
- Section 5: Study characteristics - interventions and comparisons
- Section 6: Study characteristics - outcomes
- Section 7: Data and results

General review information

Study ID:	**Report ID :**	**Date:**
First author:	Year of study:	Data extractor:
Citation:		
Further info required? Y / N	Contact details:	Contact? Y / N
Details:		

Methods of study

Study intention	**Descriptions as stated**	**Page**
Aim of intervention	*What was the problem that this intervention was designed to address?*	
Start and end date of the study		
Total study duration		
Methods		
Method of recruitment of participants	*How were potential participants approached and invited to participate? Where were participants recruited from?*	
Inclusion / exclusion criteria		
Total number of intervention groups		
Unit of randomisation	Allocation by individuals or cluster/groups	

Risk of bias assessment

Domain	**Judgement**	**Notes on rating**
Random sequence generation	***High risk*** ***Unclear*** ***Low risk***	Method used to generate the allocation sequence Including only RCTs in your review, papers marked 'High risk' should be excluded as they are not truly randomised.
Allocation concealment	***High risk*** ***Unclear*** ***Low risk***	Method used to conceal the allocation sequence
Blinding of participants and personnel	***High risk*** ***Unclear*** ***Low risk***	All measures used to blind study participants and personnel

Blinding of outcome assessment	***High risk*** ***Unclear*** ***Low risk***	Measures used to blind outcome assessors from knowledge of which intervention a participant received. Whether the intended blinding was effective.
Incomplete outcome data	***High risk*** ***Unclear*** ***Low risk***	Completeness of outcome data for each main outcome (attrition (loss to follow up, withdrawn and exclusions from analysis). Attrition and exclusions reported? numbers in each intervention group (compared with total randomized participants), reasons for attrition/exclusions, and any re-inclusions in analyses
Selective reporting	***High risk*** ***Unclear*** ***Low risk***	Possibility of selective outcome reporting, what was found.
Other sources of bias	***High risk*** ***Unclear*** ***Low risk***	State any important concerns about bias not addressed in the other domains in the tool.

Study Characteristics - participants

Participants	**Information for each group (i.e. intervention and controls) under study**	**Page**
Total number randomised		
Number allocated to each intervention group		
Where there any significant baseline imbalances?	Yes ☐ No ☐ Unclear ☐ Details:	
What percentage of patients completed the study?		
What percentage of participants received the allocated intervention or exposure of interest?		
Age (median, mean and range if possible)		
BMI (median, mean and range if possible)		
Osteoarthritis details		
Comorbidity details		
Subgroups	Any participant subgroups from this paper to be analysed in the review.	

Study characteristics – Interventions / controls

Intervention Group 1 (copy and paste table for more Intervention/control groups)

Group name	**Name for this intervention group**	**Page**
Details of intervention **or control** condition		
Setting	Multicentre, university teaching hospitals, rural, school, workplace, community, GP clinic, etc.	
Content	List the strategies intended and delivered TYPE	
Delivery	Stages (sequential or simultaneous), FITT - timing, frequency, duration, intensity	
Providers	Who, number, education/training in intervention delivery, ethnicity etc. (if potentially relevant to acceptance and uptake by participants)	
Co-interventions?		

Duration of intervention		
Duration of follow-up		
Other economic information (from a societal, non-healthcare view – e.g. lost wages, time)	Yes ☐ No ☐ Details:	
Subgroups	Enter a description of any intervention subgroups from this report to be analysed in the review.	
Control/comparison	What information is provided about what the control or comparison group received? (if not reporting in extra table)	

Study Characteristics – outcomes

Dichotomous outcome

Comparison					
Outcome					
Subgroup					
Time point					
Results	**Intervention**		**Comparison**		
	Events	No. participants	Events	No. participants	
Missing participants			Details:		
Other results reported					

Continuous outcome

Comparison						
Outcome						
Subgroup						
Time point				Details: Post-intervention or change from baseline?		
Results	**Intervention**			**Comparison**		
	Mean	SD (or other variance)	No. participants	Mean	SD (or other variance)	No. participants
Missing participants				Details:		
Any other results reported						

Question	**Outcome 1**	**Page**	**Outcome 2**	**Page**
Type of outcome				
Time points reported				

Unit of measurement (if relevant)				
How is the measure applied?	Telephone, mail, in person, trained assessor etc.			
How is the outcome reported?	Self or study assessor			
Is there adequate power for this outcome?				

Extra information

Outcomes relating to harms/unintended effects / adverse events of the intervention	
Potential for author conflict	
Key conclusions of the study authors	
Could the inclusion of this study potentially bias the generalisability of the review?	
References to other relevant studies	
Additional notes by review authors	

Data and results

Comparison:

Outcome:

Subcategory:

	Treatment group:	**Control group:**
Total randomised		
excluded*		
Observed		
lost to follow up*		

*Reasons for loss/exclusion:

Subcategory:

Treatment group:		**Control group:**	
Observed (n)	total (N)	observed (n)	total (N)

	Treatment group:	**Control group:**
Total randomised		
excluded*		
Observed		
lost to follow up*		

*Reasons for loss/exclusion

Appendix 6. Outcome measures data extraction hierarchy

Table: A6.1 Outcome (pain, function, quality of life and global health) measurement tool hierarchy for data extraction

Outcomes Extracted	Hierarchy of Measures
Pain	1. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) subscale for Pain. 2. The Short-Form Health Survey (SF-36) subscale for pain 3. The Euro QOL 5 Dimensions (EQ-5D) subscale for pain. 4. Pain during activity and Pain at rest (VAS) 5. Knee Injury and Osteoarthritis Outcome Score (KOOS) lower limb focused pain component 6. Hip Injury and Osteoarthritis Outcome Score (HOOS) pain component
Function	1. The WOMAC index subscale for physical function 2. The SF-36 survey physical functioning component 3. Disabilities of the Arm, Shoulder and Hand (DASH) upper limb focused 4. 6-Minute Walk Test (6MWT) 5. Timed get up and go test (GUG) 6. HOOS/ KOOS physical functioning component
Quality Of Life	1. The SF-36 survey 2. The EQ-5D survey 3. HOOS/ KOOS QOL subscales
Global Health Measure	1. The SF-36 general health component 2. The EQ-5D global health state component 3. Global Perceived Effect (GPE) scale, which participants rate the treatment effect from better, no change, to worse.

Informed by recommendations from the Cochrane Handbook and OMERACT OARSI recommended OA outcome measures (Higgins and Green, 2011; Smith et al., 2019).

Appendix 7. Risk of bias tool selection

Table: **A7.1** The strengths and weaknesses of the three main tools considered for assessing risk of bias in included studies.

	Strengths	**Weaknesses**
COCHRANE tool	• Strong strict structure • Easy to follow, concise • Clear instructions and empirical support for domain components • *Scoring low, high, unclear*	• Not much flexibility apart from 'other sources of bias' option which is vague • Too detailed and thus time-consuming • Risk of bias graph too general
JADAD scale	• Concise and quick to complete • Easy to understand with empirical evidence support • structured	• Point system unclear as to what scored low, or why • Too brief thus weighting is hard to justify • Not instructed in depth
CASP checklist	• Strong strict structure • Concise • Clear instructions and prompts • *Yes, no, can't tell*	• A mix of dichotomous and detailed answers • Long

Note: Although the Cochrane ROB tool was selected as the most suited to the current review to assess ROB, there were still some limitations of using this tool. The main limitation was the application of the 'blinding of participants and personnel' domain to the treatment received as this was impossible with any form of PA intervention. For this reason, the risk of performance bias due to participant and personnel delivering the intervention was consistently marked as unclear.

Table: A7.2 The Cochrane Collaboration Tool for assessing Risk of bias

Domain	Support for judgement	Review authors' judgement
Selection bias.		
Random sequence generation.	Describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.	Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence.
Allocation concealment.	Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment.	Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment.
Performance bias.		
Blinding of participants and personnel *Assessments should be made for each main outcome (or class of outcomes).*	Describe all measures used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.	Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Detection bias.		
Blinding of outcome assessment *Assessments should be made for each main outcome (or class of outcomes).*	Describe all measures used, if any, to blind outcome assessors from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.	Detection bias due to knowledge of the allocated interventions by outcome assessors.
Attrition bias.		
Incomplete outcome data *Assessments should be made for each main outcome (or class of outcomes).*	Describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. State whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomized participants), reasons for attrition/exclusions where reported, and any re-inclusions in analyses performed by the review authors.	Attrition bias due to amount, nature or handling of incomplete outcome data.
Reporting bias.		
Selective reporting.	State how the possibility of selective outcome reporting was examined by the review authors, and what was found.	Reporting bias due to selective outcome reporting.
Other bias.		
Other sources of bias.	State any important concerns about bias not addressed in the other domains in the tool. If particular questions/entries were pre-specified in the review's protocol, responses should be provided for each question/entry.	Bias due to problems not covered elsewhere in the table.

Appendix 8. Meta-analysis detail

Study selection

All studies which investigated osteoarthritis and obesity were initially considered (n=10). Meta-analysis is only possible were studies are similar enough in terms of methods and reporting (Higgins and Green, 2011). Therefore, some studies were not deemed similar enough to include in the meta-analysis. The following section describes this process of selection.

Table: A8.1 Studies to check for sufficient homogeneity for meta-analysis of OA with obesity**.**

Study	Mean BMI	BMI Range	Measures reported	SD/SE	Post-control	Post-int	Meta-analysis inclusion or exclusion (1st reason)
Casilda-Lopez et al. 2017	32	>30	WOMAC pain & function, 6MWT	Mean SD	Y	Y	Excluded Active control group
Christensen et al. 2015	37	>30	SF-36	-	-	-	Excluded Outcome measure
Jenkinson et al., 2009	33	>28	WOMAC pain & function	Mean SD	Y	Y	Excluded BMI lower limit
Lim et al. 2010	27	>25	SF-36	-	-	-	Excluded BMI
Messier et al. 2004	34	>30	WOMAC pain & function, 6MWT	Mean SE	Y	Y	Included in 2 meta-analyses
Messier et al. 2013	33	>30	WOMAC pain & function, SF-36, 6MWT	Mean SE	Y	Y	Included in 3 meta-analyses
Miller et al. 2006	34	>30	WOMAC pain & function, 6MWT	Mean SE	Y	Y	Included in 3 meta-analyses
Rejeski et al.,	34	>30	SF-36	Mean SE	N	N	Excluded Follow-up reporting style
Schlenk et al. 2011	33	>30	WOMAC function, 6MWT	Mean SD	Y	Y	Included in 2 meta-analyses
Somers et al., 2012	33	>30	WOMAC pain & function	VAS	Y	Y	Excluded Reporting style

BMI=Body Mass Index; SD=Standard Deviation; SE=Standard Error; Post=Post intervention follow-up data available for (control group / intervention group); (1st reason)=1st reason the study was not included in meta-analyses.

Of the 14 studies included in the systematic review, ten of these were exclusively in a population of OA and obesity comorbidity. From these ten studies, one was removed due to all outcome follow-up scores being an average of 6 and 18-month data (Rejeski et al., 2002). A further study was removed due to the Korean cut-off for obesity (BMI≥25) (Lim et al., 2010) and one study was removed due to the lower BMI mean of their sample (BMI>28) (Jenkinson et al., 2009)*. One study was ineligible due to the outcome measurement tool used (SF-36) (Christensen et al., 2015). The remaining studies all had used at least one of; WOMAC pain, WOMAC function or 6MWT function outcome measures (n=6). One study was subsequently removed due to the outcome measure type, which was the Visual Analogue Scale, not compatible to be combined with the other studies (Somers et al., 2012). Finally, one study was ineligible due to the active control type (physical activity control) (Casilda-Lopez et al., 2017).

It was decided that four studies provided enough homogeneity to pool the results in three random effects meta-analyses. The final meta-analyses contained three studies assessing WOMAC pain, three studies assessing WOMAC function and four assessing 6MWT function. Random effects modelling was used as it assumes that the individual studies were drawn from different populations that could impact

on the treatment effect (e.g. the intensity or duration of the intervention received). This process is shown in the flow diagram below.

*BMI ranges of each obesity study was calculated through a process of converting the mean BMI (SD or SE) to find the lower limit of each study confidence intervals (95%) to determine the actual BMI of the samples.

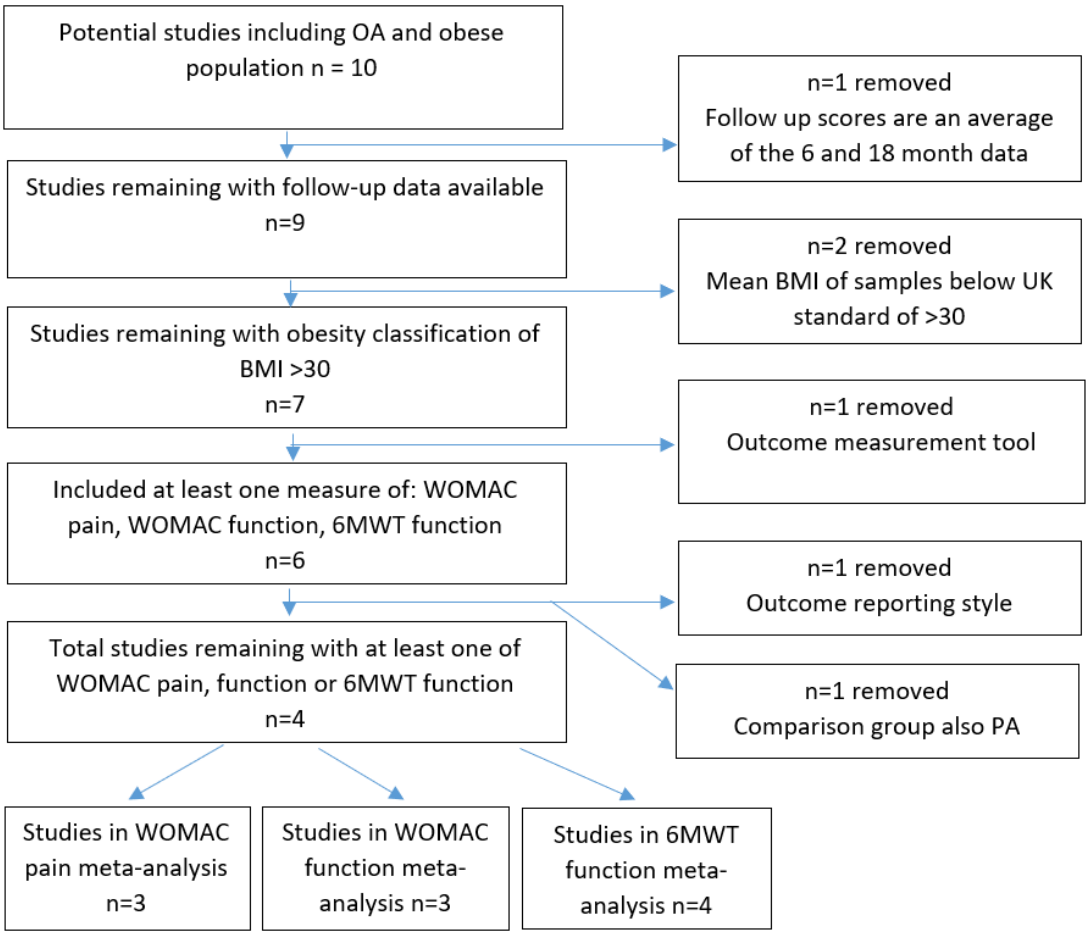


Figure: A8.1 Flow chart of study inclusion or exclusion from meta-analyses

Raw study values for meta-analyses

Table: A8.2 Raw values for WOMAC pain

Study	INT (N)	CNT (N)	Baseline INT	Baseline CNT	Post INT	Post CNT
Messier *et al.* 2004	80	78	6.64±0.39	7.25±0.39	6.24±0.47	6.02±0.45
Miller *et al.* 2006	44	43	6.5(0.5)	6.3 (0.5)	4.1(0.4)	6.1(0.5)
Messier *et al.* 2013	150	152	6.1(5.6-6.6)	6.6(6.1-7.1)	4.4(3.9-4.9)	4.8(4.2-5.3)

Table: A8.3 Raw values for WOMAC function

Study	INT (N)	CNT (N)	Baseline INT	Baseline CNT	Post INT	Post CNT
Messier *et al.* 2013	150	152	23.1±10.6	24.8±9.98	17.6(15.8-19.4)	17.7(15.7-19.8)
Miller *et al.* 2006	44	43	24.0(1.5)	26.7(1.9)	15.2(1.5)	23.8(2.0)
Schlenk *et al.* 2011	13	13	22.5±11.6	23.6±11.6	17.3±13.1	22.9±14.9

Table: A8.4 Raw values for 6MWT function

Study	INT (N)	CNT (N)	Baseline INT	Baseline CNT	Post INT	Post CNT
Messier *et al.* 2004	80	78	424.15±10.96	434.61±10.96	472.73±13.12	429.89±12.77
Messier *et al.* 2013	150	152	480 (466-495)	475(462-488)	525 (511-540)	502(488-515)
Miller *et al.* 2006	44	43	436.5(13.0)	447.8(14.9)	510.0(15.0)	459.0(17.4)
Schlenk *et al.* 2011	13	13	442.4±87.2	512.8±105.4	466.1±101.3	504.4±106.6

Int=Intervention group; CNT=Control group; N=Number; Baseline=Baseline scores; Post=Post-intervention scores

Meta analyses

The included studies in the meta-analysis had a large degree of statistical heterogeneity, therefore the estimates were pooled using a random effects approach to meta-analysis. For all meta-analyses the data was continuous, therefore the following input variables were necessary; the number of participants in each arm and the mean and standard deviation (SD) for both the intervention and control group arms at follow-up (Higgins and Green, 2009). Studies were reported as mean SD, confidence intervals (CI) and standard errors (SE), therefore the appropriate calculations were made to convert the data;

1. For Mean CI;
   SD = ((lower CI – mean)*(√ number participants)*-1)/1.96
2. For mean SE;
   SD = SE*(√ number participants)

All meta-analyses were completed using STATA 16 integrated statistical software package. First, the pooled estimates were calculated for each group; WOMAC pain, WOMAC function and 6MWT function (command metan), which provided information on the presence and magnitude of statistical heterogeneity (I squared measure: 0-100% lower value being less heterogeneity). The risk of publication bias in the meta-analysis (command metafunnel) was calculated to assess the ROB concerning effects size and power.

