EXPLORING STRENGTH EXERCISE PRESCRIPTION AND ITS DOSE IN RHEUMATOID ARTHRITIS

A thesis submitted for the degree of Doctor of Philosophy

By

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DEDICATION.

For my wife and son, Sue, and Joe Boniface.

TABLE OF CONTENTS.

ABSTRACT.

Rheumatoid arthritis (RA) is a significant global burden. It causes pain and disability and has significant socio-economic implications. Non-pharmacological interventions are commonly prescribed to mitigate the impact of the disease. Strengthening exercise, supported by evidence from randomised controlled trials (RCTs), has gained wider acceptance. The National Institute for Health and Care Excellence (NICE) recommends strengthening exercise for managing the functional impairments associated with the disease. Whilst modest benefits have been demonstrated, uncertainties persist regarding the optimal dosage. This thesis endeavours to enhance our understanding of the prescription of strengthening exercise and its dose in RA through three original interrelated studies.

Study one systematically reviewed contemporary RCTs where strengthening exercise was a main component of the intervention being evaluated. How dose of strengthening exercise was determined for the trial intervention was investigated. The majority of included RCTs did not: (1) Report piloting the intervention and its dose prior to conducting the RCT and (2) Cite any evidence underpinning the dose of strengthening exercise prescribed for participants taking part in the trial. Moreover, when evidence was cited, it varied in quality. Often the dose used or recommended in the underpinning evidence was inconsistently applied in the intervention being evaluated by the RCT. Frequently, the underpinning evidence was not directly applicable to individuals living with RA. The findings of this review cast doubt on whether dose of strengthening exercise is optimised for individuals with RA in RCTS.

Study two investigated the dose in hand strengthening exercise prescribed and completed during the **S**trengthening **A**nd Stretching For **R**heumatoid **A**rthritis of the **H**and **(SARAH)** multicentre RCT. The study utilised the area under the curve (AUC) method to quantify the overall dosage of hand strengthening exercise prescribed across the five face-to-face exercise sessions. General estimating equation (GEE) multiple regression analysis was then employed to determine: (1) The relationship between prescribed overall dose and key outcomes (overall hand function and grip strength) and (2) What factors were associated with the overall dose prescribed. Results indicated that participants who were prescribed a higher overall dose of hand strengthening exercise exhibited better overall hand function and grip strength. Factors that influenced overall dose prescribed included the professional background of the therapist (i.e. occupational therapist or physiotherapist) and baseline participant characteristics including metacarpophalangeal joint deformity, number of swollen wrist/hand joints, grip strength, participant mood, and confidence to exercise without fear of making symptoms worse.

Study three employed judgement analysis (JA) to evaluate how occupational therapists and physiotherapists (therapists) judge what intensity (a key dose parameter) of hand strengthening exercise to prescribe an individual with pain and dysfunction of the hand associated with RA. A modified Delphi process involving therapists experienced in managing hand impairments associated with RA was used to prioritise the key clinical cues included in the case scenarios. Therapists based in the United Kingdom (UK) were then invited to assess a set of sixty-nine case scenarios (54 + 15 repeats) via an online platform. Their judgements on prescribed intensity of hand strengthening exercise were explored using multiple regression analysis. Results indicated all therapists reduced the intensity of the exercise as the severity of the clinical cue increased. The cues that influenced therapists the most included: (1) Patient's pain performing the exercise, (2) Disease activity and (3) Average pain over the preceding week, (4) Hand range of movement, (5) Ulnar drift and (6) Patient grip strength. Sub-analysis employing the Cochran-Weiss-Shanteau (CWS) index of expertise identified therapists who were more consistent in their prescribing judgements relied on fewer clinical cues (1-3), implying a form of pattern recognition may be associated with their prescribing judgements.

In summary, dose is a crucial aspect of therapeutic exercise prescription. These studies provide new insights into prescribing and dosing of strengthening exercises for RA in both clinical trials and practice. Based on these findings, this thesis proposes several future research directions. First, the issues identified in study one may not be limited to strengthening exercises and RA. Investigating whether similar issues exist in RCTs evaluating other therapeutic exercise-based interventions used to manage other musculoskeletal disorders is urgently needed to understand whether dose is sufficiently optimised in rehabilitation research more broadly. Second, to actualise the full potential of therapeutic exercise-based interventions, alternative methods for optimising dose warrant investigation. Dose escalation methodology may offer healthcare researchers a viable alternative to employing past research, which for strengthening exercise in RA, is often low quality and not applicable to the clinical population of interest. Third, further exploration around how healthcare professionals optimise dose of exercise-based interventions at the point of contact is essential for optimising exercise prescription in clinical practice.

DECLARATION.

This is to certify that this thesis comprises only my original work towards the Doctor of Philosophy. Due acknowledgement has been made in the text to all other material used.

Name: Graham Boniface

Signed: G. Boniface

Date: 30/06/2024

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LIST OF PUBLICATIONS ASSOCIATED WITH THIS THESIS.

Study 1:

Boniface, G., Gandhi, V., Norris, M., Williamson, E., Kirtley, S., & O'Connell, N.E. (2020). A systematic review exploring the evidence reported to underpin exercise dose in clinical trials of rheumatoid arthritis. *Rheumatology*, *59*(11), 3147-3157. https://doi.org/10.1093/rheumatology/keaa150

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Study 2:

Boniface, G., Sanchez-Santos., M.T., Norris., M., O'Connell., N.E, Williamson., E., & Lamb, S. E. (2022). Understanding prescribed dose in hand strengthening exercise for rheumatoid arthritis: A secondary analysis of the SARAH trial. *Musculoskeletal Care*, 20(4), 899–907. https://doi.org/10.1002/msc.1646

Study 3:

Boniface, G., White, N., Tomlinson, C., Norris, M., O'Connell, N.E., Williamson, E., & Harries, P. (2023). Prescribing hand strengthening exercise for patients with rheumatoid arthritis; clinical cues influencing occupational therapists' and physiotherapists' judgements. *Musculoskeletal Care*, 22(1), e1849. https://doi.org/10.1002/msc.1849

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Study 1:

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Study 1:

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Boniface, G., Norris, M., Williamson, E., Gandhi, V., Kirtley, S., & O'Connell, N.E. What evidence is used by researchers to underpin the prescribed dose of strengthening exercise in randomised controlled trials of rheumatoid arthritis? A systematic review. *College of Health and Life Sciences Conference,* Brunel University, London. December 2019.

Boniface, G., Norris, M., Williamson, E., Gandhi, V., Kirtley, S., & O'Connell, N.E. What evidence is used by researchers to underpin the prescribed dose of strengthening exercise in randomised controlled trials of rheumatoid arthritis? A systematic review protocol. *Council for Allied Health Professionals Research (CAHPR) Meeting, Oxford,* Oxford Brookes University, Oxford. March 2018.

Study 2:

Boniface, G., Sanchez-Santos, M. T., Norris, M., O'Connell, N.E., Williamson, E., & Lamb, S. E. (2022). Understanding prescribed dose in hand strengthening exercise for rheumatoid arthritis: A secondary analysis of the SARAH trial. NHS Scotland Allied Health Professionals Research Event, Virtual poster format. November 2022.

LIST OF FIGURES.

LIST OF TABLES.

LIST OF ABBREVIATIONS.

ACPA	Anti-Citrullinated Peptide Antibody
ACSM	American College of Sports Medicine
ACR	American College of Rheumatology
BAHT	British Association of Hand Therapists
cDMARD	Conventional Disease-Modifying Anti-Rheumatic Drugs
CERT	Consensus on Exercise Reporting Template
CI	Confidence Interval
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CONSORT	Consolidated Standards of Reporting Trials
CRP	C-Reactive Protein
CWS	Cochran-Weiss-Shanteau
DAS28	Disease Activity Score in 28 Joints
EMBASE	Excerpta Medica Database
ESR	Erythrocyte Sedimentation Rate
EULAR	European League Against Rheumatism
GEE	Generalised Estimating Equations
HCP	Healthcare Professional
HCPC	Health and Care Professions Council
ICC	Intraclass Correlation Coefficient
IQR	Interquartile Range
MeSH	Medical Subject Headings
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NRS	Numerical Rating Scale
OMNI-RES	OMNI Perceived Exertion Scale for Resistance Exercise
PEDro	Physiotherapy Evidence Database
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyses
RA	Rheumatoid Arthritis
RF	Rheumatoid Factor
RCT	Randomised Controlled Trial
RoB	Risk of Bias
RPE	Rating of Perceived Exertion
RPS	Royal Pharmaceutical Society

SARAH	Strengthening And stretching for Rheumatoid Arthritis of the Hand
SD	Standard Deviation
SDM	Shared Decision Making
SMD	Standardised Mean Difference
STROBE	STrengthening the Reporting of OBservational studies in Epidemiology
TIDieR	Template for Intervention Description and Replication
UK	United Kingdom
VAS	Visual Analogue Scale
WHO	World Health Organisation

CHAPTER 1. INTRODUCTION AND THESIS OVERVIEW.

1.1. Introduction.

RA is a significant cause of pain and disability (Institute for Health Metrics and Evaluation, 2019b). The disease primarily affects an individual's synovial joints, especially the small joints of the hand (Aletaha and Smolen, 2018, Ledingham et al., 2017). Strengthening exercise is an important non-pharmacological intervention recommended for managing the physical impairments associated with the disease (National Institute for Health and Care Excellence, 2018). Whilst modest benefits for improving clinical outcomes have been demonstrated, uncertainties persist regarding the optimal dosage (Baillet et al., 2011, Osthoff et al., 2018b, Wen and Chai, 2021). In rehabilitation interventions proven to be effective, identifying what dose works best is a research priority amongst patients, carers, healthcare professionals (HCPs) and healthcare researchers (Brody, 2011, Chartered Society of Physiotherapy, 2018). To actualise the full potential of strength-based exercise interventions in RA, a thorough understanding about how dosage is both developed prior to evaluation by RCT and prescribed in clinical practice is needed. Insight into how healthcare researchers determine dose is essential to ascertain whether strength-based exercise interventions are appropriately dosed before they are assimilated by healthcare researchers in future clinical trials or implemented by HCPs in their clinical practice. Moreover, examining the prescription of strengthening exercise in clinical practice is valuable for understanding the factors that influence its prescription and consequently its effect on key clinical outcomes.