Forest plots were used to display the meta-analysis results from each study which are displayed as a square and a horizontal line, representing the intervention effect estimate together with its CI for the WOMAC pain, WOMAC function and 6MWT function meta-analysis. The area of the square reflects the weight that the study contributes to the meta-analysis. The combined-effect estimate and its CI are represented by a diamond.

In the meta-analysis, a random-effects model was used to estimate the overall adjusted effects. This included an estimate of the degree of variation between studies shown as study heterogeneity (I squared statistic). This result for each of the three meta-analysis describes the percentage of variability in effect estimates that is due to variation between studies, rather than chance. Substantial heterogeneity (>50%) was found in two meta-analyses (78.35%, 73.39%; WOMAC pain, function; respectively) and no heterogeneity was found in the 6MWT meta-analyses. Using the random-effects model for this meta-analysis was still favourable as it was practical to assume there would be statistical heterogeneity that it would account for.

Funnel plots for meta-analysis publication bias

Funnel plots seek to detect whether there is any suggestion of publication bias in the studies. The small amount of studies makes it hard to interpret the funnel plots below, but they do roughly resemble a pyramid or inverted funnel, with scatter due to sampling variation. This shape is expected because the

studies had wide standard error ranges. There is minimal suggestion of publication bias from the limited data.

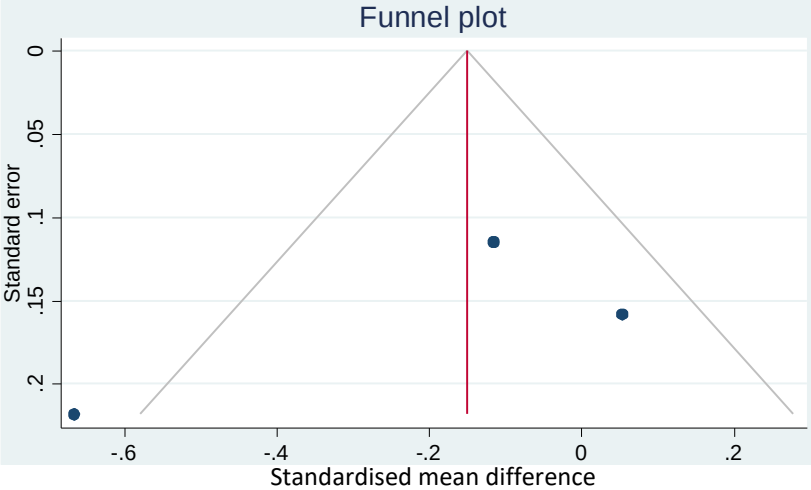


Figure: **A8.2** Funnel plot of WOMAC pain

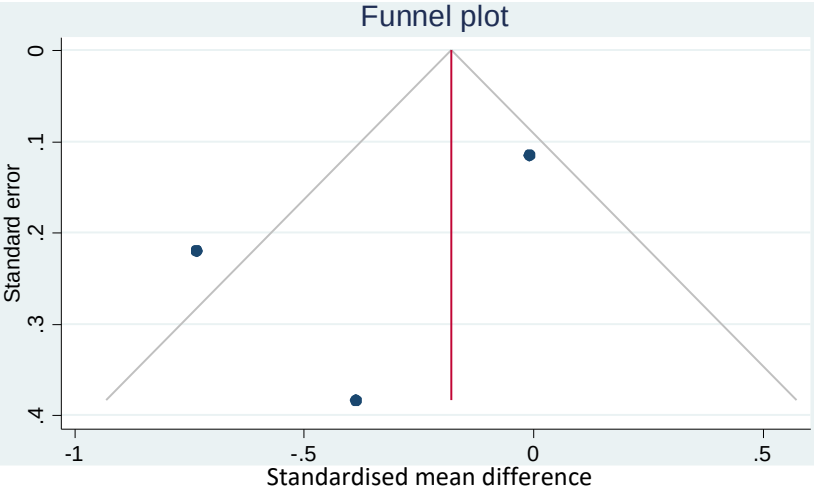


Figure: A8.3 Funnel plot of WOMAC function

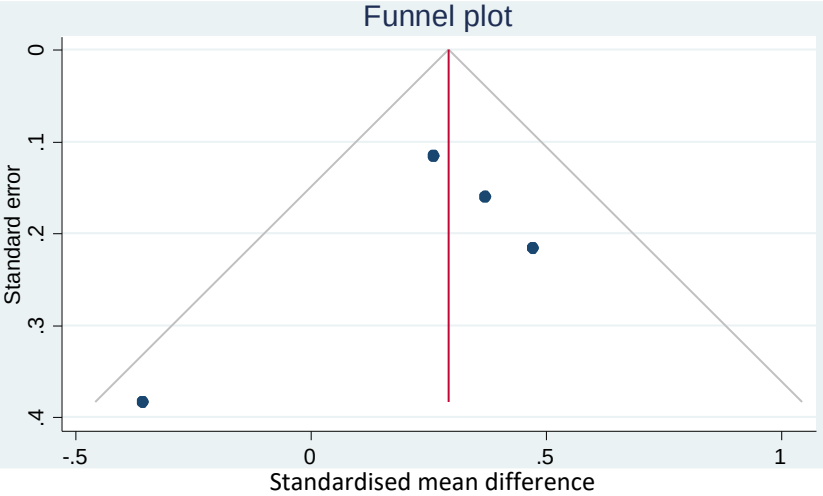


Figure: A8.4 Funnel plot of 6MWT

Appendix 9. Data request and approval

A) BEEP data request and approval (signature section redacted for thesis)

Arthritis Research UK Primary Care Centre
Keele University
Internal data request form
To be completed by the Researcher of proposed study

Proposed Study Title: Physical activity in people with osteoarthritis and comorbidity: A multi-method study.				
Researcher: Sarah Mckevitt				
Supervisor of Researcher (where applicable): Dr Jonathan Quicke, Dr. Clare Jinks and Dr. Emma Healey				
Co-authors: Trishna Rathnod				
Is the data required for practicing analysis or demonstration/ teaching only? *If so, please provide further details*	**YES**		**NO**	**x**
Research Question / Objective: 1. Is comorbidity presence associated with physical activity in adults with osteoarthritis? 2. Are different frequencies and types of comorbidity associated with physical activity level in adults with osteoarthritis?				
Outline design of analysis: 1. To investigate the physical activity levels of osteoarthritis patients with and without comorbidity I will carry out quantitative secondary data analysis (using SPSS). 2. Comorbidity, physical activity and covariate data will be statistically described (using mean and standard deviation or frequency and percentages as appropriate). To describe comorbidity frequency, a 'comorbidity count' variable will be recoded from existing comorbidity variables. 3. The crude association between a) presence of any comorbidity of interest b) comorbidity count (independent variables) and physical activity (outcome variable) will be investigated using simple linear regression models (B coefficients, 95% confidence intervals and p values will be reported). 4. In order to investigate the adjusted association between relevant comorbidities (independent variable) and physical activity (outcome variable), taking into account relevant covariates, multiple linear regression will then be used to fit the data (B coefficients, 95% confidence intervals and p values will be reported). 5. Linear regression model assumption checking will be carried out. 6. The process will be repeated with comorbidity recoded to count as the independent variable.				
Study (or studies) from which data are requested: 1. The Benefits of Effective Exercise for knee Pain (BEEP)				
Study population required *(For quantitative studies please specify if there are **specific groups of participants** required from the study e.g. age range, gender, and for qualitative studies please specify the **demographic or sample frame** and the **number of participants** you require):* • All BEEP participants (male and female adults 45 years of age or older with knee pain attributable to osteoarthritis).				

Precise data required

*(For quantitative data please be **specific** on survey wave (e.g. baseline data) and list **all variables** required and for qualitative data please detail the **type of data** required (e.g. interview transcripts, diaries etc):*

- **Survey Wave:** Baseline data
- **Variables:**

Variables	Measurement Scale	Page, part, question
Participant characteristics		
Age	Years	26.E.2
Gender	Female/Male	26.E.1
Body Mass Index	Height (centimetres) weight (kilogram) (categorical (≥30) calculated and categorised into underweight/normal/overweight/obese) and continuous.	26.E.6&7
Marital status	Tick box (categorical single/partner)	26.E.3
Employment status	Employed yes/no	26.E.5
General health and well-being		
Anxiety	GAD7 0-21	20.C1.9-15
Quality of life	EQ-5D-3L -0.59-1	21.C2.1-5
Osteoarthritis		
Duration of pain	≤12 months/ >1 ≤ 5 years/ > 5 ≤ 10 years/ >10 years	4.1.2
Knee pain	WOMAC 0-20	4.A.3-7
Knee function	WOMAC 0-68	5-7.A.10-26
Physical activity		
Physical activity	PASE 0-400+ (score calculated)	9-14.B.all
Moderate	PASE (continuous hours/week)	11.B.4
Strenuous	PASE (continuous hours/week)	11.B.5
Strength/endurance	PASE (continuous hours/week)	12.B.6
Comorbidity		
Comorbidity type	Tick box of key comorbidities; • High blood pressure • Osteoporosis • Angina • Heart failure • Stroke • Heart attack • Depression • Diabetes • Asthma • Bronchitis	23.4.1
PASE = Physical Activity Scale for the Elderly, PHQ8 = Patient Health Questionnaire 8, WOMAC = Western Ontario and McMaster Universities Arthritis Index, GAD 7 = Generalized Anxiety Disorder 7, EQ-5D-3L = Quality of Life.		

Is new REC approval required?	**YES**		**NO**	**x**

B) MOSAICS data request and approval (signature section redacted for thesis)

Arthritis Research UK Primary Care Centre
Keele University
Internal data request form
To be completed by the Researcher of proposed study

Proposed Study Title: Physical activity in people with osteoarthritis and comorbidity: A multi-method study.				
Researcher: Sarah Mckevitt				
Supervisor of Researcher (where applicable): Dr Jonathan Quicke, Dr. Clare Jinks and Dr. Emma Healey				
Co-authors: Trishna Rathnod				
Is the data required for practicing analysis or demonstration/ teaching only? *If so, please provide further details*	**YES**		**NO**	**x**
Research Question / Objective: 7. Is comorbidity presence associated with physical activity in adults with osteoarthritis? 8. Is comorbidity presence associated with sedentary time in adults with osteoarthritis? 9. Are different frequencies and types of comorbidity associated with physical activity level in adults with osteoarthritis?				
Outline design of analysis: 1. To investigate the physical activity levels and sedentary time of osteoarthritis patients with and without comorbidity I will carry out quantitative secondary data analysis (using SPSS). 2. Comorbidity, physical activity, sedentary time and covariate data will be statistically described (using mean and standard deviation or frequency and percentages as appropriate). To describe comorbidity frequency, a 'comorbidity count' variable will be recoded from existing comorbidity variables. 3. The crude association between a) presence of any comorbidity of interest b) comorbidity count (independent variables) and physical activity (outcome variable) will be investigated using simple linear regression models (B coefficients, 95% confidence intervals and p values will be reported). 4. Also, the crude association between comorbidities of interest (independent variable) and sedentary time (outcome variable) will be investigated using simple linear regression (B coefficients, 95% confidence intervals and p values will be reported). 5. In order to investigate the adjusted association between relevant comorbidities (independent variable) and physical activity (outcome variable), taking into account relevant covariates, multiple linear regression will then be used to fit the data (B coefficients, 95% confidence intervals and p values will be reported). 6. Linear regression model assumption checking will be carried out. 7. The process will be repeated with sedentary time as the outcome variable. 8. The process will be repeated with comorbidity recoded to count as the independent variable.				
Study (or studies) from which data are requested: 2. The Management of OsteoArthritis In Consultations (MOSAICS)				
Study population required *(For quantitative studies please specify if there are **specific groups of participants** required from the study e.g. age range, gender, and for qualitative studies please specify the **demographic or sample frame** and the **number of participants** you require):* • All MOSAICS participants (male and female adults 45 years of age or older with joint pain attributable to osteoarthritis)				

Precise data required

*(For quantitative data please be **specific** on survey wave (e.g. baseline data) and list **all variables** required and for qualitative data please detail the **type of data** required (e.g. interview transcripts, diaries etc):*

- **Survey wave:** Consultation data
- **Variables:**

Variable	Measurement Scale	Page, question
Participant characteristics		
Age	Years	29.F.6
Gender	Female/Male	29.F.7
Weight	weight (kilograms)	29.F.8
Employment status	Employed yes/no (retired/no categorised as no)	29.F.2
General health and well-being		
Physical & mental health	SF12 V2 0-100	8&9.B2.all
Quality of life	EQ-5D-3L -0.59-1	22.D4.1-5
Anxiety	GAD 7 0-21	19.D2.1-7
Osteoarthritis		
Hip pain	Previous 3 months yes/no	6.B.1
Knee pain	Previous 3 months yes/no	6.B.2
Hand pain	Previous 3 months yes/no	6.B.3
Foot pain	Previous 3 months yes/no	6.B.4
Pain intensity	0-10	7.B.5
Physical function	WOMAC SF-PF 0-32	8&9.2.all
Physical activity and Sedentary time		
Sedentary time	IPAQ hours and minutes per day	11.C1.7
Physical activity	PASE 0-400+ (score calculated)	12-17.C3.All
Moderate	PASE (continuous hours/week)	14.C3.4
Strenuous	PASE (continuous hours/week)	14.C3.5
Strength/endurance	PASE (continuous hours/week)	15.C3.6
Comorbidity		
Comorbidity type	MRR - identify people with comorbidities; • High blood pressure • Hypertension • Angina • Heart failure • Stroke • Heart attack • Heart disease • Depression • Diabetes • Asthma • COPD • Bronchitis • Osteoporosis	MRR
PASE = Physical Activity Scale for the Elderly, IPAQ= International Physical Activity Questionnaire, SF12 V2 = Short form 12, EQ-5D-3L = Quality of Life, GAD 7 = Generalized Anxiety Disorder 7, WOMAC = Western Ontario and McMaster Universities Arthritis Index, MRR = Medical Record Review		

Is new REC approval required?	**YES**		**NO**	**x**

Appendix 10. Example read codes: Depression

NOTE: all synonyms for codes to be included except where stated
NOTE: codes followed by "." or ".." indicate all daughter codes to be included unless stated otherwise

CODE	TERM	
1B17.	Depressed	
1B1U.	Symptoms of depression	
1BT..	Depressed mood	
2257.	O/E - depressed	
62T1.	Puerperal depression	
6G00.	Postnatal depression counselling	
9H90.	Depression annual review	
E11	Depressive psychoses	(No other terms for E11)
E112.	Single major depressive episode	(+ daughter codes EXCEPT E1126 "Single major depressive episode, in full remission")
E113.	Recurrent major depressive episode	(+ daughter codes EXCEPT E1136 "Recurrent major depressive episodes, in full remission")
E115.	Bipolar affective disorder, currently depressed	
E118.	Seasonal affective disorder	
E11y	Other and unspecified manic-depressive psychoses	
E11y0	Unspecified manic-depressive psychoses	
E11y2	Atypical depressive disorder	
E11y3	Other mixed manic-depressive psychoses	
E11yz	Other and unspecified manic-depressive psychoses NOS	
E11z2	Masked depression	
E135.	Agitated depression	
E2003	Anxiety with depression	
E204.	Neurotic depression reactive type	
E290	Brief depressive reaction	
E290z	Brief depressive reaction NOS	
E291.	Prolonged depressive reaction	
E2B..	Depressive disorder NEC	
Eu3	[X]Mood - affective disorders	
Eu31	[X]Manic-depressive illness	(PLUS all other terms for Eu31 EXCEPT "[X]Bipolar affective disorder")
Eu313	[X]Bipolar affect disorder cur epi mild or moderate depressn	

Eu314	[X]Bipolar affective disorder, current episode severe depression without psychotic symptoms	
Eu315	[X]Bipolar affective disorder, current episode severe depression with psychotic symptoms	
Eu32.	[X]Depressive episode	
Eu33.	[X]Recurrent depressive disorder	(+ daughter codes EXCEPT Eu334 "[X]Recurrent depressive disorder, currently in remission")
Eu34	[X]Persistent mood affective disorders	
Eu341	[X]Dysthymia	
Eu34y	[X]Other persistent mood affective disorders	
Eu34z	[X]Persistent mood affective disorder, unspecified	
Eu3y.	[X]Other mood affective disorders	
Eu3z	[X]Unspecified mood affective disorder	(NOT Eu3z "Affective psychosis NOS")
Eu412	[X]Mixed anxiety and depressive disorder	
Eu530	[X]Postnatal depression NOS	(NOT Eu530 "[X]Mild mental and behavioural disorders associated with the puerperium, not elsewhere classified"
Eu530	[X]Postpartum depression NOS	(NOT Eu530 "[X]Mild mental and behavioural disorders associated with the puerperium, not elsewhere classified"
Eu920	[X]Depressive conduct disorder	

Appendix 11. Physical Activity Scale for the Elderly (PASE)

Scale detail (summarized)

Leisure time activity

1. Over the past 7 days, how often did you participate in **sitting** activities such as reading, watching TV or doing handcrafts?

1a. What were these activities?

1b. On average, how many hours per day did you engage in these sitting activities?

2. Over the past 7 days, how often did you **take a walk outside your home** or garden for any reason? For example, for fun or exercise, walking to work, walking the dog, etc.?

2a. On average, how many hours per day did you spend walking?

3. Over the past 7 days, how often did you **engage in light sport or recreational activities** such as bowling, golf with a cart, shopping, fishing or other similar activities?

3a. What were these activities?

3b. On average, how many hours per day did you engage in these light sport or recreational activities?

4. Over the past 7 days, how often did you **engage in moderate sport and recreational activities** such as doubles tennis, ballroom dancing, aqua aerobics, golf without a cart or other similar activities?

4a. What were these activities?

4b. On average, how many hours per day did you engage in these moderate sport or recreational activities?

5. Over the past 7 days, how often did you engage in **strenuous sport and recreational activities** such as jogging, swimming, cycling, singles tennis, aerobic dance or other similar activities?

5a. What were these activities?

5b. On average, how many hours per day did you engage in these strenuous sport and recreational activities?

6. Over the past 7 days, how often did you do any exercises specifically to increase muscle strength and endurance, such as lifting weights or push-ups, etc.?

6a. What were these activities?

6b. On average, how many hours per day did you engage in muscle strength and endurance exercise?

Household activity

7. During the past 7 days, have you done any light housework, such as dusting or washing dishes?

8. During the past 7 days, have you done any heavy housework or chores, such as vacuuming, scrubbing floors, washing windows, or carrying wood?

9. During the past 7 days, did you engage in any of the following activities? Please answer Yes or No for each item.

- Home repairs like painting, wallpapering, electrical work, etc.
- Lawn work or garden care, including leaf removal, wood chopping, etc.
- Outdoor gardening
- Caring for another person, such as children, dependent spouse, or another adult

Work-related activity

10. During the past 7 days, did you work for pay or as a volunteer?

10a. How many hours per week did you work for pay and/or as a volunteer?

10b. Which of the following categories best describes the amount of physical activity required on your job and/or volunteer work? ***(Please put a cross in one box only)***

- Mainly sitting with slight arm movements
- Sitting or standing with some walking
- Walking with some handling of materials generally weighing less than 50 pounds
- Walking and heavy manual work often requiring handling of materials weighing over 50 pounds

PASE preliminary norms (Washburn et al., 1993)

Preliminary norms for PASE were established in a general population of older adults. In this sample scores ranged from 0 to 361. The mean score was 102.9 (standard deviation = 64.1); the median was 90. Mean scores (and standard deviations) by age and gender were as follows:

Table: A11.1 PASE preliminary norms

Gender / Age group	65-69 years	70-75 years	76-100 years
Male	144.3± 58.6	102.4 ± 53.7	101.8 ± 45.7
Female	112.7 ± 64.2	89.1 ± 55.5	62.3 ± 50.7

PASE scoring (Washburn et al., 1993)

Table: A11.2 PASE scores are calculated from weights and frequency values for each of 12 types of activity

PASE Item	Type of Activity	Activity Weight	Activity Frequency	Weight times Frequency
2.	Walk outside home	20	a.	
3.	Light sport / recreational activities	21	a.	
4.	Moderate sport / recreational activities	23	a.	
5.	Strenuous sport / recreational activities	23	a.	
6.	Muscle strength / endurance exercises	30	a.	
7.	Light housework	25	b.	
8.	Heavy housework or chores	25	b.	
9a.	Home repairs	30	b.	
9b.	Lawn work or yard care	36	b.	
9c.	Outdoor gardening	20	b.	
9d.	Caring for another person	35	b.	
10.	Work for pay or as volunteer	21	c.	
			PASE SCORE:	

Table: A11.3 Activity Frequency value calculation

Days of Activity	Hours Per Day of Activity	Hours Per Day
0. Never		0
1. Seldom	1. Less than 1 hour 2. 1-2 hours 3. 2-4 hours 4. More than 4 hours	.11 .32 .64 1.07
2. Sometimes	1. Less than 1 hour 2. 1-2 hours 3. 2-4 hours 4. More than 4 hours	.25 .75 1.50 2.50
3. Often	1. Less than 1 hour 2. 1-2 hours 3. 2-4 hours 4. More than 4 hours	.43 1.29 2.57 4.29

a. Use hours per day conversion

b. 1 = activity reported in past week, 0 = activity not reported

c. Divide work hours reported in Item 10.1 by seven; if no work hours or if job involves mainly sitting with slight arm movements (Item 10.2 = 1), then activity frequency = 0

Appendix 12. Comorbidity selection, recoding and renaming

Table: A12.1 Original comorbidity names, frequency and percentage for both datasets

BEEP (self-report)	Frequency	percentage	MOSAICS (MRR)	Frequency	percentage
High BP	240	46.7	**Hypertension**	194	37
Stroke	19	3.7			
Angina	24	4.7			
Heart failure	9	1.8	**Heart disease**	65	12.4
Heart attack	19	3.7			
Osteoporosis	37	7.2	**Osteoporosis**	5	1
Depression	114	22.2	**Depression**	38	7.2
Bronchitis	32	6.2			
Asthma	67	13.0	**Asthma/COPD**	55	10.5
Obese	189	36.8	**Obese**	161	30.7
Diabetes	66	12.8	**Diabetes**	66	12.6

Comorbidity selection

1. Osteoporosis was removed from the analysis as too few participants had this comorbidity present.
2. Hypertension/ high blood pressure was removed from the analyses as too many participants had these comorbidities additional to their other comorbidities. Also, high blood pressure alone is not thought to cause symptoms that might influence PA level.

Comorbidity recoding and renaming

1. In BEEP, Stroke, Angina, Heart failure and Heart attack were combined and recoded as 'cardiovascular'.
2. In MOSAICS, Heart disease was renamed cardiovascular.
3. In BEEP, Asthma and Bronchitis were combined and recoded as 'respiratory'.
4. In MOSAICS, Asthma / COPD was renamed respiratory.

Therefore, if a person had all four possible cardiovascular conditions, this would now count as one comorbidity: cardiovascular. Equally, if a person only had heart failure, they would count as having cardiovascular.

Table: A12.2 Final comorbidities included in the analysis

Respiratory	Cardiovascular	Depression	Diabetes	Obesity	*Additional*
Asthma	Angina	Depression	Diabetes	BMI calculated	BMI categories
Bronchitis	Heart failure			≥30	<25
COPD	Stroke				25-29.9
	Heart attack				>30

Appendix 13. Exploring collinearity

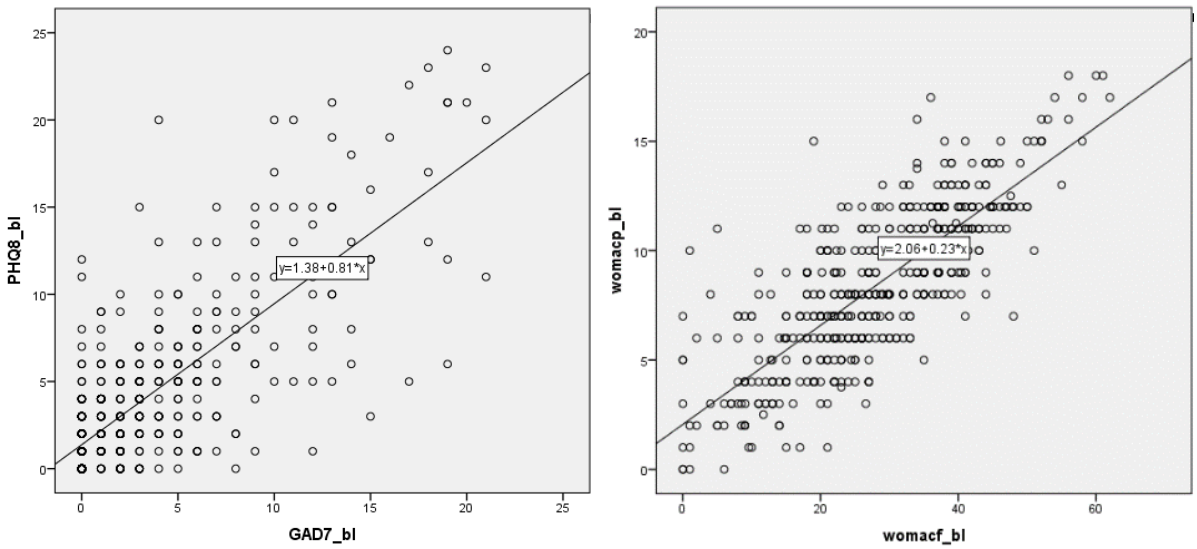
Collinearity occurs when independent variables within a linear regression model are highly correlated with each other. When highly correlated, independent variables cannot independently predict the value of the dependent variable. This can be indicated by Pearson's correlation or by variance inflation factor to measure the degree of collinearity. Multicollinearity is when more than 2 of the independent variables are strongly correlated. High levels of collinearity or multicollinearity could lead to spurious model outputs as the coefficient estimates swing wildly based on which other independent variables are in the model. Furthermore, it reduces the precision of the estimate coefficients and increases the p value (reduce the level of significance) of the regression model (Tu et al., 2005). The first step taken to reduce this risk was to assess Pearson's correlations. The correlations >0.5 in each of the datasets are shown below.

Table: A13.1 BEEP Pearson's correlations >0.5 in all variables

Variable 1	Variable 2	Pearson's correlation
EMPLOYMENT	AGE	0.553
EQ D5 5L	PHQ8	0.501
	WOMAC P	0.508
	WOMAC F	0.581
GAD7	PHQ8	0.770
WOMAC F	WOMAC P	0.798

Table: A13.2 MOSAICS Pearson's correlations >0.5 in all variables

Variable 1	Variable 2	Pearson's correlation
AGE	EMPLOYMENT	0.671
SF-12 GENERAL	SF PHYSICAL	-0.529
SF12 PAIN	SF-PHYSICAL	-0.832
	EQ-5D-5L	-0.639
	WOMAC PF	0.714
SF PHYSICAL	EQ-5D-5L	0.591
	WOMAC PF	-0.696
SF MENTAL	GAD	-0.705
WOMAC PF	EQ-5D-5L	-0.664



Figures: A13.1-2 Example highly correlated variables

It was, therefore, important to select the smallest subset of independent variables that explain as much of the variation in the regression as possible. Pearson's correlations between all the independent variables were investigated followed by the removal of variables based on high correlation, perceived clinical importance and similarity between datasets. For example, in the BEEP dataset, the PHQ8 depression and GAD7 anxiety variables were highly correlated, hence the PHQ8 was removed from the models since the PHQ8 is a measure of depressive symptomology and depression was considered as a comorbidity within the analysis (Pearson's correlation: 0.770). Another example was the WOMAC function and WOMAC pain which were highly correlated (Pearson's correlation: 0.798). Although both measures of the WOMAC are of theoretical importance, the WOMAC PF was kept as both datasets had this variable. The E-5D-5L was initially included in the multivariable models but further exploration found that it had not been recorded well and was skewing the analysis.

Table: A13.3 Variables kept in the multivariable models

Outcome	PASE score		
Independent	Comorbidity (self-report & MRR) (presence, frequency and type)		
Demographic	Gender	Age	Partner status
Clinical	WOMAC function	GAD 7	

PASE=Physical Activity Scale for the Elderly; MRR=Medical Record Review; WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index; GAD 7= Generalised Anxiety Disorder version 7

Appendix 14. Model assumption checking

Chapter 5 utilised multiple linear regression modelling. This appendix is organised so that the assumptions for multiple linear regression are addressed. For the purpose of clarity with concision, only a selection of the assumption checks for a selection of multivariable models are presented to provide evidence of the key outputs.

Multiple linear regression assumptions

Multiple linear regression models have a number of assumptions which were listed in Chapter 5 Part 2. In brief, the assumptions are;

1. The dependent variable must be interval or ratio
2. The independent and dependent variables must have a roughly linear relationship
3. The variables have normal distribution
4. The independent variables have little to no collinearity or multicollinearity
5. The residuals are not autocorrelated
6. Finally, the assumption that the data are homoscedastic

Assumption 1.

Assumption one was satisfied without the need for statistical testing since the dependent variable; PASE score is continuous.

Assumption 2.

In order to satisfy a roughly linear relationship between the independent and dependent variables, scatter plots of the independent variables (e.g. comorbidity presence, age, GAD7) against the dependent variable (PASE) were created with a line of best fit. A linear relationship of a roughly straight line of the plotted points satisfies assumption two.

Assumption 3.

In order to satisfy assumption three, histograms and P-P plots were used to check for normal variation of variable residuals around the regression line. Histograms with normal variation of data around the line, in a bell-shaped curve with vertically split symmetry and P-P plots with a linear relationship, would indicate a normal distribution of the residuals and satisfy the assumption.

Assumption 4.

In order to satisfy assumption four, first, the Pearson's correlations of all independent variables and removal of high pairwise correlations provided an initial step of removing collinearity. Additionally, collinearity statistics of Tolerance (Tol) which measures the influence of one independent variable on all other independent variables ($T<0.1$ there may be collinearity, $T<0.01$ indicates collinearity) and

Variance Inflation Factor (VIF) which is 1/Tol and indicates whether multicollinearity may be present (VIF>5 there may be multicollinearity, VIF>10 indicates multicollinearity).

Assumption 5.

In order to satisfy assumption five, the Durbin Watson test was used. A value near 2 indicates non-autocorrelation (<1 or >3 indicate autocorrelation).

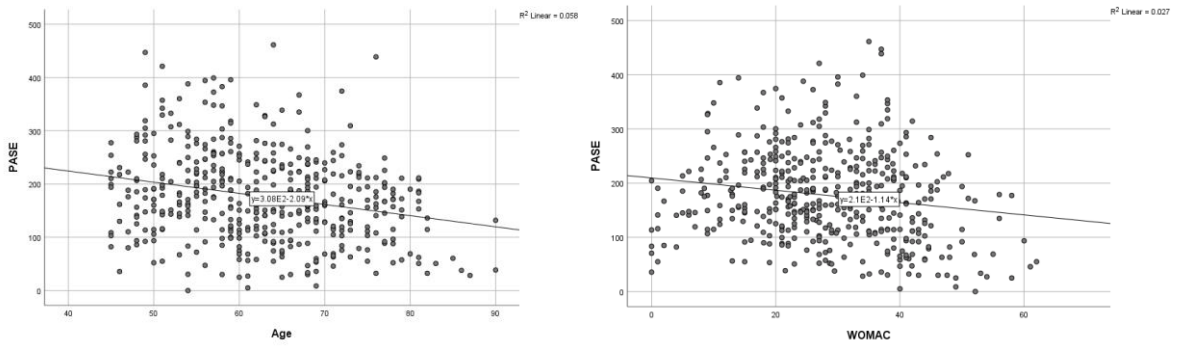
Assumption 6.

In order to satisfy assumption 6, scatter plots of the residuals against the predicted values were checked. Randomly distributed, evenly spread residuals without linear or funnel relationships meet the assumption.

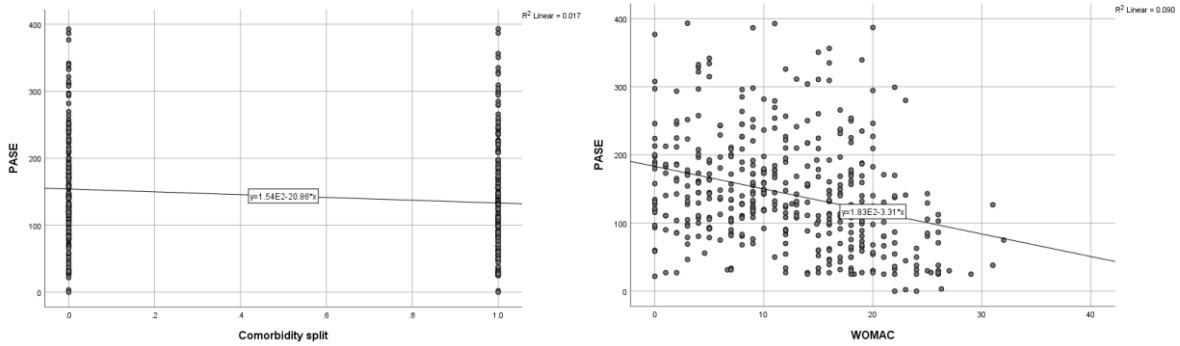
Examples of assumption checking

Assumption 2.

Checking assumption 2, the scatter plots below, show a roughly linear relationship between a selection of independent variables with PASE score. There is no evidence of a curvilinear relationship.



Figures: A14.1-2 Example scatter plots: BEEP



Figures: A14.3-4 Example scatter plots: MOSAICS

Assumption 3.

Checking assumption 3, the histograms below suggest a roughly normal distribution of residuals as indicated by the bell-shaped distribution and roughly vertical symmetry. The P-P plots show a roughly straight line suggesting a normal distribution of the residuals.