1.2. Thesis overview.

This thesis examines dose of strengthening exercise in RA through a series of three original research studies. Firstly, it explores the development of the dose of strengthening exercise before its evaluation by RCT. Secondly, using the data from the multicentre RCT that instigated the NICE recommending tailored hand strengthening and stretching exercises in RA, the factors associated with the prescribed dose and its correlation with key clinical outcomes are explored. Lastly, the thesis examines the prescribing judgments of occupational therapists and physiotherapists, HCPs who are commonly involved in managing individuals living with RA.

Knowledge gained from this thesis will produce a set of recommendations that may contribute to not only improving dosing of strength-based exercise interventions used in the management of RA, but more broadly for other exercise-based rehabilitation interventions and other musculoskeletal disorders. Furthermore, the results of this work provide greater understanding about the factors that influence its prescription. The thesis is structured in the following manner:

Chapter one presents an introduction to the topic area and an overview of the thesis.

Chapter two presents a narrative review of the literature relevant to the topic of this thesis. The chapter describes RA classification, symptomatology/clinical presentation, pathophysiology, diagnosis, prognosis, prevalence and incidence, the personal and socioeconomic impact of the disease, pharmacological and non-pharmacological management strategies for RA recommended by NICE. It then outlines the role that therapeutic exercise plays in RA management, defining both therapeutic exercise and its dose. Therapeutic strengthening exercise and its physiological effects are described before looking at how dose is determined in clinical trials and practice. Frameworks for prescribing interventions are then discussed. The chapter concludes with the aims and research questions of this thesis.

Chapter three describes the first research study in this thesis, a systematic review of contemporary RCTs in RA, where the main component of the intervention is strengthening exercise. The primary aims were to: (1) Determine what proportion of published RCTs evaluating strength-based exercise interventions in RA reported using phase I/II trials for setting dose parameters, (2) Determine what type and level of evidence is used to underpin dose parameters, (3) Explore the quality, consistency and applicability of the evidence used to underpin dose parameters and (4) Narratively explore if a relationship exists between risk of bias for RCTs evaluating strength-based interventions in RA and the level of evidence for underpinning dose parameters. This review represents the first time that the underpinnings of strength exercise dose used in RCTs of RA have been submitted to a rigorous systematic review.

Chapter four examines the data from the SARAH multicentre RCT, the results of which currently underpin the NICE recommendations for tailored strengthening and stretching hand exercise. Overall dose of hand strengthening exercise was calculated using AUC method. GEE multiple regression analysis was then used to determine (1) Therapist and participant characteristics associated with prescribed dose and (2) The impact that prescribed dose had on two key trial outcomes (hand function and grip strength).

Chapter five used JA to investigate how therapists judge what intensity of hand strengthening exercise to prescribe an individual with RA using hypothetical patient case scenarios. The best performing therapists were identified using the CWS index of expertise. Using multiple linear regression analysis,

therapists identified as the most consistent with their prescribing judgements were compared against the remaining (less consistent) therapists involved in the study.

Chapter six summarises the findings of the three studies included in this thesis, highlighting their novel contributions to research and clinical practice. It outlines the strengths and limitations of the research, provides recommendations for both HCPs and future research, and concludes with final remarks.

CHAPTER TWO. LITERATURE REVIEW.

2.1. Rheumatoid arthritis (RA).

RA is a musculoskeletal disorder that is associated with significant disability (Institute for Health Metrics and Evaluation, 2019b). Presently RA remains incurable (Gerlag et al., 2012). The optimal management of RA includes pharmacological, non-pharmacological and surgical interventions (Black et al., 2023, Ledingham et al., 2017, National Institute for Health and Care Excellence, 2018). The first part of this chapter describes RA classification, symptomatology/clinical presentation, pathophysiology, diagnosis, prognosis, prevalence and incidence, and the personal and socioeconomic impact of the disease. The second part of the chapter describes NICE recommendations for the management of RA, focusing on prescription of therapeutic exercise, in particular, strengthening exercise. The concept of dose is discussed, and a comparison made between how safe and effective dose is determined in pharmacological and non-pharmacological trials. The current practice of dose escalation methodology in therapeutic exercise-based trials is looked at, before looking at how HCPs combine the best available evidence with clinical expertise when considering dose. The chapter ends with general aims of the thesis and key research questions.

2.1.1. Definition and classification.

RA is defined as a systemic chronic auto-immune disease characterised by pain, swelling and disruption of the synovial joints and classified as an inflammatory arthropathy according the 11th revision of the international classification of diseases (Aletaha et al., 2010, Arnett et al., 1988, Black et al., 2023, Kay and Upchurch, 2012, Lindqvist et al., 2003, Lindqvist et al., 2002, Smolen et al., 2016, World Health Organization, 2019b). It's not uncommon for RA to be classified by duration of disease: 'recent-onset or early RA' (Disease duration of ≤2 years) and 'established disease' (Disease duration of >2 years) (Aletaha et al., 2002).

2.1.2. Symptomatology/clinical presentation.

Typically, individuals initially present with pain and swelling of the metacarpophalangeal, metatarsophalangeal, and proximal interphalangeal joints (Aletaha and Smolen, 2018, Ledingham et al., 2017). Symptoms are often symmetrical, meaning joints on both sides of the body are affected (Grassi et al., 1998). Prolonged stiffness in the joints, typically manifested as morning stiffness or after periods of inactivity is common (Aletaha et al., 2010). Pain, swelling and stiffness can limit individual joint range of movement (Kojima et al., 2018). Rheumatoid nodules, firm lumps under the skin near to joints are often present in 25% of individuals (Gordon et al., 1973, Sayah and English, 2005). Joint deformities like ulnar drift of the phalanges (e.g., fingers) at metacarpophalangeal joints (e.g.,

knuckles) can occur (Madenci and Gursoy, 2003), although progression has slowed with advances in pharmacological management of the disease. Other symptoms including fatigue and extra-articular manifestations of the disease including eye inflammation and cardiovascular issues are common consequences associated with chronic inflammation (Aletaha and Smolen, 2018). In addition to the above symptoms, changes in body composition have also been documented (Roubenoff, 2009, Roubenoff and Rall, 1993, Roubenoff et al., 1994). Rheumatoid cachexia (RC) where there is a loss of body cell mass, in particular skeletal muscle, is a common condition associated with RA. Despite improvement in the pharmacological management, RC persists even after joint inflammation improves (Roubenoff, 2009). Prevalence has been estimated between 15-32% depending on the criteria used to define it. It's characterised by low muscle mass and function (strength and performance) (Roubenoff et al., 1992, Santo et al., 2018, Summers et al., 2008). Increased levels of pro-inflammatory cytokines such as IL-1 beta and TNF-alpha are considered to be a key feature of RC (Roubenoff et al., 1994).

2.1.3. Pathophysiology.

The exact cause of RA is unknown, however why an individual develops RA probably involves a complex interplay of genetic, immunologic, and environmental factors (Aletaha and Smolen, 2018, Choy, 2012, Versus Arthritis, 2023). Genetic susceptibility has been identified, with certain human leukocyte antigen (HLA) alleles, such as HLA-DRB1*01 and HLA-DRB1*04 being most closely associated with RA (Aletaha and Smolen, 2018). The presence of HLA-DRB1 alleles is linked to the formation of autoantibodies and the start of an autoimmune response with the infiltration of immune cells, particularly T-cells and B-cells, into the synovial membrane that lines the joints. Activated T-cells release pro-inflammatory cytokines, such as tumour necrosis factor-alpha (TNF-α), interleukin-1 (IL-1), and interleukin-6 (IL-6). These cytokines contribute to the chronic inflammatory process. Autoantibodies play a crucial role in the pathogenesis of RA. The presence of rheumatoid factor (RF) and anti-citrullinated protein antibody (ACPA) tested as anti-cyclic citrullinated peptide, are commonly found in individuals with RA. These autoantibodies form immune complexes that contribute to inflammation and overall joint damage (Aletaha et al., 2010). Environmental triggers have also been linked to the development of RA, these include smoking, infection (e.g., periodontitis, viral etc.) and characteristics of the microbiome, the collection of microorganisms found in the gut, mouth, and lungs. All may play a role in the pathogenesis of the disease (Aletaha and Smolen, 2018, Versus Arthritis, 2023).

2.1.4. Diagnosis.

RA can be difficult to diagnose (Kay and Upchurch, 2012). The initial signs and symptoms of early RA do not substantially differ from other inflammatory arthritis (Heidari, 2011). HCPs responsible for the management of individuals with suspected RA typically make a diagnosis based on clinical signs and symptoms identified during the healthcare consultation that are supported with laboratory-based testing (e.g., blood test). Over the past forty years, two key classification criteria have been used by HCPs to help diagnose individuals with RA. The American College of Rheumatology (ACR) outlined specific criteria for diagnosing RA in 1987 (Arnett et al., 1988). For a diagnosis to be made the individual must have at least four out of the seven criteria present (Table 2.1). The top-four criterion needing to have been present for at least 6-weeks.

Table 2. 1. 1987 ACR classification criteria.

Number	Criterion
1	Morning stiffness in and around joints lasting at least 1 hour before maximal improvement
2	Soft tissue swelling of three or more joint areas observed by a physician
3	Swelling of the proximal interphalangeal, metacarpophalangeal, or wrist joints
4	Symmetric swelling
5	Rheumatoid nodules as observed by a physician
6	The presence of RF
7	Radiographic erosions and/or periarticular osteopenia in hand and/or wrist joints

The 1987 ACR classification criteria was based on comparing 262 individuals with established RA to their control (e.g., other individuals presenting with joint pain associated with diseases like gout, osteoarthritis, polymyalgia rheumatica etc.). The overarching purpose of this approach was to try and distinguish RA from other forms of arthritis (Scott et al., 2010). However, a key shortcoming of the criteria is it fails to adequately identify individuals with 'early RA'. For example, using x-ray to identify joint erosion in the early stages of the disease is not clinically useful as joint erosion is rarely present until the disease has become established. Scientific advances in understanding the disease meant the ACR 1987 was developed before the diagnostic and prognostic importance of ACPA was fully understood (Scott et al., 2010). Therefore, in an effort to improve earlier detection of the disease, an alternative criteria (Table 2.2) covering four domains was developed between the ACR and the European League Against Rheumatism (EULAR) (Kay and Upchurch, 2012, Scott et al., 2010). For an individual to be diagnosed with RA, opposed to having four out of seven criteria, a score of ≥ 6 is required to make a diagnosis of RA. The 2010 ACR/EULAR classification criteria has shown good diagnostic properties in detecting early arthritis amongst individuals presenting with inflammatory arthritis signs and symptoms (Alves et al., 2011).

Table 2. 2. 2010 ACR/EULAR classification criteria.

Domain	Criterion
A	**Joint involvement** [a] *1 large joint (0 points)* *2-10 large joints (1 point)* *1-3 small joints (large joints not counted) (2 points)* *4-10 small joints (large joints not counted) (3 points)* *>10 joints including at least one small joint (5 points)*
B	**Serology (at least one test needed for classification)** *Negative RF and negative ACPA (0 points)* *Low positive RF or low positive ACPA (2 points)* *High positive RF or high positive ACPA (3 points)*
C	**Acute-phase reactants** *Normal C-Reactive Protein (CRP) or Erythrocyte Sedimentation Rate (ESR) (0 points)* *Abnormal CRP or ESR (1 point)*
D	**Duration of symptoms** *<6 weeks (0 points)* *≥6 weeks (1 point)*

[a] Large joints refer to shoulders, elbows, hips, knees, and ankles. Small joints refer to wrists, thumb interphalangeal joints, metacarpophalangeal joints, proximal interphalangeal joints, second through fifth metatarsophalangeal joints.

2.1.5. Prevalence and incidence.

It's estimated (in 2020) that 17.6 million (95% uncertainty interval 15.8 - 20.3) individuals of all ages are living with RA worldwide. This represents an increase of 121% (117 - 125%) since 1990 (Black et al., 2023). It's forecast that 31·7 million (25·8-39·0) individuals will be living with RA worldwide by 2050 (GBD 2021, 2021). Across all ages (in 2020), RA is more common in females, with a global age-standardised prevalence rate of 293·5 (95% uncertainty interval 262·7 - 336·3) per 100,000 population compared to 119·8 (106·3 - 140·0) per 100,000 for males (Black et al., 2023). Global prevalence, disability-adjusted life-years (DALY), and years lived with disability (YLD) rates of rheumatoid arthritis in 2020 by sex and age are reported in figure 2.1 (Black et al., 2023). Across all metrics females are negatively impacted to a greater extent than males. In keeping with global trends, in the UK, the estimated prevalence of RA is greater in females (1.14%) than in males (0.44%) (Symmons et al., 2002). Evidence supports genetic and sexual chromosomes playing a role in determining the female prevalence (Gerosa et al., 2008). The incidence of RA in the UK is low. Approximately 15-25 men and 36-54 women develop RA per 100,000 individuals per year in the UK. Based on the UK population at mid-2022 being 67.6 million (34,492,000 women and 33,105,000 men), this would approximately equate to 4,964-8,275 men and 12,384-18,576 women being newly diagnosed each year (Office for National Statistics, 2024). Incidence peaks for both genders in the 70's, but with a long tail (large

confidence interval) on either side, RA can develop across all ages (Humphreys et al., 2013, Symmons et al., 1994).

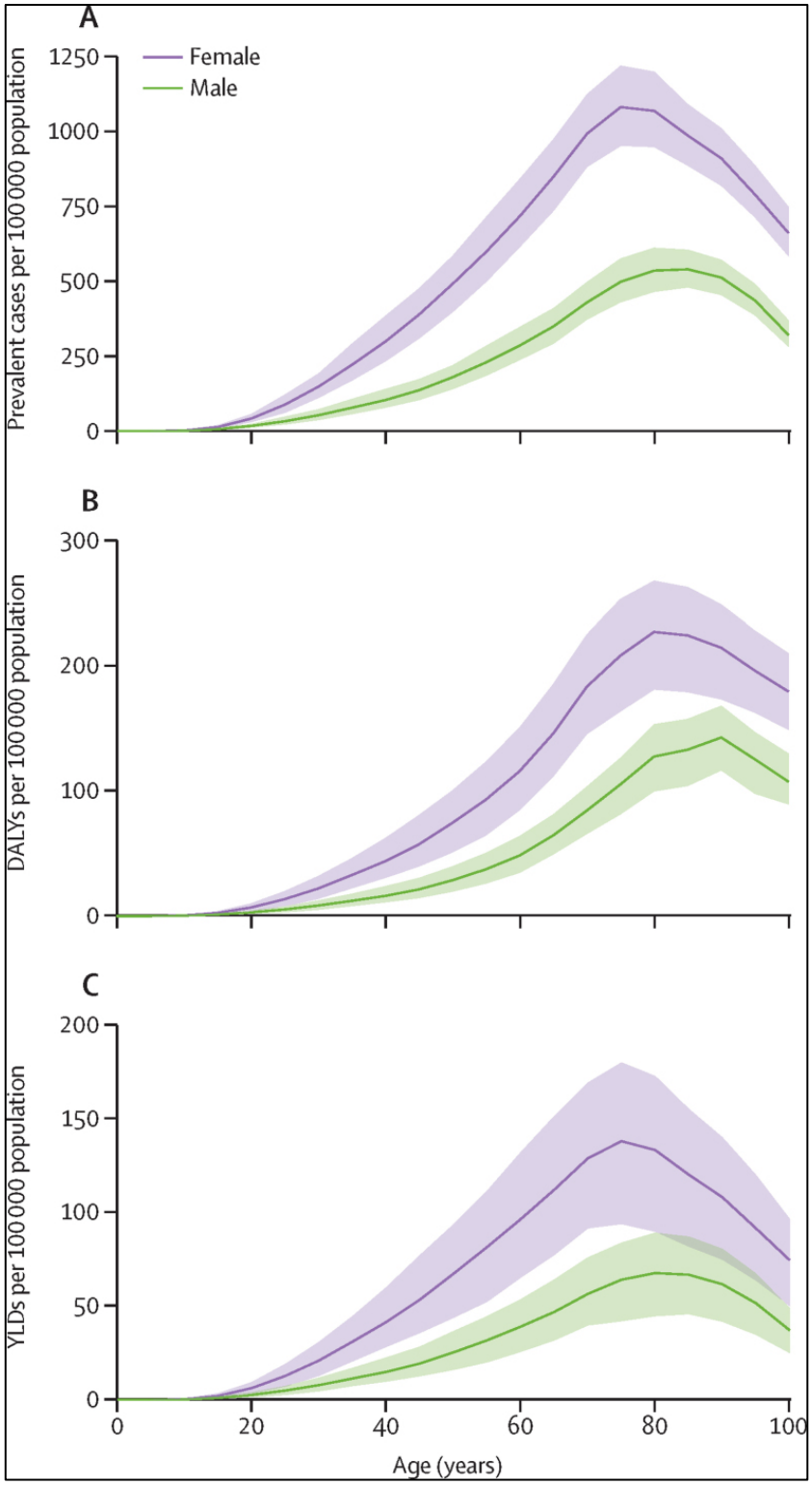

Figure 2. 1. Global prevalence, DALY, and YLD rates of rheumatoid arthritis in 2020 by sex and age. (A) Prevalent cases per 100 000 population; (B) DALYs per 100 000 population, (C) YLDs per 100 000 population. Shaded areas represent 95% uncertainty intervals. Reproduced with permission from: *(Black et al., 2023)*.

2.1.6. Prognosis.

Improvement in and greater availability of pharmacological interventions like methotrexate, a conventional disease-modifying anti-rheumatic drug (cDMARD) or etanercept, a biological DMARD (bDMARD), has meant remission or low disease activity can be achieved in about 75% to 80% of patients (Aga et al., 2015, Shams et al., 2021). As a consequence, most individuals can continue to participate in social and work activities and have normal life expectancy (Listing et al., 2015). However, disease remission or low disease activity is not achieved in approximately a quarter of individuals, particularly in lower income countries where access to biologic and synthetic disease modifying drugs is lower (Putrik et al., 2014). Inequality in the level of care across a countries healthcare system or difficulty in diagnosing the disease is also associated with poorer clinical outcomes as a consequence of higher disease activity at the start of treatment (Blüml et al., 2015, Burmester et al., 2018, Cheung and McInnes, 2017). If the disease is left untreated, disruption of the synovial joints may occur leading to deformity and physical impairment (Lindqvist et al., 2003, Lindqvist et al., 2002).

2.1.7. Personal and socioeconomic impact of RA.

Whilst RA can affect individuals of any age, most are diagnosed between forty and sixty-five years of age (Nilsson et al., 2021, Versus Arthritis, 2023). Disease course is similar for both sexes across all ages (<40, 40-54, 55-69 and ≥70 years) regardless of the treatments provided (Nilsson et al., 2021). RA is the 61st leading cause of years lived with disability (YLD) worldwide (Institute for Health Metrics and Evaluation, 2019b). Given the chronic nature of RA, individuals often live for many years in a state of disability, often with significant burden at both a personal and socioeconomic level.