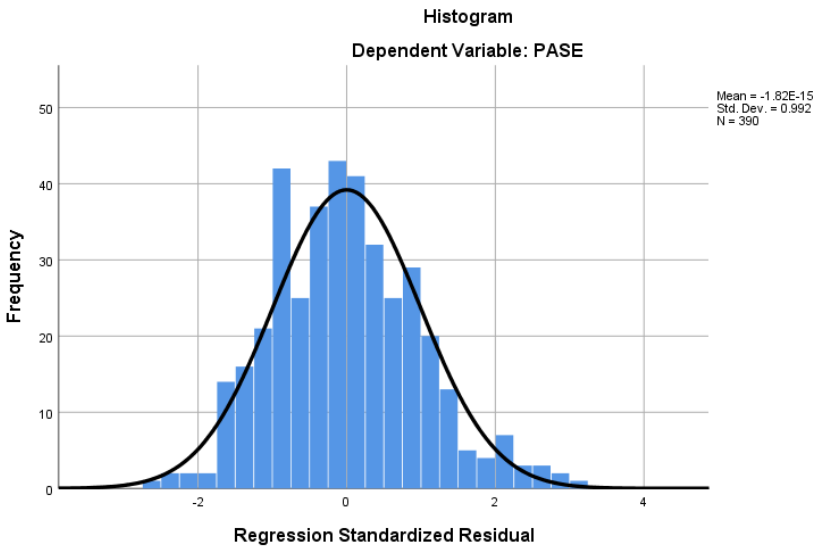


Figure: A14.5 Example of Objective 1. BEEP: Histogram of residuals

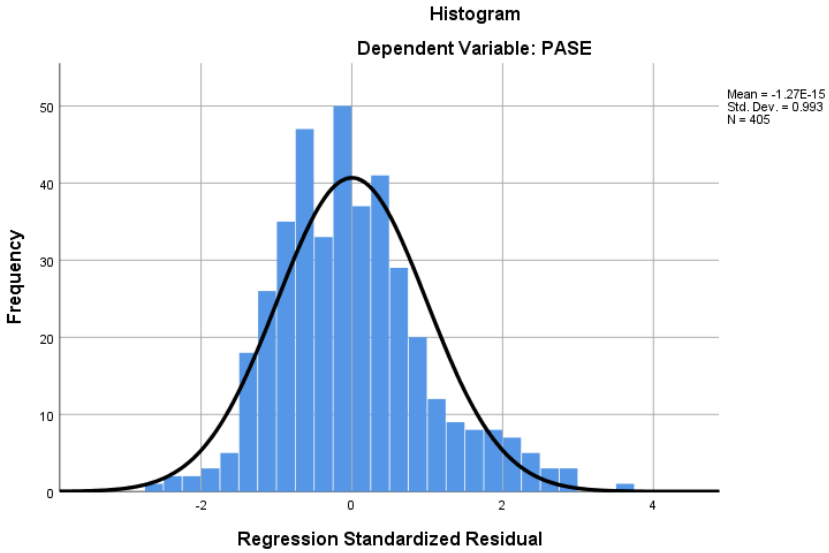


Figure: A14.6 Example of Objective 1. MOSAICS: Histogram of residuals

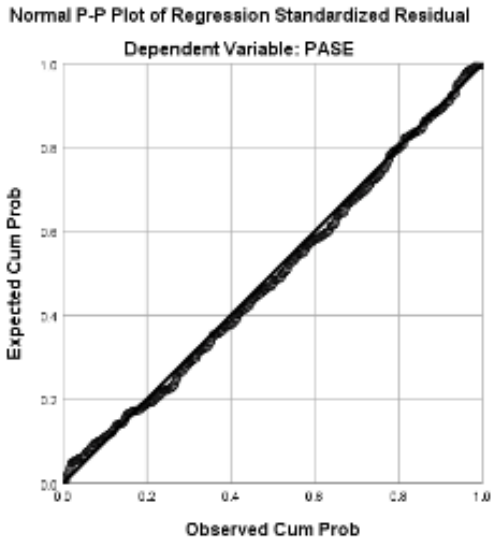


Figure: A14.7 Example of Objective 1. BEEP: normal probability plot (P-P)

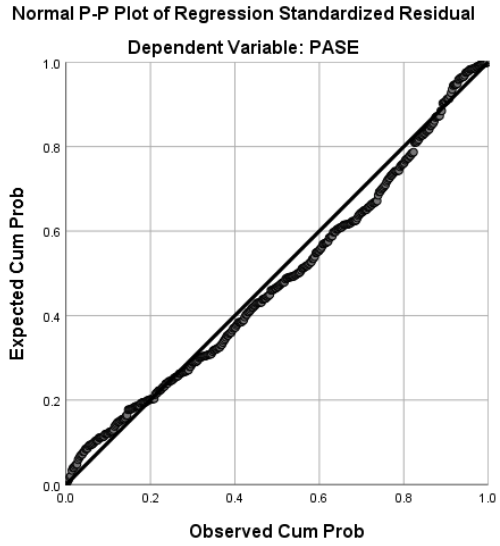


Figure: A14.8 Example of Objective 1. MOSAICS: normal probability plot (P-P)

Assumptions 4 and 5.

The tolerance in both datasets was well above the cut-off of suggested or certain multicollinearity in the data. The Variance Inflation Factor tests of the regression are also well below the cut-offs to suggest or confirm multicollinearity among the variables.

The Durbin Watson test results are both close to the value of 2. This indicates that there is little autocorrelation of the data and the residuals are independent of each other. The BEEP result is slightly more positively autocorrelated and MOSAICS is slightly more negatively autocorrelated, however, the values are not below the cut-offs of <1 or >3 to indicate any autocorrelation concern.

Table: A14.1 Example of Objective 1. BEEP and MOSAICS: Durbin Watson, Tolerance and Variance Inflation Factor tests results.

Objective 1.	**TOL**	**VIF**	**DW**
BEEP	0.949	1.054	1.752
MOSAICS	0.906	1.104	2.077

Assumption 6.

The examples below show the final check for homoscedasticity through scatter plots of residuals against the predicted values. The scatter plots show the data to be roughly randomly distributed, with evenly spread residuals. On inspection, throughout all scatter plots of residuals against predicted values, the MOSAICS dataset appears to have more indication of funnelling, but not of an unacceptable homoscedastic level.

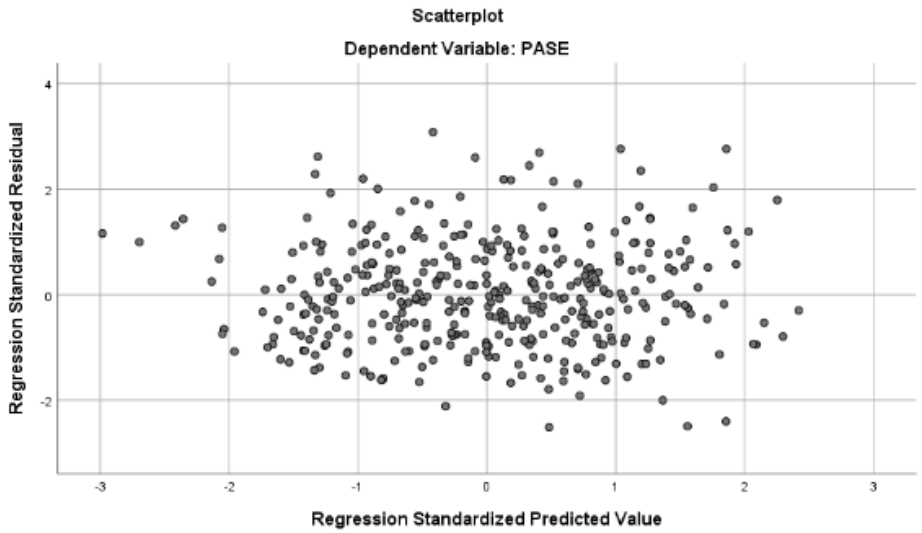


Figure: A14.9 Example of Objective 1. BEEP: Residual versus predicted value plot for homoscedasticity

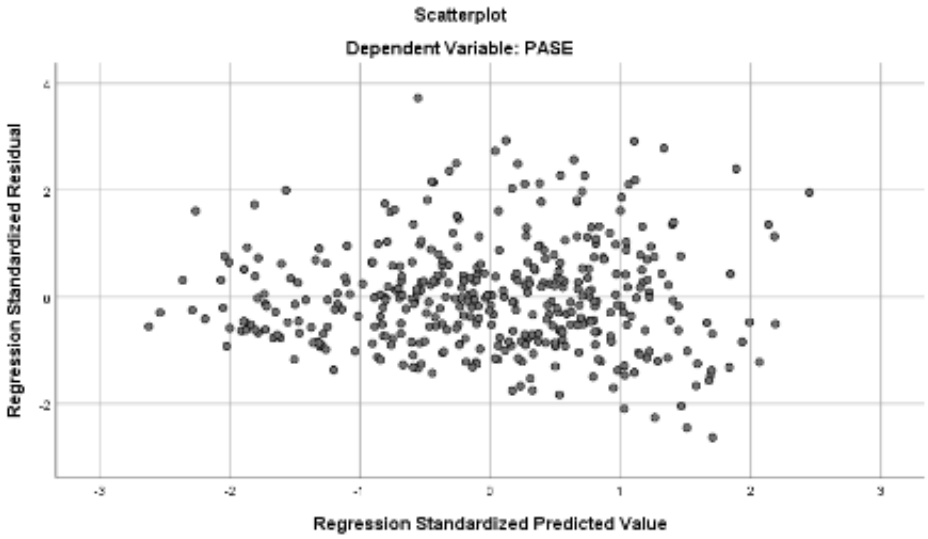


Figure: **A14.10** Example of Objective 1. MOSAICS: Residual versus predicted value plot for homoscedasticity

Appendix 15. Qualitative ethics review panel approval letter

05/01/2018

Dear Sarah

PI: Sarah Mckevitt
Title: Attitudes and beliefs about physical activity in people with osteoarthritis and comorbidity: A qualitative study.
Ref: ERP3128

Thank you for submitting your application for review. The proposal was reviewed by the Panel Chair. I am pleased to inform you that your application has now been approved by the Ethics Review Panel.

If the fieldwork goes beyond the date stated in your application, or there are any amendments to your study you must submit an 'application to amend study' form to the ERP administrator at research.governance@keele.ac.uk. This form is available via http://www.keele.ac.uk/researchsupport/researchethics/

If you have any queries please do not hesitate to contact me, in writing, via the ERP administrator, at research.governance@keele.ac.uk stating **ERP3128** in the subject line of the e-mail.

Yours sincerely

(signature redacted for thesis)

Appendix 16. PPIE involvement

Patient and Public Involvement and Engagement (PPIE) input into the research design

1. Overview
2. PPIE meeting request form summary
3. Plain English summary
4. PPIE meeting presentation slides
5. PPIE meeting minutes
6. Brainstorm slide created from meeting

1. Overview

A meeting with members of the PPIE group (n=3) at the Research Institute for Primary Care and Health Sciences (iPCHS) was organised to gain the important lay perspective regarding all public-facing items and methods for data collection. The study and planned methods were presented to the group and opened the discussion. The PPIE members helped with the development of the interview guides by emphasising themes and specific questions, recruitment posters (e.g. adding a photo of the researcher), study information (simplifying and adding clarity to complex terminology) and methods for recruitment (e.g. specific leisure centres and contacts) to reach potential participants.

2. Patient and Public Involvement Request form summary

A Patient and Public Involvement request form was completed. In brief, this form intends to more efficiently support the incorporation of PPIE into the research process as well as considerations to assist the researcher in ensuring the best experience possible for public involvement. The form consists of;

1. A plain English summary to inform the Research User Group members about the study
2. The overall aims and objectives of the project including start date and study duration
3. The overall aim of having PPIE involvement and how they would inform the research
4. The specific role and tasks that would be undertaken by PPIE
5. How many individuals would be necessary to fulfil the PPIE aims
6. The expertise and patient characteristics to fulfil the intended study population
7. The stages of the research process that would require PPIE
8. An outline of topics intended to be covered in the meetings

3. Plain English summary

Osteoarthritis is one of the most common musculoskeletal conditions and has a negative impact on a patient's life in terms of pain, function and Quality of life. Osteoarthritis is rarely experienced on its own. Other conditions often exist alongside osteoarthritis, and this existence needs to be accounted for within management strategies such as physical activity treatments as additional conditions may interfere with the application of exercise therapy. There is a recognized requirement for research to determine the effects of additional conditions on treatment outcomes, guidelines for care and treatment plans and practice. This study aims to explore the attitudes and beliefs of adults with osteoarthritis and the existence of additional conditions regarding physical activity. This study focuses

on how people with OA experience physical activity and how this population could be encouraged to increase their physical activity levels.

The primary aim of this research is to explore individuals with OA and comorbidity to gain an in-depth insight into their attitudes and beliefs regarding PA through the use of qualitative interviews.

Objectives:

1. How do people with OA experience PA in the context of other health conditions?
2. How can people with OA and other health conditions be encouraged to increase PA levels?

Methods:

These objectives will be met through interviews with adults with osteoarthritis and at least one other health condition.

Patient and Public Involvement and Engagement (PPIE) is an initial strategy used to inform and shape the project. The researcher will be arranging suitable dates to meet with PPIE members throughout the research process. The target PPIE members will be adults with osteoarthritis (and comorbidity?). In the initial meet, the PPIE members will assist in the formation of the study process and methods chosen from recruitment through to analysis plans. Feedback will be sought for the documentation regarding participant information and guides used in the interviews to ensure the language used and information is comprehensive from a patient perspective. Throughout the research process, PPIE input would be sought regarding how to analyse and interpret the data, as well as feedback regarding how well they feel the data represents the population. The PPIE member insight would also be sought following the completion of the qualitative research regarding how the research could be disseminated and used in practice, in the next stage of the PhD project.

What roles and tasks will be undertaken?

Most importantly the public-facing documents – the interview guides. I have outlined in my whole PhD project that I wish to include the public in my decisions and the application of my research.

What characteristics are needed?

Those with OA and of age 45 and over.

Project stages requiring PPIE

At the very beginning of this project, ideally before submission of ethics. I would like to have the input on all public-facing documents. I would also like to include them in the analysis / interpretation phase.

4. PPIE presentation slides for group meetings

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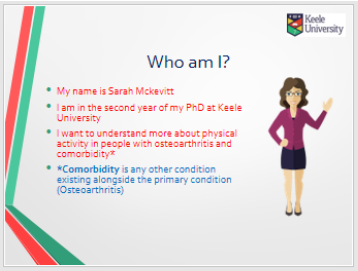

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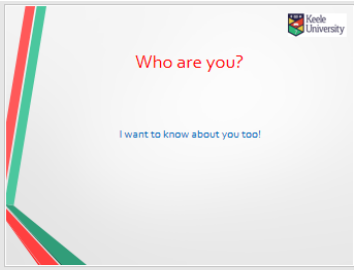

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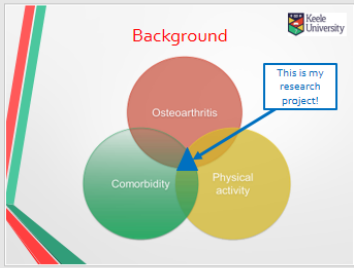

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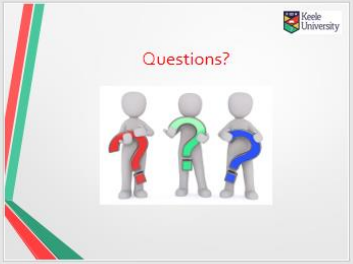

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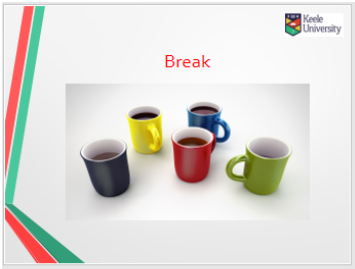

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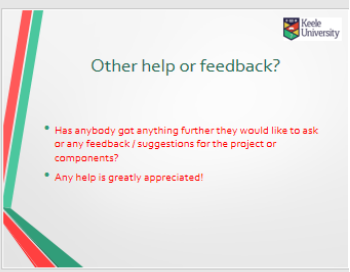

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5. PPIE meeting minutes

Sarah McKevitt PPIE meeting minutes: 3rd October, 10am – 1pm, Room 0.79

Attendees:

Sarah McKevitt (SM), Laura Campbell (LC), Alice Moult (AM)

General conversations in group

Participant C has OA and Rheumatoid Arthritis, she doesn't do formal exercise but 'potters' about.

Participant J has Osteoporosis and mental health problems, she attends exercise classes such as yoga and tai-chi.

Participant K (Spine / neck spondylosis). Attends various exercise classes and has tailored the exercises to meet her needs.

Exercise doesn't work fast; you've got to persevere with it. Even if pain if halved it's a huge thing, it's important to tailor exercise to your own way. It's important for someone starting off to do exercise.

SM opened the meeting with an introduction into her PhD research.

Recruitment locations:

C - **Haywood, NRAS** group – once every three months.
ARM group / society meeting 4 times a year, meet at Haywood.
Haywood have **the PEER** room – Haywood would promote and make people aware of it.

June Brammer – she oversees the PEER room and attends ARM and NRAS. Member of RUG ask Laura for contact details.

NRAS society also runs an **online forum**.
Exercise class at **Newcastle Leisure centre**.

People afraid to do exercise because they don't know the damage that it can cause. Funding might be a barrier to attending the gym. No information unless you seek it out.

Better for me (researcher) to meet people, rather than to go through gate-keeper.

K – **Leisure centres** for people who already do exercises.
GP surgeries for perhaps people who don't do exercise.

People don't like being told what to do, people put off being told to do exercise. The way that the exercise is communicated, it needs to be suggested not dictated to the person. People need to be motivated to exercise it's not an easy route. Barriers may prevent exercise and each person's barrier to exercise may be different. Comorbidities may prevent exercise, need to consult a GP before engaging with exercise e.g. if the person has a heart condition. Confidence goes after diagnosis, less likely to try something you know is going to be difficult. Mental health conditions are also comorbidities, people didn't have mental health conditions before a diagnosis of a physical condition. Depression may come from needing help from others, group therapies would be good.

Leighton hospital, Occupational health department do classes for newly diagnosed people, classes include hand and arm exercises and how to use aids for things such as using bottles.
Meditation and mindful classes to work on techniques to work on mind control.

Online forums are second best to face to face communication.

'Rehabilitation' Classes at leisure centres for individuals with physical problems, **Congleton leisure** centre. Work through circuits an easy one and a hard one, an element of choice for the individual, can tailor to the individual's needs.

J – **Haywood hospital** steered to RUG group.
Working Education Association – sent from GPs.
U3A groups around North Staffordshire, they do holidays and crafts.
Recruit from **Women's institute.**
West End Village in Stoke do a lot of classes.

People learn from things due to word of mouth.

Recruitment Poster:

K: Likes the colour and the use of boxes, easy to read and is clear.
Do not need any more information.
Re-arrange boxes with contact details, reuse space for the photograph.
Perhaps use a bigger font.

C: Include a photo of SM to put a face to the research.

If SM goes prepared with participant information sheets, people will be more likely to give contact details.

LC – Needs to put the new logo on it.

Invitation letter:

J – Likes the layout and the inclusion of the phone number.

K – Middle paragraph doesn't quite read right *(If you were willing to be interviewed* sentence) Need to be more specific and state 'the return of the participant information sheet' not just information.
No extra words if you don't need them.
Include the Keele and ARUK logo.