2.1.7.1. Personal impact.

At the personal level, the burden of RA can vary significantly. Partly because RA is unpredictable, often exhibiting both periods of increased disease activity and disease remission (Hewlett et al., 2012, Van Riel, 2014). Individuals living with RA have described a variety of consequences associated with the disease. These include pain, restricted mobility, ability to work, systemic fatigue, sleeplessness, eating difficulties and emotional disturbance (Hughes, 2009, Lütze and Archenholtz, 2007, Sokka et al., 1999). Mental health disorders such as anxiety, depression and cognitive impairment are also more common when compared to the general healthy population (Lwin et al., 2020). In addition, behavioural factors may also play a role in rheumatoid cachexia. Individuals with RA have lower physical activity levels which have been attributed to pain and fear of aggravating symptoms (Mancuso et al., 2007). A longitudinal cohort study concluded that 41% of individuals with established RA met the World Health Organisation recommendations for moderate to vigorous physical activity per week (Bremander et al.,

2020, World Health Organization, 2010). Research has identified links between rheumatoid cachexia and metabolic syndrome (Elkan et al., 2009). Metabolic syndrome is a group of health problems that places an individual at greater risk of conditions type-II diabetes or cardiovascular disease (Cornier et al., 2008). Elevated diastolic blood pressure and obesity in RA have been identified as strong predictors of cardio-respiratory fitness, an important determinant of cardiovascular disease (Cooney et al., 2019). Across both sexes, cardiovascular disease is the primary cause of death in those individuals living with RA (Aletaha and Smolen, 2018). Deaths associated with RA are documented to be 0.6 (0.4 - 0.7) per 100,000 (Institute for Health Metrics and Evaluation, 2019b). Deaths associated with cardiovascular diseases, across both sexes are 239.8 (219.4 - 254.9) per 100, 000 (Institute for Health Metrics and Evaluation, 2019a).

2.1.7.2. Socioeconomic impact.

The societal and economic burden of RA is thought to be substantial, ranging from the individuals living with the disease, the health and social care system helping in their management and society as a whole (Cooper, 2000). The economic impact of RA may be measured in terms of direct, indirect, and intangible costs (Markenson, 1991). Examples of direct costs may include diagnostic tests to detect the disease, the prescription of medicines, consultations with members of the multi-disciplinary team and surgery. Indirect costs represent the cost of disability associated with the disease, such as lost productivity associated with the inability to work and other forms of welfare and disability support. Work disability is recognised as an important outcome in individuals of working age. A longitudinal cohort study involving 160 patients examined the impact of RA on employment status in the early years of the disease. One-third stopped working on the grounds of ill-health within the first few years of being diagnosed with the disease. Whilst the peak for stopping work was in the early years of the disease, the study also identified individuals continue to leave work for several years after disease onset (Barrett et al., 2000). Intangible costs represent the impact of RA on domains such as quality of life and emotional well-being (Markenson, 1991). For 1992-93, the total economic cost of RA in England was estimated to be £1.256 billion. Fifty-two percent was attributed to disability and the inability to work (McIntosh, 1996). In 2009, the National Audit Office estimated direct and indirect costs being £560 million and £1.8 billion per year respectively (Leigh, 2010). Considering RA's prevalence and its associated personal and socioeconomic impacts, safe and effective management of the disease is essential.

2.2. Management of adults living with RA in the UK.

2.2.1. NICE evidence-based guidelines.

NICE is responsible for helping healthcare professionals and policy makers get the best care to patients, while ensuring value for the taxpayer (National Institute for Health and Care Excellence, 2023). In the UK (excluding Scotland), NICE publishes clinical practice guidelines, offering recommendations for HCPs how to care for individuals with specific conditions. The recommendations are based on evidence reviews and expert consensus (National Institute for Health and Care Excellence, 2012).

2.2.2. NICE guidance for managing adults with RA.

In adults living with RA, NICE first published its guidance in 2009. The guideline has been updated three times since then (2015, 2018 and 2020). Individuals are commonly managed in the community by a multi-disciplinary team depending on their needs. These may include the rheumatologist, general practitioner, specialist nurse and members from the allied health professionals including occupational therapy, physiotherapy and podiatry (National Institute for Health and Care Excellence, 2018). Currently, the optimal management of RA requires a combination of pharmacological and non-pharmacological interventions (National Institute for Health and Care Excellence, 2018).

2.2.2.1. NICE recommendations for the pharmacological management of RA.

Improvements in pharmacological interventions have led to changes in the guidance over the last fourteen years (Singh et al., 2009, Suarez-Almazor et al., 2000). Key drug classes used in managing RA are analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), conventional disease-modifying anti-rheumatic drugs (cDMARDs), biological and targeted synthetic disease-modifying anti-rheumatic drugs (DMARDs) and glucocorticoids (National Institute for Health and Care Excellence, 2018). cDMARDs are the predominant treatment for RA (Donahue et al., 2008). The NICE guideline recommends that adults with newly diagnosed active RA receive cDMARDs such as oral methotrexate, leflunomide or sulfasalazine should be started ideally within 3 months of onset of persistent symptoms, with dose being escalated as tolerated (National Institute for Health and Care Excellence, 2018). Individuals with severe RA measured by the disease activity score (DAS28) of ≥5.1 may be treated with biological DMARDs (bDMARDs) such as upadacitinib, sarilumab, tofacitinib, adalimumab, etanercept, infliximab and abatacept (National institute for Health and Care Excellence, 2017b, National Institute for Health and Care Excellence, 2017a, National Institute for Health and Care Excellence, 2020, National Institute for Health and Care Excellence, 2021a). Analgesics may also be considered for the chronic pain associated with the condition, but clinical judgement is recommended

to inform shared decision making about management options (National Institute for Health and Care Excellence, 2021b). In addition to advances in pharmacological management of RA, non-pharmacological interventions have also become more widely used in clinical practice (Scott et al., 2010).

2.2.2.2. NICE recommendations for the non-pharmacological management of RA.

NICE recommends adults living with RA should have access to three specialist HCPs depending on their needs. These include occupational therapy, physiotherapy and podiatry (National Institute for Health and Care Excellence, 2018). NICE recommends individuals have access to specialist occupational therapy where they are experiencing difficulties with everyday activities or having problems with hand function. Occupational therapists plays a role in the comprehensive management of RA, offering tailored interventions to enhance individuals' ability to engage in daily activities and improve their overall quality of life (Ekelman et al., 2014). The second profession recommended is specialist physiotherapy. Physiotherapists help individuals through movement and exercise, manual therapy, education and advice (The Chartered Society of Physiotherapy, 2018). As such, NICE recommends individuals have access to physiotherapy to improve general fitness and encourage regular exercise, learn exercises for improving joint flexibility, muscle strength and for managing other functional impairments. In addition, NICE recommends individuals see a physiotherapist to learn about short-term pain relief using transcutaneous electrical nerve stimulators (TENS) and where needed, wax baths (National Institute for Health and Care Excellence, 2018). The third profession NICE recommends individuals have access to is podiatry for assessment of foot health needs, functional insoles, and therapeutic footwear for making walking less painful (Laitinen et al., 2022, Royal College of Podiatry, 2024). In 2015, initiated following the publication of the SARAH multicentre RCT (Lamb et al., 2015), NICE updated its recommendations to also include tailored strengthening and stretching hand exercise for individuals with pain and dysfunction of the wrists or hands. This time it did not stipulate the type of HCP required, only that they possess training and skills in this area (National Institute for Health and Care Excellence, 2018). In the National Health Service (NHS), these may be occupational therapists or physiotherapists who specialise in the rehabilitation of individuals with disorders affecting the hands and upper limbs or who have been trained to deliver hand exercise programmes such as the SARAH hand exercise programme (British Association of Hand Therapists, 2020, Srikesavan et al., 2018). The recommendations contained in the non-pharmacological section of the NICE guideline reflects growing acceptance and evidence for prescribing therapeutic exercise-based interventions in RA.

2.3. Defining therapeutic exercise.

Exercise in general is considered a subset of physical activity. Whilst it shares a number of common elements with physical activity (e.g., bodily movement caused by the skeletal muscles, energy expenditure etc.), the traditional aim of exercise is to improve, or maintain components of physical fitness (e.g., cardiovascular fitness, strength, flexibility, balance etc.) using a planned approach that is both structured and repetitive (Caspersen et al., 1985, World Health Organization, 2019a). It's common to use one form of exercise to improve a particular component (e.g., aerobic exercise to improve cardiovascular fitness or strengthening exercise to improve muscular strength), however in reality, the different forms of exercise may produce changes in more than one component simultaneously, for example, strengthening exercise may also improve an individual's cardiovascular fitness (Wasfy and Baggish, 2016). The distinction between exercise and therapeutic exercise hinges on the context and intent behind its application. Whilst exercise is used to improve or maintain physical fitness, it may also be used to improve or maintain non-physical components of fitness. For example, exercise is therapeutically prescribed to manage chronic musculoskeletal pain and mental health conditions such as anxiety and depression associated with RA (Booth et al., 2017, Cooney et al., 2011, Geneen et al., 2017). Therefore, therapeutic exercise aims to restore movement and function when an individual is affected by injury, illness, or disability (Barker and Eickmeyer, 2020, Taylor et al., 2007, The Chartered Society of Physiotherapy, 2018). Humphrey and Colby (2018) define therapeutic exercise as *"the systematic, planned performance of physical movements, postures or activities intended to provide the patient/client with the means to: 1) Remediate or prevent impairments of body functions or structures, 2) Improve, restore, or enhance activities and participation, 3) Prevent or reduce health-related risk factors and 4) Optimise overall health, fitness, or sense of wellbeing."* (Humphrey and Colby, 2018 :p2). A key type of therapeutic exercise recommended in the non-pharmacological management of RA is strengthening exercise (National Institute for Health and Care Excellence, 2018).

2.4. Therapeutic strengthening exercise prescribed in the management of RA.

Therapeutic strengthening exercise is prescribed by HCPs for addressing the impact of rheumatoid cachexia (Cooney et al., 2011, Liao et al., 2021) and other effects associated with reduced physical activity, such as low bone mineral density (Cooney et al., 2011). A meta-analysis evaluating strength-based exercise interventions versus interventions without a strengthening component identified based on three RCTs (76 patients in the intervention group and 72 patients in the control group) that strengthening exercise was associated with increases in isokinetic strength (weighted mean difference (WMD) = 23.7%, 95% CI 11 – 36.4%, $p < 0.001$, $I^2 = 0\%$) and isometric strength (WMD = 35.8%, 95% CI

24.4 – 47.1%, p < 0.001, I^2 = 68%). Five RCTs (126 patients in the resistance exercise group and 117 patients in the control group) indicated improvements in isometric grip strength (WMD = 26.4%, 95% CI 12.3 – 40.5%, P<0.001; I^2=0% (Baillet et al., 2011). Isokinetic strength refers to the ability of muscles to generate force at a constant speed or velocity throughout a range of movement. Isometric strength refers to the ability of muscles to generate force without changing their length or causing movement at a joint (Newton et al., 2011). In the meta-analysis that informed the 2018 EULAR recommendations for physical activity in people with rheumatoid arthritis, spondyloarthritis and hip/knee osteoarthritis (Osthoff et al., 2018a), twenty-five RCTs including 936 participants indicated a moderate effect for strengthening exercise on quadriceps muscle strength (standardised mean difference (SMD) = 0.54, CI 0.35 to 0.72, I^2 = 67%). Whilst Baillet et al (2011) didn't report publication bias, Osthoff et al (2018a) found evidence of small study effects for RA and indicated the analyses may overestimate the effect of strengthening exercise on clinical outcomes.

2.4.1. The physiological mechanisms associated with strengthening exercise.

Strengthening exercise specifically targets the musculoskeletal system, prompting physiological adaptations in skeletal muscles responsible for human movement. These adaptations correlate with increases in strength, power, and functional performance, as noted by (Deschenes and Kraemer, 2002). The mechanisms driving these physiological adaptations are attributed to a combination of neural and muscular factors, as outlined by Aagaard (2011). Neural adaptations resulting from strengthening exercises encompass alterations in spinal motor neuron recruitment, motor neuron excitability, corticospinal excitability, and co-activation of antagonist muscle groups (Aagaard, 2011). The belief is that increased motor neuron recruitment influences muscle strength. Strengthening exercises prompt the nervous system to recruit a greater number of motor units, leading to enhanced force production and consequent strength gains. Improved motor unit synchronization contributes to more efficient and coordinated muscle contractions. Additionally, greater frequency at which motor units are recruited is associated with the nervous system becoming more adept at regulating motor unit activation, resulting in improved force production and control. While these neural changes are more prominent in the initial stages of strengthening exercises, contributing to early strength improvements, sustained engagement in such exercises over the long term further enhances these adaptations. However, it is acknowledged that other factors, particularly muscle hypertrophy, likely become more significant contributors to strength gains in the longer term (Aagaard, 2011). Muscle hypertrophy involves an increase in skeletal muscle size. Although not fully understood, strengthening exercises stimulate the release of specific growth factors, including insulin-like growth factor 1 (IGF-1), which has been associated with muscle hypertrophy. IGF-1 serves as a key activator of the protein

kinase B (Akt)/mammalian target of rapamycin (mTOR) signalling pathway, a critical regulator of protein synthesis (Tricoli, 2011). While understanding how strengthening exercise affects muscle physiology in healthy individuals is more established, its impact on pathological tissues is less understood (Brody, 2011). The optimal combination of dose parameters like intensity, frequency, and type of strengthening exercise prescribed remains uncertain, and further research is recommended to clarify exercise prescriptions across different populations (Kraemer et al., 2017).

2.5. Defining dose of therapeutic exercise.

Dose has long been considered a fundamental concept of exercise prescription. The earliest record of dose as a concept can be traced back to ancient Greece. Hippocrates (460-377 BC), widely recognised as the father of modern medicine, is credited as one of the earliest examples of a healthcare professional recognising the importance of using and tailoring exercise for its health benefits when he said *"if we could give every individual the right amount of nourishment and exercise, not too little and not too much, we would have found the safest way to health"* (Buford et al., 2013 :p157).

Dose is a non-specific term referring to a quantity or amount (Oxford English Dictionaries, 2019, Rowbotham et al., 2019) and is made up of several different dose parameters that may be manipulated depending on the individual and the desired outcome/s (Scott et al., 2016). This is reflected in the American College of Sports Medicine (ACSM) recommendations and the 'FITT' principle for guiding exercise prescription. FITT refers to F= Frequency (how often is exercise done each week), I = Intensity (how hard is the exercise), T = Time (how long is the exercise duration), T = Type (what is the mode of exercise) (American College of Sports Medicine, 2010). This principle later evolved to FITT-VP, where V = Volume (what is the total amount of exercise), and P = Progression (how is the programme advanced) were also recognised as important dose parameters (American College of Sports Medicine, 2014). In applying the FITT-VP principle, the ACSM recommends the prescriber (e.g., HCP) consider the following: 1) Individual health status (including clinical conditions), 2) Physical ability, 3) Age, 4) Training responses and 5) Individual's goals (American College of Sports Medicine, 2020, Bushman, 2018). Owing to individual response to therapeutic exercise being highly variable (Ross et al., 2019), the complexities of personalising exercise prescription based on individual characteristics remains an area of scientific interest (Gronwald et al., 2020, Herold et al., 2019, Herold et al., 2021, Noone et al., 2024, Ramírez-Vélez et al., 2017, Ross et al., 2019).

2.6. Determining dose of interventions evaluated by clinical trial.

Whether the intervention is pharmacological (i.e. drug) or non-pharmacological (i.e. therapeutic exercise), dose is recognised as a key driver for producing positive clinical outcomes (Brody, 2011, Holden and Barton, 2019, Moore, 2004, Nilsen et al., 2018, Noone et al., 2024, Piantadosi, 2017, Pinheiro and Duffull, 2009, Swisher, 2010). One of the many decisions made when developing and refining interventions for clinical trials is choosing the intended dose. Insufficient dosing of an intervention may lead to premature conclusions about its ineffectiveness (Voils et al., 2012). Conversely, too much may give rise to potential harms. Developing the interventions evaluated by clinical trials is a critical stage of the research process (Piantadosi, 2017). An integral part of this process focuses on determining safe and effective prescription of dose (Buford et al., 2013, Piantadosi, 2017). Yet the approaches used by healthcare researchers appear to differ depending on the type of intervention being evaluated (e.g., drug vs. therapeutic exercise).

2.6.1. Determining safe and effective dose in pharmacological trials.

Healthcare researchers evaluating investigational medicinal products (i.e. drugs) commonly use early phase clinical trials (e.g., phase-I/II), employing different dose-escalation designs (Hansen et al., 2014, Le Tourneau et al., 2009) as an essential step to safeguard participants and optimise potential for efficacy (European Medicines Agency, 2017, Health Research Authority, 2017). Early pharmaceutical trials (phase I) often employ dose-finding strategies when testing new drugs to identify the appropriate dose for phase II trials. Researchers may be interested in the minimum effective dose (i.e. the lowest dose of a drug that produces the desired effect) (Piantadosi, 2017), or in the example of cytotoxic drugs (e.g., cancer therapies), the maximum tolerated dose (i.e. the highest dose of drug that can be tolerated with an acceptable or manageable level of toxicity) (Piantadosi, 2017). Various dose escalation methodologies may be used, such as the traditional 3 + 3 design, where successive cohorts of participants will be started on a fixed dose and if no dose-limiting toxicity (DLT), the following cohort of participants will be enrolled at the next dose level. The overarching principle for dose escalation is to avoid unnecessary exposure of participants to sub-therapeutic doses of a drug whilst preserving safety (Le Tourneau et al., 2009, North et al., 2019). Ideally, prior to phase III, the optimal therapeutic dose (OTD) has been identified. OTD is defined as the dose which can provide the best possible outcomes with a tolerable onset of adverse events for most participants. Later development trials (phase III) often ask questions related to clinical outcome and address treatment tolerability, where tolerability has three components: 1) Feasibility (i.e. practicality and likelihood of successfully developing, manufacturing and delivering a new drug), 2) Safety (i.e. potential risks and adverse effects) and 3) Efficacy (i.e. producing the desired therapeutic effect) (Piantadosi, 2017).

2.6.2. Determining safe and effective dose in non-pharmacological trials.

Healthcare researchers typically don't adopt the dosing approach described above. Instead, many may follow the Medical Research Council (MRC) framework for developing and evaluating complex interventions used to improve health (Craig et al., 2008, Medical Research Council, 2000, medical Research Council, 2006, Skivington et al., 2021). This framework draws parallels with the phases used for evaluating drugs: 1) Pre-clinical (Theory), 2) Phase-I (Modelling), 3) Phase-II (Exploratory trial), 4) Phase-III (Definitive RCT) and 5) Phase-IV (Long-term implementation). Phases 1-3 specifically relate to developing the intervention and include setting prescription parameters (i.e. recommended dose and/or schedule of administration). The MRC first published its framework over two decades ago, it has been recently updated and continues to advocate for piloting and exploratory testing to address key uncertainties (Craig et al., 2008, Medical Research Council, 2000, medical Research Council, 2006, Skivington et al., 2021).

2.6.2.1. Feasibility and pilot studies.

Feasibility and pilot studies serve as preliminary steps for healthcare researchers prior to conducting a phase-III (definitive) RCT. While the terms are sometimes used interchangeably, both have subtle differences in their objectives (Drummond, 2017). Feasibility studies assess logistical feasibility for conducting a definitive RCT of the intervention, identifying potential issues related to recruitment, data collection, and participant safety (Abbott, 2014). Feasibility studies may lack randomisation procedure or a control group (Harvey, 2018). Pilot studies aim to replicate the planned full-size clinical trial on a smaller scale, testing the overall research design and provide training and experience in running the trial prior to the main trial beginning (Abbott, 2014, Whitehead et al., 2014). Consequently, they are not adequately powered to enable firm statistical conclusions (Drummond, 2017). Sometimes healthcare researchers conduct a pilot study as an 'internal' component of the main study, constituting the initial stage of a larger RCT (Avery et al., 2015, Whitehead et al., 2014). The use of pilot studies in particular to optimise dose-response is a topic of debate in the development of pharmacological interventions. Some argue that dose optimisation should wait until after the RCT and the efficacy of the intervention has been established (Korn et al., 2023). Others argue for using dose-escalation methodology to guide the dose used in the definitive RCT (Aouni et al., 2020, Papathanasiou et al., 2019). Given that the MRC recommends healthcare researchers address key uncertainties, it's useful to identify whether healthcare researchers designing rehabilitation trials that involve therapeutic exercise-based interventions employ dose-escalation methodology prior to evaluating the intervention by RCT.