Information sheet:

J – Make font bigger.

C – *What is the purpose of the study* - define comorbidity and explain that they are in that section.

Do I have to take part - Additional 3 months will be given to withdraw the data – need to reword to make it clear.

Not everyone knows what a peer review – needs more clarification.

K – *What does the Study involve – This would be about your **experiences** of physical experiences* – Word it differently to capture people who don't exercise. Change the word 'experiences' to views or perspectives or attitudes or beliefs.

Signpost at the end to the participant information sheet: 'If you would like to take part fill in the participant information sheet'

Be consistent and use the word 'participant information sheet.'

Participant Information Sheet:

K – Font size is big enough. Do not need the word 'unfortunately' in the sentence **Please note, unfortunately, if you do not have another health condition' …*

The group recognised that people need time to read the sheets.

The Interview – group brainstorm (prior to viewing interview guides)

K – Need to know what they're doing first, **are they doing exercise currently**?

What prevents them from doing the physical activity? People don't **associate housework with exercise**, need to be clear in questions using the wording activity and exercise.

Need to explore the relationship between comorbidity and exercise. People need to get the okay from **HCP** that they can exercise with their comorbidity.

J – Open the interview by asking about their **typical day.**

K - being physically active is using the body and muscles, need to explore the perceptions**, purpose of activity, motivation** for physical activity, how **willing a person** is to exercise.

K – People are motivated to exercise to improve their quality of life. You '**use it or lose it.**'

C - Explore how conditions impact **upon daily life and routine.**

K – Once a person has had a flare up they need more motivation to exercise. **Encouragement** is also needed to exercise**, support** from **HCP or groups** may encourage exercise. Useful to **talk to people** who have been **through the same thing**, this might encourage and motivate the individual to exercise more.

C – People may attend groups if people are **friendly and social**, explore the **social nature** of community groups.

K – The **expectations** an individual has might affect the exercise that they engage in, they expect the exercise would be beneficial but the **exercise might hurt** at first, they may need encouragement **to carry on.** People feel good after exercise because they release Endorphins, the feel good hormones and exercise **may make them look better** and fit in clothes they couldn't have a year ago. These are **incentives to exercise**.

C – People might not want to exercise because of the immediate pain. It needs to be **clear that exercise may hurt** immediately**, but will be beneficial in the long term**, then they will **be mentally prepared for the pain**.

K – People have **targets and milestones**, this could help them **to regain their QoL**. **Family** such as grandchildren may motivate them to exercise.

C – Before the barriers in the interview, explore **what the motivations to do exercise are**.

Interview – what question would you ask?

K would ask: Are you content with the QoL you have now, would you like to improve it? Would you like to improve your QoL or reduce your pain?

J would ask: What do you miss? Is there something you would like to do? What did you get your fulfilment from and can we start little steps towards getting back to doing that?

C would ask: What do you aim to get from physical exercise? What are your expectations of exercise?

Interview Guide (after time for reading and familiarisation with guide)

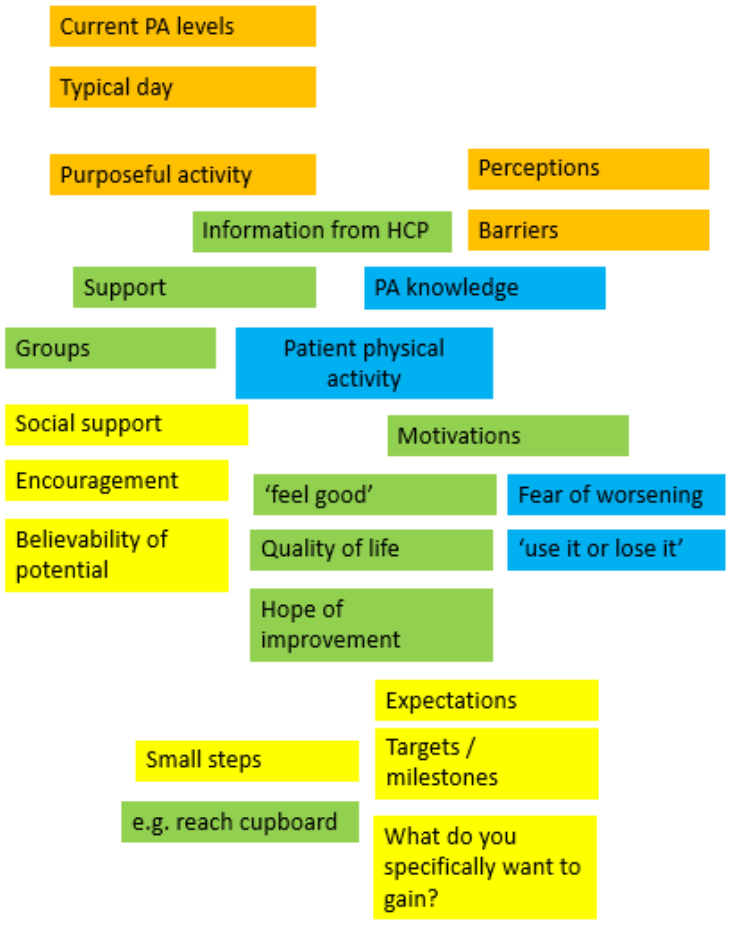
K – Need to know if the person is **retired and need to ask about job**. Don't just assume everyone is retired. Likes how the guide includes themes. Need a strategy to ensure that SM doesn't ask the **same question twice.**

C - Make it **clear** at the beginning that if they don't understand anything that **they can ask** SM a question.

Nothing to add or change. Need to include that the interview will last **'approximately' one hour**.

SM concluded by thanking the group and invited them to attend another meeting that would focus on the analysis of the interviews. The group agreed.

6. PPIE meeting brainstorm



Appendix 17. Participant recruitment locations

1. Original recruitment location contacts

Name of group	**Location**
Newcastle 50+ forum	Newcastle Under Lyme
Beth Johnson Groups	Stoke-on-Trent
Age UK groups	Newcastle Under Lyme
Arthritis Care UK	Stafford
Arthritis Action	UK-wide
Green door activities	Stoke-on-Trent
Royal Voluntary Service	Stoke-on-Trent
Newcastle Under Lyme Friendship Centre	Newcastle Under Lyme Library
College of the third age	Newcastle Under Lyme
Stoke Health older persons group	Stoke Heath Community Centre
Royal Voluntary Service	Stoke-on-Trent
Royal Voluntary Service	Parish Church of St Andrews Church Hall, Stoke-On-Trent
Woman's Institute	Stoke-On-Trent

2. Additional recruitment contact made

Name of group	**Location**
Friends activity group	Coven Memorial Hall
Age UK	St. Giles Church
Age UK	Burton
Age UK	South Staffordshire
Age UK	North Staffordshire
Diabetes UK	North Staffordshire
Staffordshire Football Association	Staffordshire
Approach Staffordshire	Staffordshire
Hayward befriending group	Stafford
Burton Albion Football Club	Burton
Critterish all sorts UK	Stoke-On-Trent
SSOTP	Stoke-On-Trent
Arthritis Care	Staffordshire
Arthritis Action	Staffordshire
Midland Heart Association	Stoke-On-Trent
Diabetes UK	North Staffordshire
Weight-Watchers	UK

Appendix 18. Recruitment poster

ARTHRITIS RESEARCH UK

Could you take part in my research?

Keele University

Who am I?

Sarah Mckevitt, a PhD student at Keele University. Please read the following information and see or rip off my details at the bottom of the page.

The project

Many people with **osteoarthritis** also have other health conditions.

1. I am interested in what impact having osteoarthritis and other conditions has on your view of physical activity.

2. I am interested to know what your physical activity preferences are.

Your views will inform future research about how to help people with osteoarthritis and other health condition be more active.

Your help

Do you have Osteoarthritis and at least one other long term health condition?

I would like to invite you to **a short interview** with me about your physical activity experiences.

There are **no physical activity level pre-requisites.**

I would meet you at a time and place convenient for you. I would like to audio record the interview for my research project. Any information would be kept **confidential and anonymous**.

Sarah Mckevitt, Research Institute for Primary Care and Health Sciences, Keele University.
Email: s[redacted]
Phone: [redacted]

Sarah Mckevitt, Research Institute for Primary Care and Health Sciences, Keele University.
Email: [redacted]
Phone: [redacted]

Sarah Mckevitt, Research Institute for Primary Care and Health Sciences, Keele University.
Email: s[redacted]
Phone: [redacted]

Contact me:

Sarah Mckevitt

Research Institute for Primary Care and Health Sciences, Keele University.

Email: s[redacted].uk

Phone: 0[redacted]

Appendix 19. Recruitment presentation

primary care centre

Keele UNIVERSITY

Could you take part in my research?

Who am I?

- My name is Sarah Mckevitt
- I am in the second year of my PhD at Keele University
- I want to understand more about physical activity in people with osteoarthritis and comorbidity*
- *Comorbidity is any other condition existing alongside the primary condition (Osteoarthritis)

Keele UNIVERSITY

My Research

An investigation of the attitudes and beliefs regarding physical activity of people with OA and comorbidity.

Keele UNIVERSITY

Background

Osteoarthritis is one of the diseases which most commonly has comorbidity

Comorbidity is any other condition existing alongside the primary condition (Osteoarthritis)

Physical activity is one of the core treatments for osteoarthritis

Keele UNIVERSITY

So what is the problem?

- Physical activity interventions are underused for patients with OA and barriers such as comorbidity exist.
- More people with OA are living with comorbidity.
- People with OA find it hard to be physically active but it is not fully understood why or how to help.

Keele UNIVERSITY

Research questions

1. How do people with OA and comorbidity experience PA?
2. How can people specifically with OA and comorbidity be encouraged to increase PA levels?



Keele UNIVERSITY

How could you help?

I would like to invite you to an interview to find out about your physical activity experiences.

Keele UNIVERSITY

Count me in!

Do you have osteoarthritis and at least one other long term health condition?

Or do you know someone who could participate in my project?

There are no physical activity pre-requisites

Could you participate in a short interview at your convenience?

I would really appreciate your help!

Keele UNIVERSITY

Thank you!

- Please don't hesitate to ask questions or have a discussion with me!
- Sarah Mckevitt
- 01782 734525
- S.a.mckevitt@keele.ac.uk

Keele UNIVERSITY

primary care centre

Keele UNIVERSITY

Acknowledgements

Arthritis Research UK | primary care centre

Dr Jonathan Quicke, Dr Clare Jinks, Dr Emma Healey, my peers and colleagues at Keele university.

Thank you for listening

Appendix 20. Participant invitation

Letter of invitation

Ref: *Insert Study ID*

>Insert prospective address<

>Insert Date<

Dear >Insert Name<,

Thank you for taking an interest to participate in my study;

Research Study: Attitudes and beliefs about physical activity in people with osteoarthritis and comorbidity: A qualitative study.

My name is Sarah Mckevitt and I am a PhD student studying at Keele University. I am inviting you to take part in a research study looking at how people over the age of 45 with osteoarthritis view physical activity when they also have other health conditions. I would be grateful if you would read the attached information sheet.

If you would be willing to be interviewed please return the reply slip in the pre-paid envelope. I will then call you to arrange a meeting.

Please contact me if you would like more information. I am very happy to discuss the research and answer any questions you may have.

Yours sincerely,

Sarah Mckevitt

PhD Researcher

Telephone: 01782 734985

Email: s.s.mckevitt@keele.ac.uk

Attached: ***Study information sheet and Participant information sheet, reply slip and pre-paid envelope***

Appendix 21. Participant information

Information sheet

You are being invited to take part in a research study. Before you decide, it is important that you understand why the research is being done and what it will involve. Thank you for taking the time to read the following information.

Who is funding and organising the research?

Sarah Mckevitt, a PhD student at Keele University is being funded by Keele University through an ACORN PhD Studentship to undertake the study.

What is the purpose of the study?

Previous research has shown that osteoarthritis (OA) is a very common disease that has a large impact on people's lives. Often people who have OA also have other conditions at the same time. Physical activity is an effective form of treatment for osteoarthritis. Physical activity includes everyday activities such as; walking to work, housework, gardening, working out, and playing active games and sport. However, the impact of having other health conditions alongside osteoarthritis on the physical activity people carry out is not clear. This research aims to find out what the patient perspective is, what they think of physical activity, their experiences and suggestions for encouraging a more physically active life.

Why have you been invited to take part?

I have invited you to take part in an interview about your attitudes and beliefs regarding physical activity. You have been invited because you have osteoarthritis and at least one other health condition at the same time. I am investigating whether this combination of osteoarthritis and other health conditions impacts on attitudes and beliefs and ability to be physically active. My research is to find out;

1) What are your attitudes and beliefs toward physical activity?
2) How can you be helped to be more physically active?

Do I have to take part?

Participation in this study is entirely voluntary. You do not have to take part and you can change your mind at any time without consequence. An additional period of one month from the interview date will be given for you to withdraw from the study.

What does the study involve?

I will meet you at a time and location convenient for you. I would like to do a face-to-face or telephone interview which I would audio-record. This would be about your perspectives of physical activity. This could take approximately 60 minutes.

There are no direct benefits to you by taking part, however you will be helping in research to identify better ways to tailor physical activity recommendations for people with osteoarthritis and comorbidity. There are no right or wrong answers and no preparation for the interview is necessary.

Confidentiality

I will type the interview up and anonymise it by removing any names or details which could identify you, anyone else or places. The anonymised information will be used in my thesis research report and for journal articles and presentations.

On completion of the research, the information such as interview transcripts, audio-recordings and personal information will be destroyed. However, if you consent to it, anonymised information will be kept for 5 years so that this may be used in future research by researchers at Keele or our collaborators.

You don't have to answer any questions you do not wish to and you may stop the interview at any time point. All data gained from the study will be kept strictly confidential. Access to the information will only be given to myself and my supervisors at the University.

Who has reviewed the study?

The Keele University Ethics Committee has reviewed and approved this project. The quality of the study has also been reviewed by topic specialists as part of the research approval process.

Contact for further information

If you require more information I am happy to discuss the research via phone or email contact. My contact details are;

Sarah Mckevitt
Research Institute for Primary Care and Health Sciences
Keele University
Staffordshire
ST5 5BG
Email: s.s.mckevitt@keele.ac.uk
Phone: 01782 734889

For any other concerns or a matter you wish to discuss outside of the research team please contact;

Research Integrity Team

Directorate of Research, Innovation and Engagement

IC2 Building, Keele University, ST5 5NE

Email: research.governance@keele.ac.uk

Tel: 01782 733371

Thank you for taking the time to read this participant information sheet.

If you would like to take part please fill in the reply slip.

Appendix 22. Participant reply slip

Name

Date of birth

☐☐/☐☐/19☐☐

Contact number

Is there a best time to contact you?

Have you ever been diagnosed with osteoarthritis by a health professional? YES / NO

(Please circle one answer)

Do you currently have any other health condition? YES / NO

If so, which condition(s) do you have (e.g. obesity, diabetes, heart disease, depression, chronic obstructive pulmonary disease, hypertension)?

_____

_____

Please note, if you do not have another health condition, you are not eligible for this study

Thank you again for taking the time to read and provide information for this study,

Sarah Mckevitt.

Please return this reply slip in the prepaid envelope supplied.

Appendix 23. Consent form

Title of project: **An investigation of attitudes and beliefs towards physical activity in people with osteoarthritis and comorbidity: A qualitative study.**

Name of Researcher: Sarah Mckevitt

Study ID number: *(Insert study ID number)*

Participant name: (*Insert name)*

Please initial each box if you agree with the statement

1. I confirm that I have read and understood the information sheet dated <*insert date*> for the above study and have had the opportunity to ask questions. ☐
2. I understand that my taking part in an interview is voluntary and that I am free to not answer any question or withdraw at any time, without giving a reason. ☐
3. I understand that if I do take part, I can ask for my information to be removed for up to one month after my interview. After that, it will not be possible to remove it, as data analysis will have started. ☐
4. I understand that the interview will be taped and transcribed, and that the tapes will be securely stored in the Research Institute for Primary Care and Health Sciences at Keele university, but will bear no personal identifying information. ☐
5. I agree to allow my anonymous information to be used in future research projects. ☐
6. I agree to my anonymised quotes being used in the publication of any results, but that these will be anonymous and I will not be identified. ☐
7. I agree to take part in the study. ☐

_____	_____	_____
Name of participant	Signature	Date
_____	_____	_____
Researcher	Signature	Date

Appendix 24. Interview guide with tracked changes

The following statements to be read out before each interview
Explanation of who you are:

I am Sarah Mckevitt, a student from Keele University undertaking PhD study to explore Osteoarthritis and comorbidity. This interview study will inform part of my PhD and is entitled;

'Attitudes and beliefs about physical activity in people with osteoarthritis and comorbidity: A qualitative study.'

Confidentiality statement

You can be reassured that any information disclosed to me the researcher, will be kept confidential and that it will not be possible for you to be identified. Your participation in this project is voluntary and therefore you may withdraw from it at any time without penalty. You have the right not to answer specific questions and to ask for the audio-recording or note taking to stop at any point.

Interview begins

Theme A) Introduction
Let me start by asking you some questions about yourself (*Demographic questions):*

- Age
- Marital status
- Education
- Occupation

Can you tell me about your osteoarthritis (how long had it, which joints, what caused it?)

Can you tell me about other conditions you have

- Can you tell me a bit about your experience living with osteoarthritis and other health conditions at the same time? (Pain, function, other comorbidity related reductions in QOL)

Theme B) General challenges of comorbidity and PA

The next few questions are about physical activity and exercise and how this has been influenced by your other health conditions.

Can you tell me about any physical activity or exercise that you do at the moment?

- What role does PA have in your life and has this been influenced by having both OA and comorbidity? (Fitness, social, psychological, therapeutic etc.)
- Have you changed the type of PA you do because of OA and other long term conditions?
- ~~What affects your PA levels? Has this changed over time?~~
- How do you feel about doing PA in the presence of your OA and other long-term conditions?