2.6.2.2. Current practice of dose escalation methods in therapeutic exercise-based trials.

Following a search conducted using Ovid MEDLINE (R) ALL 1946 to 2019 using the following search terms (exercise$.m_titl or rehabilitation.m_titl and dose escalation.m_titl or de-escalation.m_titl or dose-finding.m_titl or early phase 1 trial.m_titl or phase 1 trial.m_titl or phase 2 trial.m_titl) and using GOOGLE scholar, four exercise-based dose-escalation studies (Table 2.3) in the healthcare literature were identified (Colucci et al., 2017, Dite et al., 2015, Peiris et al., 2017, Wallis et al., 2015). Notably, none involved RA. Most of these studies were conducted in Australia (n=3). The remaining study was conducted in the UK. Two centred on the neurological condition of stroke (Colucci et al., 2017, Dite et al., 2015). The remaining two studies, one investigated tolerance of physical activity after hip fracture (Peiris et al., 2017) and one study investigated walking-based exercise for knee osteoarthritis (Wallis et al., 2015).

The first study conducted by Dite et al (2015) was a phase-I study that investigated a 12-week exercise intervention which included balance, strength, and endurance exercise. The study used a cumulative 3 + 3 dose escalation design involving increasing doses in successive cohorts of three participants. Six participants took part before the escalation of exercise was stopped owing to two participants in the third cohort not coping with the dose escalation, reporting fatigue and diminishing (74%) adherence with the programme. Four participants tolerated up to 10·5 hours of exercise per week, which included 283 minutes of endurance exercise, 182 minutes of task practice, 138 minutes of strengthening exercise, and 28 minutes resting. Participants clinical outcomes included increased walking distance measured by the six-minute walk test and faster mobility measured by the four-square step test and timed up and go test. Whilst Dite et al (2015) planned a phase-II study, using forward citation tracking in GOOGLE scholar, no associated study was identified.

The second study conducted by Colluci et al (2017) aimed to develop a rule-based, dose-finding design for stroke rehabilitation research. As such no further study was planned. A 3+3 rule-based design was used where five cohorts of three participants took part in performing a seated task aimed at enhancing ability to use the paretic hand. Each cohort was set with a different number of repetitions per day (50, 100, 167, 209 and 251 repetitions). The first cohort started with a dose of 50 repetitions performed five days per week over a two-week period. The maximal tolerated dose for the exercise task was 209 repetitions per day. Colluci et al (2017) concluded that the dose-finding approach was a viable method to use in stroke rehabilitation research.

The third study conducted by Peiris et al (2017) was a phase-I study that investigated how much moderate-intensity walking could be prescribed to community dwelling participants following hip fracture. A 3+3 ruled based design was used to escalate the dosage. Twenty-one participants took part. It was found that participants were unable to tolerate walking doses greater than 100 minutes per week, substantially less than the 150 minutes recommended for physical activity/exercise (World Health Organization, 2010).

The final study conducted by Wallis et al (2015) aimed to identify the maximum tolerated dose of walking exercise in people with severe knee osteoarthritis. Researchers found that the maximum tolerated dose of walking was 80 minutes less per week than the 150 minutes of physical activity recommended by the World Health Organisation for healthy adults aged 18 – 64 (World Health Organization, 2010). Wallis et al (2015) indicated that healthcare professionals who follow general physical activity guidance (i.e. WHO) may be over-prescribing physical activity in this cohort of patients. The consequence of this, as discovered in this dose-finding study, was higher doses of walking increased the risk of exacerbating knee pain in those patients with more severe osteoarthritis. Flare-up of pain has been identified to impact on work and social participation and health-related quality of life (McAlindon et al., 2014, Zhang et al., 2008). The results from this study were implemented in a phase II single-blind RCT (Wallis et al., 2017) comparing a walking programme plus usual care to a control group receiving usual care (23 participants in each group). Participants in the intervention group were prescribed 70 minutes of walking per week and completed this for 12 weeks in the community. Wallis et al (2017) identified no difference for knee pain between the groups, however, participants in the intervention group had increased odds of achieving a healthy systolic blood pressure (Odd Ratio = 5.7, 95% CI 1.2 to 26.9), faster walking speed (Mean difference (MD) = 0.12 metres per second, 95% CI 0.02 to 0.23) more daily steps (MD = 1345 steps, 95% CI 365 to 2325), more time walking (MD = 18 min/day, 95% CI 5 to 31), reduced waist circumference (MD = −5.3 cm, 95% CI −10.5 to −0.03) and increased knee stiffness (MD = 0.9 units, 95% CI 0.07 to 1.8).

Table 2. 3. Characteristics of studies using dose-escalation methods in exercise.

Study + Country of origin (Research area)	Primary aim of study	Sample characteristics	Dose-escalation metho used	Main study conclusions
Dite et al (2015) **Australia (Stroke)**	To identify the maximum tolerated dose of targeted multimodal exercise in a group of community-dwelling stroke survivors with impaired balance and walking.	n=6 Mean age: 56 ± 5 Male/female 83%/17%	Phase I cumulative 3 + 3 design.	▪ Cumulative 3 + 3 model feasible for non-drug dose maximization. ▪ Maximal dose of exercise identified significantly higher that the dose delivered to stroke survivors in current trials.
Wallis et al (2015) **Australia (Knee osteoarthritis)**	To determine how much physical activity, in the form of walking, can be safely and feasibly tolerated for people with severe knee osteoarthritis.	n=24 Mean age: 67 ± 8 Male/female 45%/55%	Phase I dose–response study, an algorithm based (A + B) design	▪ 70 min per week of moderate intensity supervised walking was safe and feasible. ▪ People with severe osteoarthritis of the knee, for higher doses there was a risk of exacerbating knee pain levels.
Colucci et al (2017) **UK (Stroke)**	To develop a rule-based, dose-finding design for stroke rehabilitation research.	n=15 Mean age: 68 (48 - 81) Male/female 53%/47%	Single arm 3+3 rule-based, dose-finding study.	▪ Dose-finding design a feasible method for use in stroke rehabilitation research.
Peiris et al (2017) **Australia (Hip fracture)**	To determine how much moderate-intensity physical activity, in the form of walking, could be prescribed for people living in the community after hip fracture in terms of safety, tolerability, and feasibility.	n=21 Mean age: 75 ± 9 Male/female 24%/76%	Phase I dose-response design using an algorithm-based A+B design: the 3 + 3 design.	▪ The maximum tolerated dose of walking for adults after hip fracture before significant discomfort was experienced (e.g., breathlessness, pain, and fatigue) by any participant was 100minutes/week. ▪ No adverse events occurred, but participants began to be unable to tolerate higher doses beyond 100minutes/week.

Since the publication of study one (chapter three) in 2020, the above search was re-run (15/02/2024). This identified five additional rehabilitation studies and one protocol employing dose escalation methodology (Table 2.4). The five studies focused on stroke rehabilitation (Bajuaifer et al., 2023, Galloway et al., 2023, Kramer et al., 2020, Mackie et al., 2021a, Mackie et al., 2021b) while the protocol focused on therapeutic exercise for patients with metastatic castrate-resistant prostate cancer (Bultijnck et al., 2021). While healthcare researchers in stroke rehabilitation are exploring the use of dose escalation methods more extensively, only one further study identified in the initial search (Peiris et al, 2017) employing dose-escalation methodology has integrated the dose-escalation results into a

follow-up study. In a feasibility RCT, thirty-eight participants were recruited following hip fracture (Taylor et al., 2023). Twenty were assigned to the experimental group, where they were prescribed 100 minutes of walking per week identified by Peiris et al (2017) in addition to standard care, which included an information handout on staying safe at home and continued with existing exercise programmes and other services. The control group received standard care. Both groups had similar characteristics at baseline. Despite participants finding it challenging to achieve the weekly target, all completed it, usually spread over six sessions. No serious adverse events related to the intervention were reported, and researchers observed clinically significant improvements in physical activity levels among those receiving the intervention compared to the control group. However, demand for the intervention was low, with 69 (44%) of the 158 potentially eligible participant declining, citing reasons such as lack of interest or being too busy.

Table 2. 4. 2024 update - Characteristics of studies using dose-escalation methods in exercise.

Study + Country of origin (Research area)	**Primary aim of study**	**Sample characteristics**	**Dose-escalation metho used**	**Main study conclusions**
Kramer et al (2020) **Australia (Stroke)**	To determine the maximum safe and tolerable intensity of CRF training early post-stroke.	Not applicable as protocol	Phase I, 5+5 dose ranging trial	▪ Not applicable as protocol
Bultijnck et al (2021) **Belgium (Metastatic castrate-resistant prostate cancer)**	To determine the start exercise prescription dose in metastatic castrate-resistant prostate cancer patients receiving second-line hormone treatment and recommended phase I(Kramer et al., 2020, Mackie et al., 2021b)I exercise prescription	n=9 Mean age: 69 (64-78) Male/female 100%/n/a	Phase I study used monocentric 3 + 3 research design	▪ Dose limiting safety concerns were observed in 2 out of 3 patients in dose level 2 and 1 patient out of 6 in dose level 1 due to VAS > 3 during resistance training and/or flexibility training. No tolerance issues were observed in the two dosing cohorts. ▪ The optimal start exercise prescription dose was set at dose level 1 due to safety issues at dose level 2. ▪ Findings suggest that exercise is perceived tolerable in patients receiving second-line hormone therapy. Caution is indicated on safety during performance of the exercises.