Theme C) Advice about PA for OA and comorbidities

What do you know about physical activity treatment options for someone like yourself with OA and other health condition(s)?

- How much physical activity do you think you should do? What are the reasons for your answer?
- What types of physical activity do you think you should do? (probe reasons for answers)

Where do you get information and ideas about physical activity? (Doctor, family, books, self—help group etc.)

~~Have you spoken to anyone about PA such as how much to do, what type or when to do it? Who?~~

- ~~How do you feel about discussing physical activity with others? Caregiver? Professional? Family?~~

What has been the advice you have had about physical activity?

- How do you feel that this advice suits your situation of OA and *other condition*

How confident are you that you can follow advice to be physically active?

Did you try any instruction for PA you received? Did it help? If not, why?

Theme D) Priority of conditions and PA

Do you feel that any one of your conditions are more important than others? Can you explain the reasons for your answers?

~~Where does physical activity sit in your priorities?~~

How does having this combination of conditions impact on PA? (In what way? Why?)

~~What factors determine whether you do any physical activity or not on a daily basis? (Anything encourage / discourage you?)~~

What is different about having conditions together than alone?

Do you think it would be the same for other people with this combination of conditions?

Theme E) Impact of OA and comorbidity on sedentary time

Do you spend any time sitting, for example reading, watching television or on the computer?

- How do you feel about the amount time you spend sitting?
- Does having OA and another condition affect this amount of time you spend sitting, reading etc, why?

What would make physical activity more appealing for somebody like you who has ~~OA and other long term conditions?~~ this combination of conditions? What makes it worse?

- What is it about having OA and other conditions that make it hard to exercise?
- What are the problems that crop up when you want to be active but can't?

Theme F) Facilitating PA for someone with OA and comorbidity

Can you tell me what supports you with regards to physical activity and maintaining a physically active lifestyle? (family, friends, community, internet, healthcare)

- How has this been supportive?

Are there other sorts of support that you would find helpful, or that you think other people with ~~OA and long term conditions~~ this combination of conditions might find helpful?

Is there any other kind of physical activity, exercise programme or opportunity that you have heard of, know someone else does it, or would like to try? Why haven't you tried it?

What would make you want to try a new type of physical activity or take up activity you have previously done?

If you were asked to do a programme of exercise by a healthcare professional or if you we advised to go swimming or walking, what would you want to know about? What would help you to do that activity with regards to your conditions?

Have you ever heard of an intervention or programme which tries to encourage or make physical activity experiences better for people with OA and comorbidity? What would feature in an intervention if you helped to design it?

Do you have any future plans or goals for physical activity with your ~~OA and comorbidity?~~ combination of conditions?

Have you got any thoughts about what would help people with the combination of OA and other health conditions exercise more or be more physically active?

Theme G) Concluding questions

What are your thoughts about PA for people with OA and other health conditions (Including, work, housework, gardening, and hobbies) Do you think it is safe, good for you and achievable? (Prompt for good or bad, if so what does good mean?)

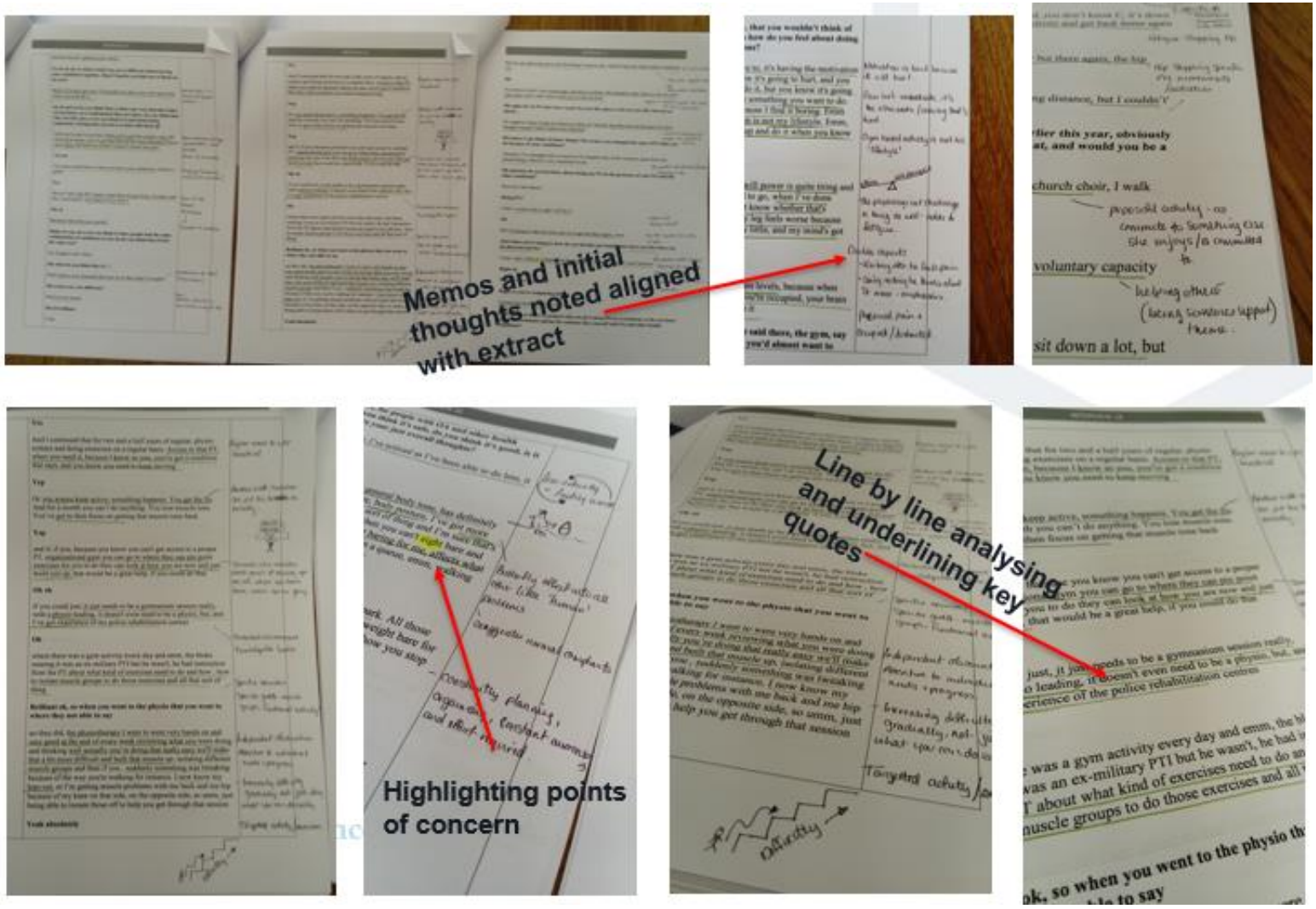
Would you like to say anything further, that you consider to be important and I haven't asked?

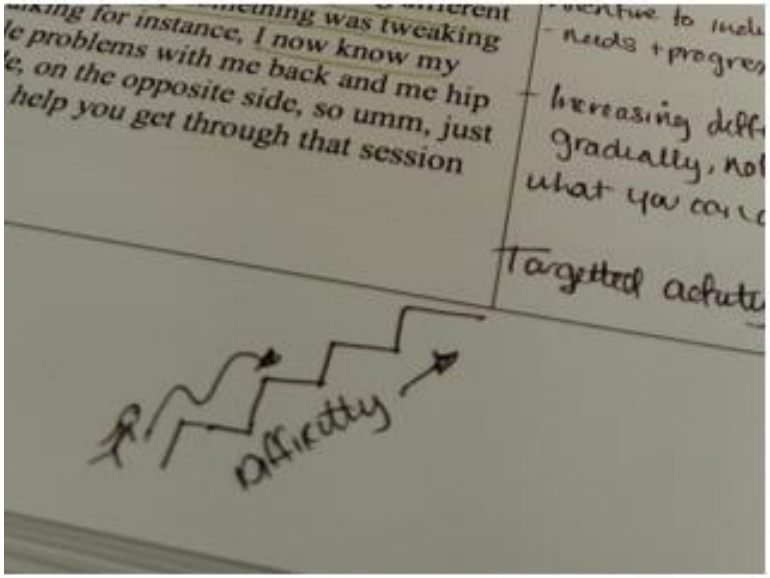
Check consent is still in place.

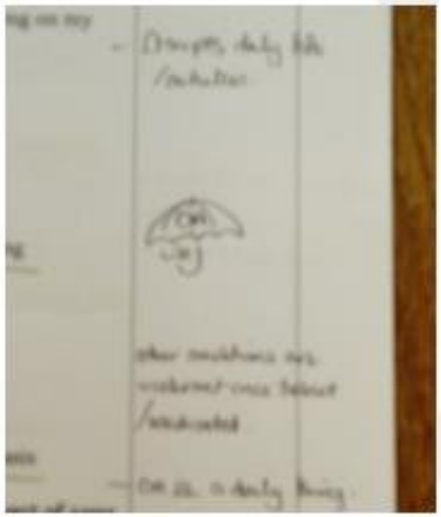
Check if participant would like to receive a summary of the interview findings.

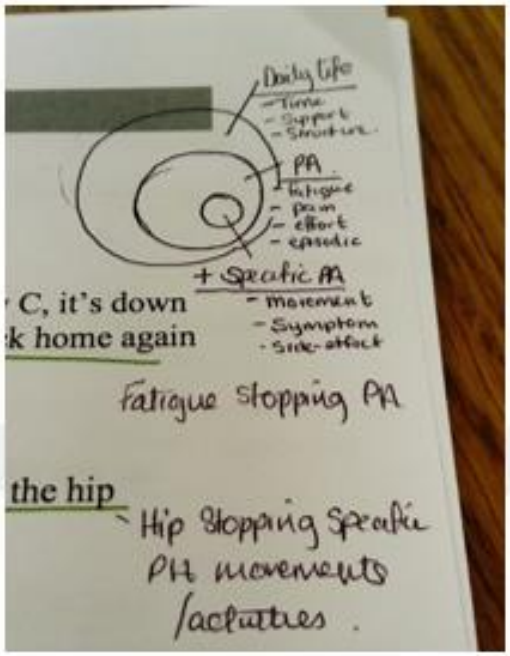
Thank you very much for taking the time to participate in this research project.

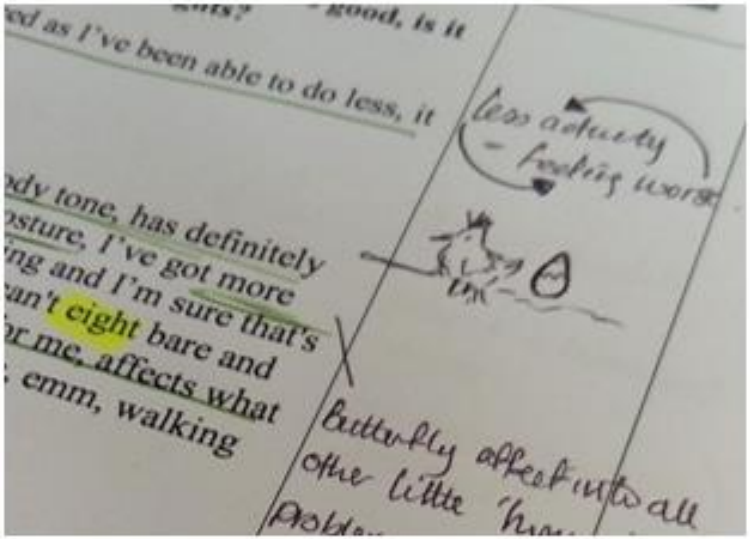
Appendix 25. Analysis process examples

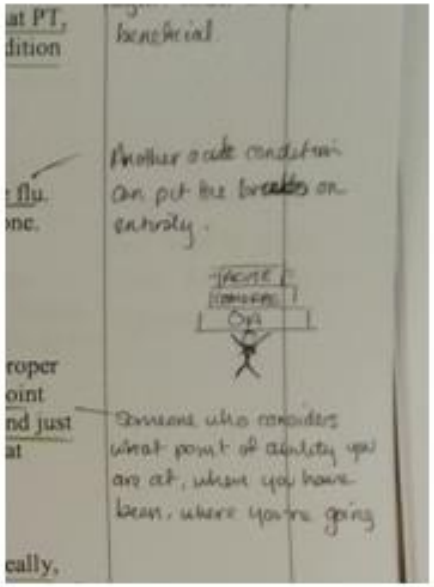


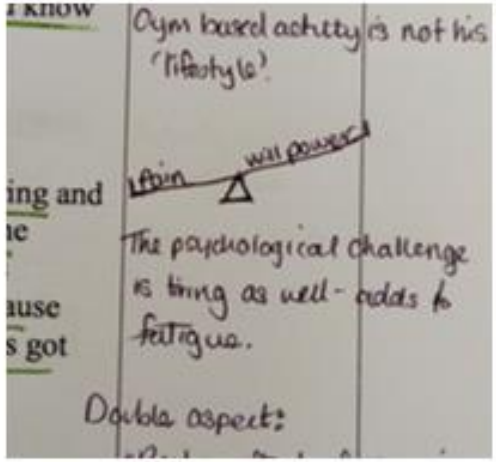

for instance, I now know my
problems with me back and me hip
on the opposite side, so umm, just
help you get through that session
Targetted
activity

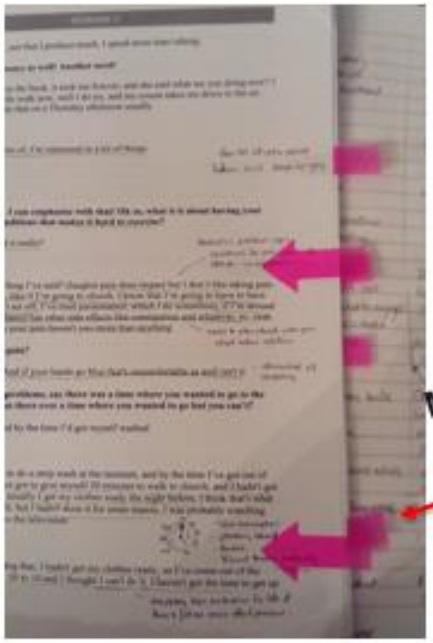


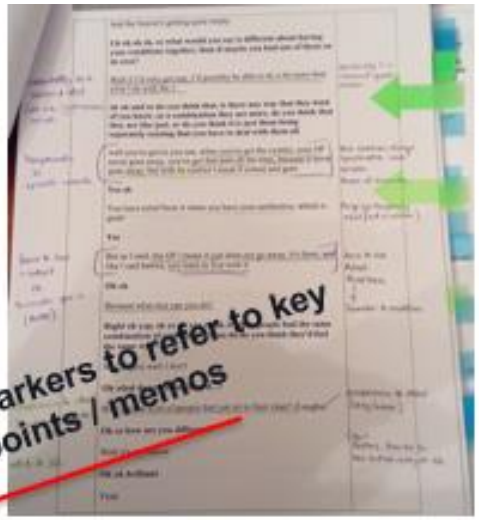

Daily life
PA
+ Specific PA
C, it's down
k home again
Fatigue stopping PA
the hip
Hip stopping Specific
PH movements
/activities

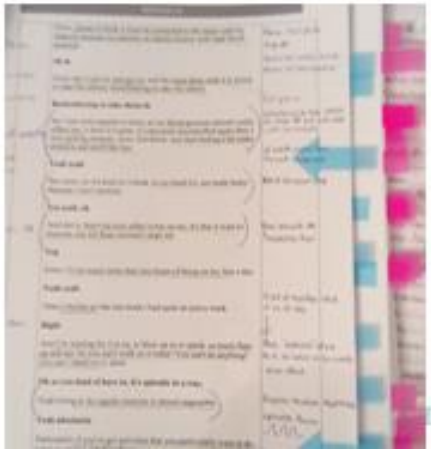

as I've been able to do less, it
less activity
- feeling worse
dy tone, has definitely
sture, I've got more
ng and I'm sure that's
an't eight bare and
r me, affects what
emm, walking
Butterfly affecting all

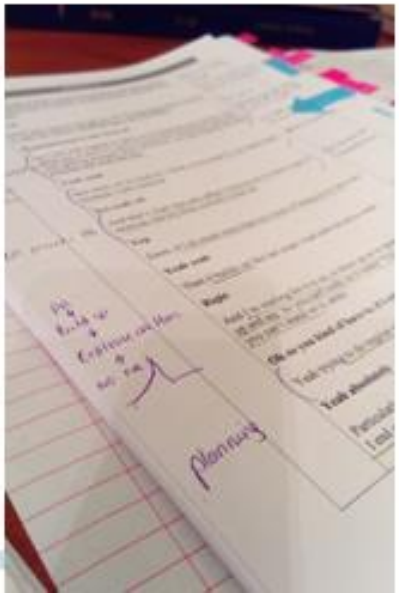

Beneficial
Another acute condition
can put the brakes on
entirely.
Someone who considers
what point of activity you
are at, where you have
been, where you're going


Gym based activity is not his
('lifestyle')
will power
The psychological challenge
is living as well - adds to
fatigue.
Double aspect:

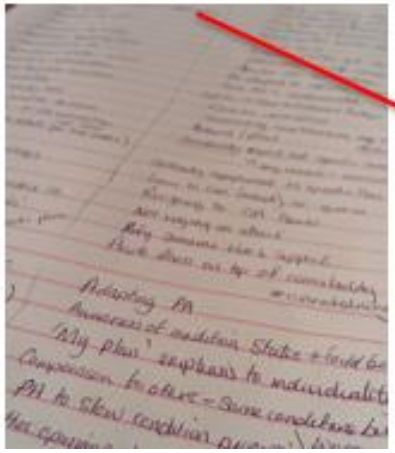


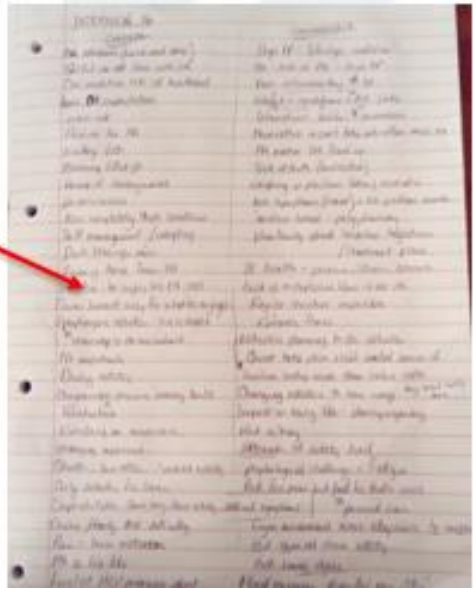






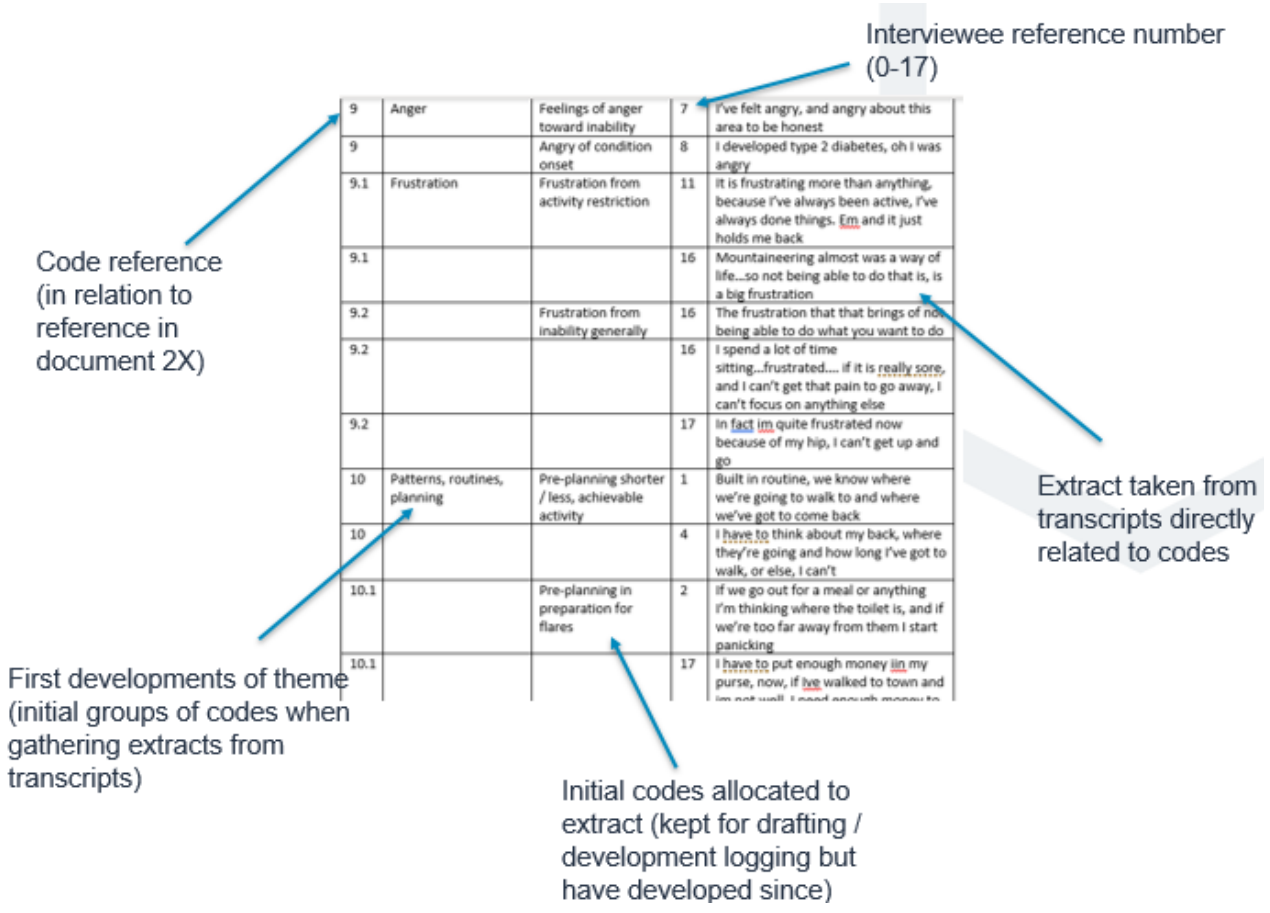
Codes and memos noted down from each separate account



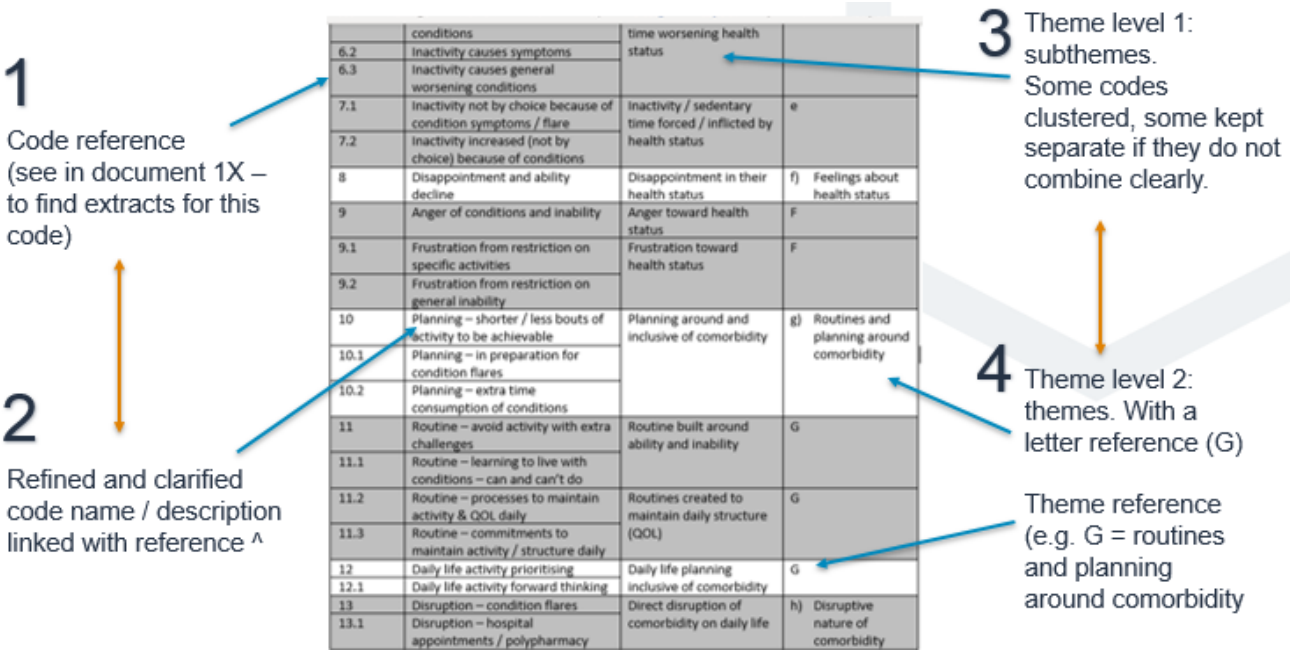


Initial coding, note taking examples

Interview	*Extract*	*Coding*
15	*They affect you, make you down, they make you depressed, if you let it*	Comorbidity and ill mental health
15	*Then I open then I do them blinds, so that's my little routine, to get me going*	Enforcing routines, positive habits to get through
15	*It's gentle exercise, which is, with, OP I think you need*	Specific comorbidities require specific PA / limit PA abilities
15	*Well if I'd only got one, I'd possibly be able to do a bit more than what I do with the 2*	Accumulative comorbidity affect
15	*Your OP never goes away, you've got that pain all the time, because it never goes away, but with the cystitis I mean it comes and goes*	Symptomatic vs episodic comorbidities
15	*It just does not go away…you learn to live with it*	Learn to live, adapt or surrender to conditions
15	*Last year I got a real bad dose of the flu…and I just didn't want to get up*	Acute illness on top of comorbidity, OA, overwhelming
16	*With taking anti-inflammatory drugs…that can have a long term effect on your blood pressure*	Needs pain relief to do PA, pain relief increases BP
16	*I get problems with acid reflux…I can't take AI medication anymore*	Side effects from OA management



9	Anger	Feelings of anger toward inability	7	I've felt angry, and angry about this area to be honest
9		Angry of condition onset	8	I developed type 2 diabetes, oh I was angry
9.1	Frustration	Frustration from activity restriction	11	It is frustrating more than anything, because I've always been active, I've always done things. Em and it just holds me back
9.1			16	Mountaineering almost was a way of life...so not being able to do that is, is a big frustration
9.2		Frustration from inability generally	16	The frustration that that brings of not being able to do what you want to do
9.2			16	I spend a lot of time sitting...frustrated.... if it is really sore, and I can't get that pain to go away, I can't focus on anything else
9.2			17	In fact im quite frustrated now because of my hip, I can't get up and go
10	Patterns, routines, planning	Pre-planning shorter / less, achievable activity	1	Built in routine, we know where we're going to walk to and where we've got to come back
10			4	I have to think about my back, where they're going and how long I've got to walk, or else, I can't
10.1		Pre-planning in preparation for flares	2	If we go out for a meal or anything I'm thinking where the toilet is, and if we're too far away from them I start panicking
10.1			17	I have to put enough money iin my purse, now, if Ive walked to town and



	conditions	time worsening health status	
6.2	Inactivity causes symptoms		
6.3	Inactivity causes general worsening conditions		
7.1	Inactivity not by choice because of condition symptoms / flare	Inactivity / sedentary time forced / inflicted by health status	e
7.2	Inactivity increased (not by choice) because of conditions		
8	Disappointment and ability decline	Disappointment in their health status	f) Feelings about health status
9	Anger of conditions and inability	Anger toward health status	F
9.1	Frustration from restriction on specific activities	Frustration toward health status	F
9.2	Frustration from restriction on general inability		
10	Planning – shorter / less bouts of activity to be achievable	Planning around and inclusive of comorbidity	g) Routines and planning around comorbidity
10.1	Planning – in preparation for condition flares		
10.2	Planning – extra time consumption of conditions		
11	Routine – avoid activity with extra challenges	Routine built around ability and inability	G
11.1	Routine – learning to live with conditions – can and can't do		
11.2	Routine – processes to maintain activity & QOL daily	Routines created to maintain daily structure (QOL)	G
11.3	Routine – commitments to maintain activity / structure daily		
12	Daily life activity prioritising	Daily life planning inclusive of comorbidity	G
12.1	Daily life activity forward thinking		
13	Disruption – condition flares	Direct disruption of comorbidity on daily life	h) Disruptive nature of comorbidity
13.1	Disruption – hospital appointments / polypharmacy		

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9	Anger	Feelings of anger toward inability	7	I've felt angry, and angry about this area to be honest
9		Angry of condition onset	8	I developed type 2 diabetes, oh I was angry
9.1	Frustration	Frustration from activity restriction	11	It is frustrating more than anything, because I've always been active, I've always done things. Em and it just holds me back
9.1			16	Mountaineering almost was a way of life...so not being able to do that is, is a big frustration
9.2		Frustration from inability generally	16	The frustration that that brings of not being able to do what you want to do
9.2			16	I spend a lot of time sitting...frustrated.... if it is really sore, and I can't get that pain to go away, I can't focus on anything else
9.2			17	In fact im quite frustrated now because of my hip, I can't get up and

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9	Anger of conditions and inability	Anger toward health status	F
9.1	Frustration from restriction on specific activities	Frustration toward health status	F
9.2	Frustration from restriction on general inability		

Extract from interview
Reviewed & refined code for extract
Code reference
Subtheme
Theme (theme reference)

Example: Code book (example not exhaustive code list)

Ref	Code	Description	Does / doesn't include -extra	Example excerpt
2	Medication role and complexity in comorbidity	Contradictions, side effects, role, preferences, dependence	Reliance as well as problems (contradicting relationship)	*'don't take this with grapefruit juice' it counteracts your heart tablet* *I have cocodamol...i have two before I start the day you know*
4	Feelings /beliefs about their health status	Stoicism toward comorbidity, disappointment, anger, frustration, acceptance, rejection, avoiding stigma	As well as comorbidity feelings, this includes feelings about weight and age	*I have got it like…you know, it's just another one of those things you've gotta get on with I suppose* *People don't see me as a disabled person…and saying that in itself is quite a big thing…because I don't you know, but I am*
7	Planning life around comorbidity	~~Shorter bouts of activity~~, planning achievable activity, preparing for flares, extra time	Doesn't include PA mode of intermittent activity.	*Built in routine, we know where we're going to walk to and where we've got to come back* *I have to put enough money in my purse, now, if Ive walked to town and im not well, I need enough money to get a taxi to bring me back home again*
9	Routines to maintain QOL inclusive of comorbidity	Daily processes, commitments to give day structure		*I have patterns…Sunday walk, Mondays yoga, Tuesday the friendship group…things that I enjoy. And social elements*
10	Disruption to general life with having comorbidity	Condition flares, healthcare, effort, restrictions, halts, acute illness overwhelming	Also unpredictability and flares of one condition, sleep/ life disruption	*If you've got appointments or anything, then I work around them, I work around the appointments, the doctors. Doctors and hospital. Then I have a rest between them.* *It stops me doing what I want to do…even like, just walking*
11	Prioritising conditions	Threat, life impact, fluctuating, shifting, controlled vs not controlled, not prioritising	Includes fluctuating / changing priorities	*My cancer returning, that's a condition…that sort of up there on the top of the list, m other is my AF, if I can keep that under control*
14	Single condition focus problem	Cannot do prescribed PA for one condition because of another. Discordance, multiple practitioner communication problems	Single disease focus overrides other codes (e.g. practitioner single condition focus here rather than 15 / 18).	*I've been shown one lot of exercises and that was for me knees. But what she was expecting me to do, I couldn't do because of the pain in me back.*
20	Intermittent PA mode	Rests / recharge, forced rest, small and often, or not sitting long, intermittent sitting		*I can walk so far…you can have a good walk and a little sit down in between and I'm raring to go again*
22	Activity modes for someone with comorbidity	Functional activity, keep moving, PA definition to them	Focus on functional ability, general movement	*Keep yourself moving, em, and just keeping your body mobile, as much as possible* *The other PA that no one ever thinks about is driving a car…because you're using your legs all the time*

25	Self confidence in person with conditions and PA	In their knowledge, ability, lack of confidence, lack of connection with body	Confidence and lack of confidence And body-mind separation	*Its very inhibiting if you're at all self-conscious…you've got to overcome that to begin with to, to gain that confidence…and not to be aware of other people*
				With having done it for so long, em, I know really what, what I'm capable of and you know, it, confident in doing it
26	PA support	Buddy, PT, social, family	Fundamental PA support	*Having other people…you encourage one another, you can lift your knee a bit higher you know? You can encourage one another*
27	Endorsement of PA as a treatment option	From HCP, PT, socially, having references	Are they being advised to use PA as a treatment	*I've never seen anybody with a condition, come out of it any better, with any activities or special classes…I've never known anybody to benefit in any real terms*
28	Meaningful PA instruction	PA explained, meaning, personal, self-manage	A method of intervening, not just instructing, having negotiations, conversations, mutual	*Knowing what exercise would benefit me the best and having it, it comes down to physiotherapy*
				Teaching people short routines they can do at home, having regular checks with them through the internet
30	Group facilitation	Social, like-conditioned people together, like aged, gender		*The opportunity to exercise with people with the same complaint*
				Have a specific group of people with the same conditional and older people as well really
31	Negative PA experiences / thoughts	PA image, unrealistic, advertisement, weight / body image focus, negative impact on them / conditions	Connotations with PA, bad previous PA history, PA stigmas	*You can really put people off exercise if you tell them they have to lose weight first*
				I suppose you could go to these classes where you sit around in a circle and you go waaay ehh ohh! (swings arms)… i'm not going to get to that stage.
33	Tailored / adjusted PA to suit them	To age, gender, level, abilities	The ways PA has been or could be adapted to be inclusive	*Its mixed ages and mixed abilities…she's aware that people have different strengths, weaknesses..*
				If you can't move a lot then chair based activity
34	Environment effects on their PA participation	Gym environment, weather	Access to equipment, adaptable, weather bad, barrier	*I should start doing the gym because it's maybe more controllable, I can stop, get in the car and go home*
				Weather, sometimes. So I mean, that determines how long a walk I do
36	Condition uncertainty	Prognosis unknown, unsure of medications, unsure of symptoms, lack of knowledge about conditions	This is an initial barrier before patients can even consider PA.	*I can't tell much about, honest and truthful, and I don't know that much about it*
				I'm waiting for a knee replacement so if I have that done and get back to doing some exercise, riding a bike and things like that, whether I can get to the point where m blood pressure's under control without medication I don't know
38	Fears and cautious behaviour in life and PA in those with comorbidity	Fears of conditions, pain	Also being self-protective from this fear: pain avoidance, careful, over cautious	*If I went on one of these physical things…it'd probably do more harm than good.*
				I probably don't push myself as much as I should…I won't do anything that gives me pain.

Example: Queries and investigation into the codes and data

Question 1: Are code 7 and 20 distinct from one another?

Points: instead of shorter bouts, the code could be; planning achievable activity within comorbidity constraints.

Decision: To keep 7 and 20 separate, but to remove the detail of 'shorter bouts' in code 7 and replace this with 'planning achievable activity'.

Official code name and number	Original code number	Original code name	Code extract
7 – Planning life around comorbidity (~~shorter bouts~~, planning achievable activity, preparing for flares, extra time)	10	~~Planning – shorter / less bouts of activity to be achievable (specifically planning it around conditions)~~ planning achievable activity within comorbidity constraints	*Built in routine, we know where we're going to walk to and where we've got to come back*
7	10		*I have to think about my back, where they're going and how long I've got to walk, or else, I can't*
7	10.1	Planning – in preparation for /	*If we go out for a meal or anything I'm thinking where the toilet is,*

Question 2: Do the codes accurately reflect the stories in the interviews? Example interview: 17.

Points: Participant 17 (Female, 77) had OA, Raynaud's, blood pressure, Thyroid and palpitation conditions. She prioritised conditions based on the impact they had on her life, but these priorities seemed to fluctuate as we progressed through the interview. There were four main topics that came across in her story which were; **1)** Contradictions between not only her medication (Raynaud's and blood pressure), but also prescribed treatment for one condition contradicted by another (hip stopped shoulder PA), **2)** the identification of solutions, but new different barriers in the way of these solutions (use of walking sticks → avoiding disability stigma; wanting to take action → waiting lists), **3)** The uncertainty she had around her conditions (how tired should she be? Where does she get information? Is it controlled? 'I don't know') **4)** There's 2 outcomes from her situation: where she is (lack of function, frustration, depressed feelings, 'time running out' and fears of unpredictability and falling) and where she wants to be (an instructor that understands conditions, more options rather than medication, understanding and control).

Decision: The extracts coded under the current headings do capture the concept of the interview. However, I think it will be important to go through a process when reporting the results to ensure that the stories from the interviews are demonstrated through the results, but that these stories are broader than just a single occurrence from one interview. I will work on how I can link and connect the problems risen from each interview to search for broader patterns and themes.

Code ref	Code description	Old code	Extract	Notes
2	Medication role and complexity in comorbidity	2	They were going to give me medication for my Raynaud's…that impacts on my life, because sometimes my fingers…are white, and numb and I have to kind of sit on them…but If I had medication for my Raynaud's, apparently it will impact on my	Medication contradiction between Raynauds and blood pressure

Matrix development

Draft one (left) and two (right) of matrix structure including themes and subthemes.

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Matrix structure draft 1.

	Theme	Subtheme
A	Hospitalisation / healthcare negative association and avoidance	• Hospitalisation avoidance • Avoiding healthcare – waiting until problem is insistent
B	Comorbidity and medication	• Medication intolerance, contradiction, complexity • Medication side-effect • Pain relief role
C	Comorbidity and mental health	• Negative mental health from conditions • Negative mentality / mental health status*
D	Attitude – PA, comorbidity, life	• Stoicism toward conditions / comorbidity • Strong willed attitude: pushing through, determined, adjusting, seeking solutions • Cautious, safe, avoiding risk • Negative mentality / mental health status* • Positive mentality
E	Sedentary time	• Inactivity / sedentary time worsening health status • Inactivity / sedentary time inflicted by health status • Sitting discomfort
F	Feelings about health status – comorbidity, abilities	• Disappointment in their health status • Anger toward health status • Frustration toward health status • Condition acceptance • Condition stigma rejection • Weight awareness*

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Matrix structure draft 2.

Theme ref	Theme name	Code ref	Codes included in theme
A	Candidacy and the CCM Chronic care M (health systems)	1	Hospital avoidance
		15	Healthcare professional (HCP) problems
		18	Healthcare structure problems
B	Unique nature of comorbidity Biographical descriptions and Complexity	2	Medication
		3	Mental health
		11	Prioritising conditions
		13	Condition combinations
		14	Single condition focus problem
C	Narrative and identity in OA and comorbidity Psychological burden	4	Feelings /beliefs about their health status
		16	Social comparison
		19	Loneliness
D	PA and self	21	Attitude / readiness toward PA
		23	Comparison to previous PA / abilities
		31	Negative PA experiences / thoughts
E	Activity status impact	5	Inactivity impact
		12	Aftermath of PA
F	Ownership of comorbidity (disruption, adapting and everyday life)	6	Inactivity forced
		7	Planning life around comorbidity
		8	Adjustments to life with comorbidity
		9	Routines to maintain QOL
		10	Disruption
G	PA characteristics / components	20	Intermittent PA
		22	Activity modes
		24	Goals and motivations to do PA
		29	Enjoyable PA
		32	Independence
		33	Tailored / adjusted PA
		34	Environment
H	Barriers and premature ageing	17	Exhaustion, fatigue /energy
		25	Confidence
		36	Condition uncertainty
		38	Fear
		35	OA impact
		37	Falls
I	Facilitators	26	PA support
		27	Endorsement of PA
		28	PA instruction
		30	Group facilitation

Final matrix structure

Theme	Subthemes	Codes included
1. Barriers to PA	1. Lack of concept of "comorbidity" and LTC prioritisation	Healthcare professional (HCP) problems Healthcare structure problems Condition combinations Prioritising conditions Single condition focus problem
	2. Uncertainty about the management of health conditions and PA effectiveness	Medication Confidence Condition uncertainty Fear OA impact
	3. Negative perceptions concerning LTCs and ageing, and PA	Hospital avoidance Feelings /beliefs about their health status Attitude / readiness toward PA Comparison to previous PA / abilities Negative PA experiences / thoughts
	4. Multiple co-existing biopsychosocial barriers to PA	Mental health Inactivity impact Aftermath of PA Disruption Inactivity forced Exhaustion, fatigue /energy Falls
	5. Solutions to barriers and barriers to solutions	Triage of barrier – solution – barrier Common co-existing Participant diagrams – participant examples
2. Facilitators of PA	1. Social support through shared learning and homogeneity	Combatting loneliness Group facilitation Social comparison
	2. Healthcare professional support to facilitate self-management of PA	PA support Endorsement of PA PA instruction
	3. PA mode and type that is intermittent, adapted, and fits into daily life	Planning life around comorbidity Adjustments to life with comorbidity Routines to maintain QOL Intermittent PA Activity modes Goals and motivations to do PA Enjoyable PA Independence Tailored / adjusted PA Environment

Example matrix theme: Facilitators of PA

Subtheme references were gathered into final subthemes for inclusion in the qualitative study

Theme reference	Theme name	Subtheme reference	Subtheme name
2	Facilitators of PA	26	PA support
		27	Endorsement of PA
		28	PA instruction
		30	Group facilitation
		20	Intermittent PA
		22	Activity modes
		24	Goals and motivations to do PA
		29	Enjoyable PA
		32	Independence
		33	Tailored / adjusted PA
		34	Environment

Example codes included in matrix theme

Code references according to their original label in the coding process

OLD code reference	Code	NEW sub-theme reference
35	PA support – having a PA buddy	26
35.1	PA support - from instruction & review from PT	26
35.2	Social comparison PA support – motivation, encouragement	26
35.3	Community, family, group support	26
36	References for PA – seeing results / someone else experienced & endorsed	27
36.1	Opposite to 36 - No references / recommendations from peers for PA	27
38	PA not endorsed / encouraged / advertised / promoted	27
38.1	Expert opinion value on whether they promote PA or not	27
38.2	Not enough Instruction/ encouragement on PA from HCP	27
39	Teaching – Explained to give them understanding and meaning to PA	28
39.1	Teaching with a personal touch on how it directly helps them specifically – personalised (conditions, age, ability, level)	28
39.2	Taught to self-manage, do it themselves, despite conditions	28
39.3	Their specific information needs	28
39.4	Their specific instruction needs	28
52.1	HCP positive – i**ntervene**s, not just instructs & negotiation PA specific	28
41.4	Social, group facilitation	30
50	Like-conditioned individuals together	30
50.1	Like in other ways – age, gender, level	30
28	Intermittent PA – active until needing rest / recharge during activity	20
28.1	Intermittent – condition symptoms during activity forces them to rest	20

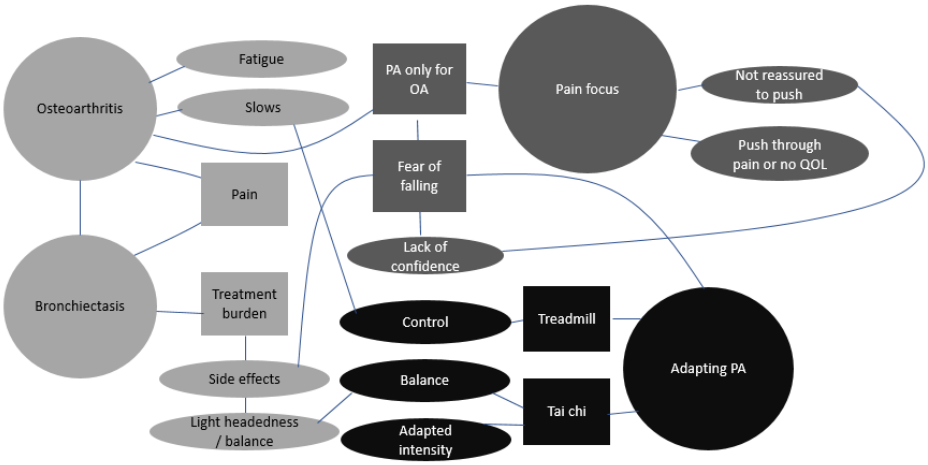
Example matrix data (original code reference) and participant reference number

Colours represent participant excerpts included in draft one of qualitative results

Old code	Participant reference	Extract
35	1	If someone was knocking on the door every week saying 'common ***, we're off swimming!' I'd go…need that, somebody saying to them come on
35.1	3	Come back and see me in 6 months (PT)
35.2	3	Having other people…you encourage one another, you can lift your knee a bit higher you know? You can encourage one another
35	4	I wouldn't like to go on my own, and ive lost all my confidence to go
35	4	I haven't got the confidence to go on my own…if somebody's with me, I'd have a go at anything really
35	11	Friends, they say, come on don't be miserable, let's go
35.3	9	I go out with my daughter and son in law, they know my limits and we have a good walk
35.3	8	As a community as a whole, if you tell us we need to lose weight or get fit to look better we do not respond, but everybody I know in this community who has been told they need to tackle their health for numerous reasons, has done so.
35.3	8	Absolutely bloody awesome husband…he's very supportive about what I can and can't do
35.3	8	I'm also lucky that in my social community is disproportionately oriented to people with chronic illnesses and disability
35	10	Oh yes, when I'm walking 'straighten your back!' 'straighten your back you look like an old lady!' (laughs)
35	10	I'm only interested in my friend you know, so I don't sort of get, I go to 2 classes, you know that classes and all that
35.1	12	There would be someone there from the NHS…just to make sure you're alright
35.3	12	Well certainly my son will nag me if I don't go!...when you say about keeping myself fit, it's for them
35	12	Someone to go with them to go…a friend to come with me, you always go more if somebody's joining you than if you're going on your own. It takes quite a bit of courage to join something
35.3	14	Its mainly my family…they tend to do the things that I can't
35.3	16	A lot of close friends understand, if I say I've got to sit…they understand
35.3	16	Me wanting to do it I think is the main thing and having friends that are willing to…go for a walk for only 3 hours rather than all day
35.3	17	My cousin, comes and picks me up and takes me, and I want to spend time with her as well
35.3	17	The church supports with the keep fit thing for sure
35.3	17	You can learn so much…from other people…its meeting them, and speaking with them
35.3	8	Those groups are very good on low impact exercise with suggestions of different types of exercise and ways to stay moving and ways to motivate yourself
36.1	15	Most of my friends don't exercise
36.1	1	I've never seen anybody with a condition, come out of it any better, with any activities or special classes…I've never known anybody to benefit in any real terms
36	3	The reference of somebody who had tried it

Appendix 26. Example diagrams of analysis

12 *'She just says if it hurts, stop. And I just thought well in that case I'm not doing anything'* *'If I can't have a quality of life, I no longer want to live'*

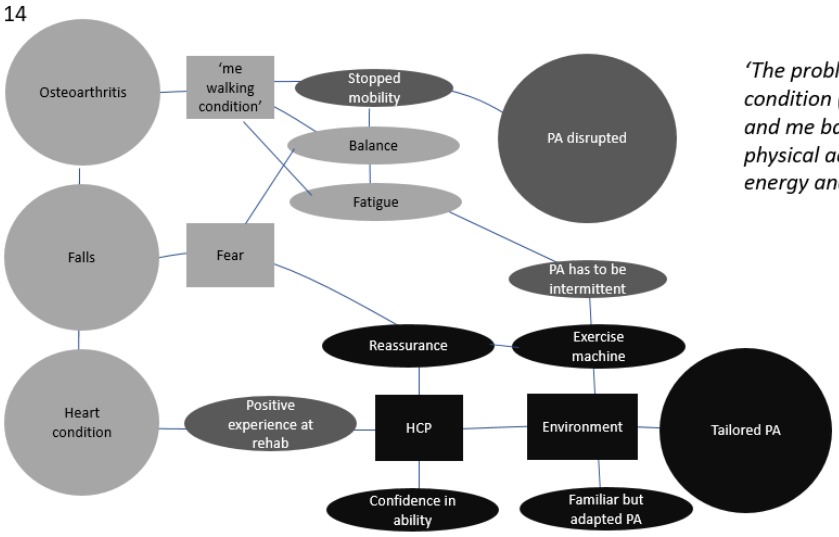


'There is a tai chi class locally, but I can't do tai chi as it is, real tai chi, the one that I went to, she adapted…and it makes a big difference'

'The treadmill that's it, where you can hold on, because it makes a big difference…when you are outside like me, you have to watch where you're walking'

Figure: A26.1 Participant 12 map

14



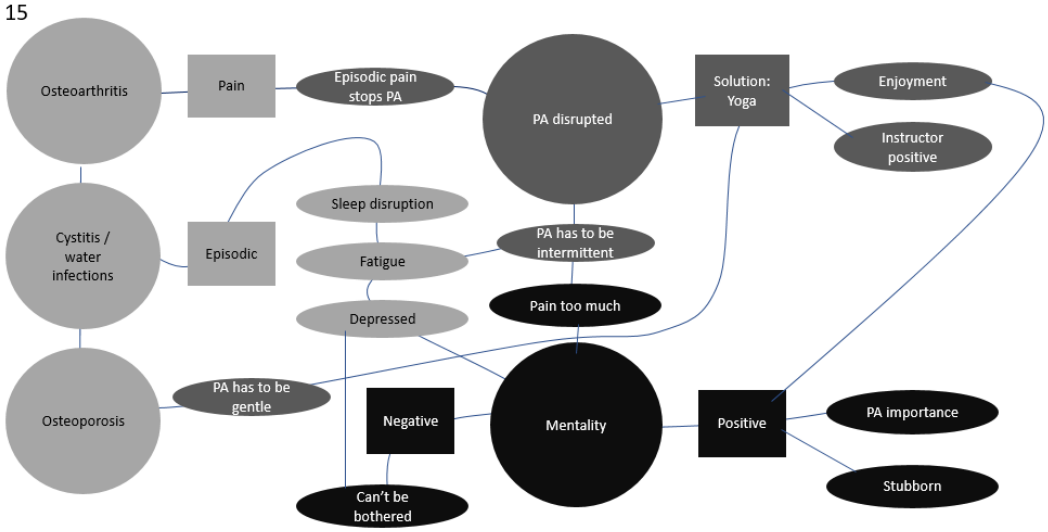
'The problem with umm, me walking condition (OA), is what bothers me mostly and me balance….it impacts a lot on me physical activities, because I haven't got the energy and I can't do things'

'Well the heart condition I could, I could just cope with that alright it didn't, didn't seem to bother me but the walking is, very detrimental to me'

'My balance mainly, stops me doing things, which I am frightened, I'm very frightened of falling over again you know'

Figure: A26.2 Participant 14 map

15



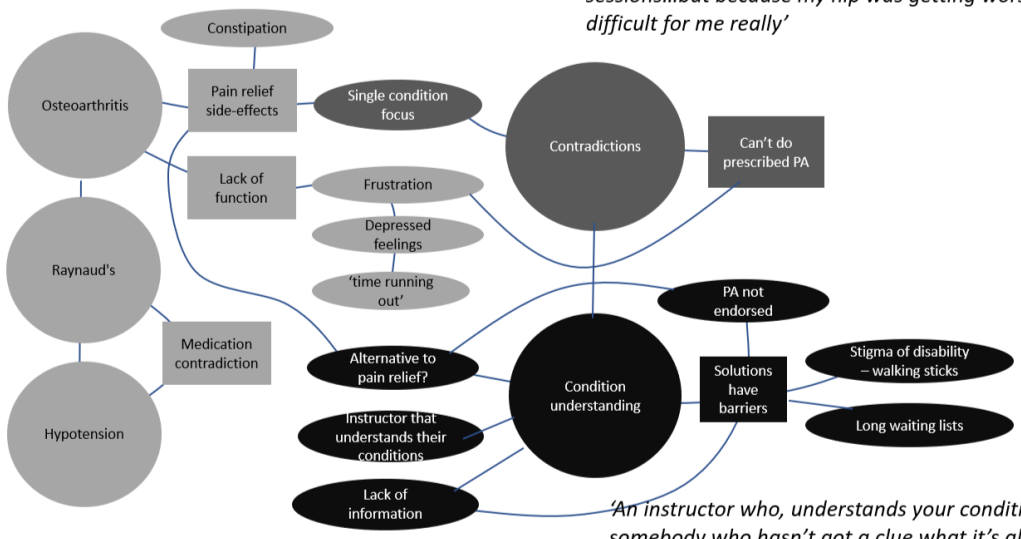
'When I have the cystitis bad that really does, when I'm up, at least about 6 times in the night going to the loo…the next day I am, you know, I feel really tired'

'I keep having the infections…because they affect you, make you down, they make you depressed, if you let it'

Figure: A26.3 Participant 15 map

17 *'Cocodamol has other side effects like constipation and whatever so, yeah you've got to deal with your pain'*

'I did go to the hospital for a little while, but that was just to do exercise because I had a frozen shoulder…it was just a few sessions…but because my hip was getting worse, it was too difficult for me really'



'I don't want to be seen as some poor old weak old thing that needs sticks to get down from A to B'

'An instructor who, understands your condition…better than somebody who hasn't got a clue what it's all about…so they would know your limitations…to devise a programme around, various conditions that existed within the group'

Figure: A26.4 Participant 17 map