Mackie et al (2021) **Australia (Stroke)**	To investigate different doses of light-intensity standing exercises that interrupt prolonged sitting and reduce blood pressure immediately and over 24 hours in stroke survivors.	n=29 Mean age: 66 ± 12 Male/female 52%/48%	Within-participant, laboratory-based, dose escalation design.	▪ Interrupting prolonged sitting with more frequent bouts of standing exercises lowers systolic and diastolic blood pressure in stroke survivors. ▪ 4-6 x 5min bouts of standing exercises were more effective than 2 x 5minn bouts of standing exercise.
Mackie et al (2021) **Australia (Stroke)**	To investigate the effects of interrupting 8 hours of prolonged sitting with increasingly frequent bouts of light-intensity standing-based exercises on the postprandial glucose response in stroke survivors.	n=28 Mean age: 67 ± 13 Male/female 54%/46%	Within-participant, laboratory-based, dose escalation design.	▪ Interrupting 8 hours of prolonged sitting at least every 90 minutes with light-intensity standing-based exercises attenuates postprandial glucose in stroke survivors. ▪ During the morning, postprandial glucose is attenuated when sitting is interrupted every 60 and 90 minutes.
Bajuaifer et al (2023) **United Kingdom (Stroke)**	To identify the maximum tolerable dose a day (MTD) of lower limb mirror movement therapy	n = 15 Mean age: 61 ± 9 Male/female 33.3%/66.6%	3+3 cohort rule-based, dose escalation/de-escalation study.	▪ The identified MTD of lower limb mirror therapy was 35 minutes daily when frequency was set at seven days a week and duration as two weeks.
Galloway et al (2023) **Australia (Stroke)**	To determine the dose-response of an 8-week home-based telehealth-supervised aerobic exercise program on post-stroke cardiorespiratory fitness.	n=20 Mean age: 66 ± 11 Male/female 60%/40%	Phase I modified 3+3 dose-escalation design.	▪ Target exercise doses were well adhered to, and the intervention was safe (480 exercise sessions delivered; one fall resulting in minor laceration) and tolerable (no participants met the dose-limiting threshold). ▪ None of the exercise doses met our criterion for efficacy.

The results of both searches demonstrate that dose escalation as an approach for determining dosage has not been used in RA. It also demonstrates that it is feasible to determine tolerance to different dosages of therapeutic exercise-based interventions across various clinical populations prior to evaluation by RCT. However, as the follow-up study to Wallis et al (2015) indicates, it's unclear whether this approach produces better clinical outcomes compared to alternative methods employed by healthcare researchers (e.g., using past evidence to support dose choices). Although prescribing dosages that participants can better tolerate, may in turn contribute towards better outcomes by improving an individual's adherence to the intervention of interest (Collado-Mateo et al., 2021).

The low uptake of formalised testing of dose indicates healthcare researchers may be opting to rely on using past research evidence to support dose choices. This is not without issue. Today's research often relies on past research discoveries (Krieger et al., 2024). In the context of therapeutic exercise and its dose, once a published study enters the evidence base, it may be used to support dose choices in later studies, underpin guidelines and ultimately be implemented into clinical practice. However, this may have negative consequences. This can be seen in rehabilitation research with the propagation of core stability in the field of low back pain, where research combined with human bias lead to an industry built on training certain abdominal muscles (e.g., transversus abdominus) (Lederman, 2010). Alternatively, it is possible no formalised testing or past research is used. A systematic review of 187 RCTs evaluating therapeutic exercise interventions for individuals with clinical conditions or high health risks found that healthcare researchers justified their dose choices in only 68 (36%) of the studies (Gallois et al., 2017). These RCTs covered various rehabilitation specialties, including cardiovascular (n=25, 13.4%), endocrine and metabolic (n=23, 12.3%), neurology (n=23, 12.3%), public health (n=23, 12.3%), and rheumatology (n=23, 12.3%). The findings are a cause for methodological concern. Firstly, dose development seems overlooked. However, Gallois et al (2017) only focused on the evidence used across three dose parameters (intensity, frequency, and duration). It is unknown whether other dose parameters (e.g., type, volume and progression) may be better supported with underpinning evidence. Additionally, Gallois et al (2017) did not assess the quality of the underpinning evidence, how well it was applied to the doses used in the RCTs, or whether it was applicable to the clinical populations under investigation. Considering all of the above, presently, individuals will still go on to develop RA and need management and HCPs will still need to make judgements about the therapeutic exercise interventions and their dose.

2.7. Prescribing therapeutic exercise and its dose in clinical practice.

Prescribing therapeutic strengthening exercise in RA typically takes place at the point of contact, normally as part of the healthcare consultation, a two-way face-to-face interaction between the HCP and the patient (Byrne and Long, 1976, Hobbs et al., 2016, Keller and Carroll, 1994, Pawlikowska et al., 2007, Pendleton, 1984, Silverman et al., 2016, Stewart et al., 2024, Stott and Davis, 1979). The consultation enables essential clinical information to be gathered for making accurate diagnosis, comprehending impairments, prioritising intervention targets and making shared decisions (Elwyn et al., 2017, Wood et al., 2024). It also serves to guide prescribing decisions by balancing potential benefits versus harms (American College of Sports Medicine, 2020, Japp et al., 2018, Peterson et al., 1992). During healthcare consultations, HCPs may opt to choose a framework to guide and structure

their prescribing decisions, with the aim of achieving better clinical outcomes (Anemaet and Hammerich, 2014).

2.7.1. Frameworks for prescribing interventions.

2.7.1.1. Royal Pharmaceutical Society (RPS) competency framework.

Prescribing pharmacological interventions in the UK, the RPS competency framework outlines the knowledge, skills, characteristics, qualities, and behaviours required for safe and effective prescribing regardless of professional background (Royal Pharmaceutical Society, 2021). The framework is designed to be universally applicable, supporting prescribers at any stage of their career and is a mandatory part of prescriber education (Rae, 2024). The competencies within the framework are presented as two domains and describe the knowledge, skill, behaviour, activity, or outcome that prescribers should demonstrate. The first domain addresses the competencies that the prescriber should demonstrate during the consultation (1. Assess the patient, 2. Identify evidence-based treatment options available for clinical decision making, 3. Present options and reach a shared decision, 4. Prescribe, 5. Provide information and 6. Monitor and review). The second domain addresses the competencies that the prescriber should demonstrate with respect to prescribing governance (7. Prescribe safely, 8. Prescribe professionally, 9. Improve prescribing practice and 10. Prescribe as part of a team) (Royal Pharmaceutical Society, 2021). Whilst the framework is designed for prescribing pharmacological interventions, it may also serve to guide HCPs in prescribing therapeutic exercise due to its focus on safe, effective, and patient-centred care.

2.7.1.2. WHO International Classification of Functioning, Disability and Health (ICF).

The ICF aims to provide a unified, standardised language and a structured approach for describing health and health-related states. The introduction of the ICF marked a shift from a biomedical model to a biopsychosocial approach, emphasising functionality over disability (World Health Organization, 2024). Unlike earlier WHO classifications that linked disability to the absence of health, the ICF assesses individuals' societal performance regardless of their limitations. This change values individuals' functioning and potential, making the ICF a versatile tool with broader applications than traditional health classifications. The ICF plays a role not only in assessing an individual's functional status but may also help HCPs match interventions and their dosage to specific health needs (Gómez-Salgado et al., 2018, Stucki et al., 2002, World Health Organization, 2024).

2.7.1.3. Operationalising frameworks for exercise prescription in RA.

Exercise is a core intervention in the management of RA (National Institute for Health and Care Excellence, 2018). Drawing on the RPS would support a focus on key competencies while also emphasising shared decision making and a need to stay evidence based. The ICF more strongly recognises the influence between biological, psychological and social factors which are known to be important in exercise interventions and has a focus on function. For conditions like RA, blending the RPS prescribing competency framework and the WHO ICF may offer HCPs a holistic, structured, comprehensive, and individualised approach to exercise prescription:

1. **Focus on impairments**: By detailing common impairments like muscle weakness and joint stiffness, specific targets for exercise interventions may be identified.
2. **Functional focus**: Evaluating what the individual can or cannot do (e.g., opening jars or lifting a kettle) gives HCPs insights into the disease's impact, guiding exercise prescriptions that improve meaningful, everyday outcomes.
3. **Consideration of social and environmental factors**: By including factors like family support and workplace demands, exercise prescription can be tailored to the individual's lifestyle, fostering greater adherence and engagement.
4. **Patient-centred goal setting**: Setting goals aligned with the individual's needs and preferences, exercise prescription can be linked to daily activities, which boosts motivation.
5. **Tracking and adjusting progress**: Using a structured approach to documenting improvements, frameworks support tracking progress and refining exercise prescriptions as needed.
6. **Enhanced multidisciplinary communication**: Using a standardised language, improves coordination across multidisciplinary team, ensuring continuity and consistency in care.

Adopting a framework by which to prescribe therapeutic exercise in RA may enhance confidence, motivation and trust, key mechanisms that have been identified in exercise prescription for other chronic musculoskeletal disorders (Wood et al., 2024). The combination both frameworks (Royal Pharmaceutical Society, 2021, World Health Organization, 2024) may facilitate equal prioritisation on individual based prescription while remaining embedded in evidence-based practice which has been shown to produce positive clinical outcomes and returns on investment (Connor et al., 2023).

2.7.2. Combining the best available evidence with clinical expertise.

It's common for occupational therapists or physiotherapists to be involved in the management of individuals living with RA (National Institute for Health and Care Excellence, 2018). Occupational

therapists and physiotherapists are regulated by the Health and Care Professions Council (HCPC) which sets and maintains standards for the sixteen professions it oversees (Health and Care Professions Council, 2024). Both professions must adhere to these professional standards, including engaging in evidence-based practice (EBP). EBP involves using current best evidence, skills, knowledge, and experience to make care decisions (Health and Care Professions Council, 2023a, Health and Care Professions Council, 2023b). EBP is linked to improved quality of care, patient safety, and positive clinical outcomes (Connor et al., 2023). Defined as the *"the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients"* (Sackett et al., 1996: p71), EBP has gained prominence amongst HCPs over the last thirty years (Lehane et al., 2019).

Therapists generally have positive attitudes towards EBP (Scurlock-Evans et al., 2014, Thomas and Law, 2013). However, implementing EBP in clinical practice is challenging due to reasons such as limited time for consultation, limited access to specialist services and HCP or patient preferences (Bishop et al., 2015, Fischer et al., 2016, Spitaels et al., 2017). For example, physiotherapists treating musculoskeletal disorders, follow guidelines only 50% of the time (Zadro et al., 2019). A study in New South Wales, Australia found that while 96% of physiotherapists valued EBP, factors like patient expectations, colleagues' treatment choices and time constraints hindered implementation (Gleadhill et al., 2022). In Canada, a longitudinal study showed a decline in EBP among 64% of occupational therapists and physiotherapists over the three years following graduation, with therapists increasingly relying on personal and peer experiences due to time constraints and the practicality of applying guidelines (Iqbal et al., 2023). This reliance on familiar experience and peer feedback, especially in complex cases, often takes precedence over searching the scientific literature to make care decisions (Lindström and Bernhardsson, 2018, Walston et al., 2022).

Other challenges exist for HCPs involved in prescribing strengthening exercise for RA. The NICE guideline lacks detailed information on prescribing strengthening exercise and its dose (National Institute for Health and Care Excellence, 2018). Lack of information on dosage is noted across other guidelines in RA (Hurkmans et al., 2011) indicating there is a need for better implementation support (Gagliardi and Brouwers, 2015). Additionally, the quality of evidence may also impact implementation. Examining the evidence used by NICE to underpin its recommendations for therapeutic exercise, twenty-one evidence sources included exercise-based interventions: sixteen single-centre RCTs (Bearne et al., 2002, Buljina et al., 2001, Cima et al., 2013, Delhag et al., 1992, Dogu et al., 2013, Eversden et al., 2007, Häkkinen et al., 2001, Hall et al., 1996, Hansen et al., 1993, Harris and Millard,

1955, Neuberger et al., 2007, O'Brien et al., 2006, Rapolienė and Kriščiūnas, 2006, van den Berg et al., 2006, Van den Ende et al., 1996, van den Ende et al., 2000), four multi-centre RCTs (De Jong et al., 2003, Hammond et al., 2004, Hoenig et al., 1993, Lamb et al., 2015), and one Cochrane systematic review with meta-analysis (Han et al., 2004). Two sources were included in both the 2009 and 2015 guidelines for hand exercise (Hoenig et al., 1993, O'Brien et al., 2006). In 2009, NICE employed the levels of evidence scoring system (Table 2.5). The methodological quality of evidence varied. Four RCTs were rated '1++' (De Jong et al., 2003, Hammond and Freeman, 2004, Han et al., 2004, O'Brien et al., 2006), eight RCTs and the one systematic review were rated '1+' (Bearne et al., 2002, Buljina et al., 2001, Eversden et al., 2007, Hall et al., 1996, Hansen et al., 1993, Hoenig et al., 1993, Neuberger et al., 2007, van den Berg et al., 2006, van den Ende et al., 2000) and four RCTs were rated '1-' (Häkkinen et al., 2001, Harris and Millard, 1955, Rapolienė and Kriščiūnas, 2006, Van den Ende et al., 1996).

Table 2. 5. NICE levels of evidence scoring system.

Level of evidence	Type of evidence
1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias.
1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias.
1-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias.[a]
2++	High-quality systematic reviews of case-control or cohort studies. High-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal.
2+	Well-conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal.
2-	Case-control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal.*
3	Non-analytic studies (for example case reports, case series).
4	Expert opinion, formal consensus.

[a] Studies with a level of evidence '–' should not be used as a basis for making a recommendation.

In the 2015 update where tailored hand exercise was added, the grading of quality shifted to the GRADE system, which rates the quality of evidence for outcomes across studies as 'high', 'moderate', 'low', or 'very low' (National Institute for Health and Care Excellence, 2012). The SARAH multicentre RCT, was rated 'moderate quality' (Lamb et al., 2015) and the remaining five RCTs rated as 'very low quality' (Cima et al., 2013, Delhag et al., 1992, Dogu et al., 2013, Hoenig et al., 1993, O'Brien et al., 2006). The 2009 RCTs (Hoenig et al., 1993, O'Brien et al., 2006) were downgraded to 'very low quality'

for the outcomes of interest (Hoenig et al., 1993, O'Brien et al., 2006), highlighting the impact of the methodological change to assessing quality.

Even where HCPs choose to implement interventions tested by RCT over the recommendations contained in guidelines, they may struggle to replicate the intervention due to poor descriptions of the intervention and its dose parameters (Gallois et al., 2017, Hansford et al., 2022, Hoffmann et al., 2013, Yamato et al., 2016).

2.8. General aims of thesis.

To actualise the full potential of therapeutic strength-based exercise interventions in RA, a thorough understanding about how dosage is both developed prior to evaluation by RCT and prescribed in clinical practice is needed. Therefore, the broad aim of this thesis was to gain a better understanding about the dose of strengthening exercise prescribed with individuals living with RA. To achieve this, the thesis set out to identify how dose has been determined in exercise-based interventions that have been formally evaluated in RCTs. Then, using data from a landmark clinical trial, the dose of hand strengthening exercise prescribed in the SARAH RCT was analysed to identify what dose works best. Lastly, the thesis examined the prescribing judgements of therapists related to hand strengthening exercise in the clinical setting. These aims were achieved through three related studies. The key research questions addressed in this thesis are:

2.8.1. Key research questions.

1. What evidence do researchers use to underpin dose parameters in RCTs evaluating strength-based exercise interventions in RA?

2. Using data from the SARAH RCT:
    a. What factors are associated with the prescribed dose of hand strengthening exercise?
    b. Was prescribed dose of hand strengthening correlated with key clinical outcomes?

3. What factors influence occupational therapists and physiotherapists when prescribing hand strengthening exercise in RA?

A multi-methods approach was taken. The approach and specific aims of each individual study contained in this thesis will be described in the relevant thesis chapter.

CHAPTER THREE. STUDY ONE. A SYSTEMATIC REVIEW EXPLORING THE EVIDENCE REPORTED TO UNDERPIN DOSE IN CLINICAL TRIALS OF RA.

3.1. Study overview.

This chapter provides a rationale for selecting systematic review methodology for this study, a description of the review objectives, the methods used, results and discussion. The review is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher et al., 2015). The protocol was both pre-registered with the International Prospective Register of Systematic Reviews (PROSPERO): PROSPERO 2018 CRD42018090963 and published (Boniface et al., 2018) (Appendix 1). The review was published in Rheumatology (Boniface et al., 2020) (Appendix 2), presented at the virtual physiotherapy UK 2020 conference (Boniface et al., 2021) and reported via social media (i.e. Twitter/X).

3.2. Introduction.

To expand current understanding of how healthcare researchers develop strength-based exercise interventions in RA, systematic review was selected as the appropriate method to investigate the underpinning evidence used to underpin the dose of strength-based exercise interventions evaluated by RCT. Systematic review is a scientific method that draws together evidence meeting pre-specified eligibility criteria to answer the research question/s of interest (Cumpston et al., 2023). Most systematic reviews conducted in health and social care sciences consider the effects of interventions. Consequently, the primary focus is the RCT (Cumpston et al., 2023). Whilst this process was ideal for identifying RCTs using strength-based interventions in RA, additional steps were required to achieve the overarching aim of this study (i.e. to better understand the supporting evidence underpinning dose of strength-based interventions). These are described in the methods.

3.3. Study objectives.

To review all contemporary RCTs evaluating strength-based exercise interventions in adults living with RA. The key objectives of the review were:

1. To determine what proportion of published RCTs evaluating strength-based exercise interventions in RA report using phase-I/II trials for setting dose parameters.
2. To determine what type and level of evidence is used to underpin dose parameters.
3. To explore the quality, consistency and applicability of the evidence used to underpin dose parameters.

4. To narratively explore if a relationship exists between risk of bias for RCT's evaluating strength-based interventions in RA and the level of evidence for underpinning prescription parameters.

3.4. Methods.

3.4.1. Search design.

The following databases were searched: 1) Allied and Complimentary Medicine Database (AMED) via OVID, 2) Cochrane Central Register of Controlled Trials (CENTRAL), 3) Cumulative Index to Nursing and Allied Health Literature (CINAHL) via EBSCOhost, 4) Excerpta Medica Database (EMBASE) via OVID, 5) MEDLINE via OVID and 6) Physiotherapy Evidence Database (PEDro). Search strategies for each database were developed iteratively and included relevant controlled vocabulary terms (e.g., MeSH and EMTREE headings) and free-text terms searched in the title, abstract or keyword fields for variants of 'rheumatoid arthritis', 'exercise' and 'strength' or 'resistance training'. Where available, validated RCT search filters were used including the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE (sensitivity-maximizing version (2008 revision) Ovid format), the McMaster EMBASE RCT search filter (Best balance of sensitivity and specificity) and the SIGN Search Filter for identifying randomised trials in CINAHL (for EBSCO). The review examined the state of contemporary practice in prescribing the dose of strengthening exercise in clinical trials. Therefore, the search was limited to identify RCTs published after 01/01/2000. This date was selected to coincide with the year the Medical Research Council published their original framework for developing and evaluating randomised controlled trials for complex interventions used to improve health (Medical Research Council, 2000). The initial search was run on the 18/05/2018. An update search was run on the 03/04/2019 to identify RCTs that had been published since the initial search. No language restrictions were applied to the searches. The database search strategies used are available as supplementary material (Appendix 3).

3.4.2. Eligibility.

3.4.2.1. Types of studies.

Published RCTs evaluating exercise interventions where a main component (i.e. key feature) of the intervention and/or control included land-based strengthening exercise were included.

3.4.2.2. Types of participants.

RCTs involving adults (males and females ≥18 years old) with a diagnosis of RA were included. Purposefully, the eligibility criteria for diagnosis using one of the common classification criteria's (e.g.,

ARA 1987 revised criteria for the classification of rheumatoid arthritis or 2010 ACR-EULAR Classification Criteria for Rheumatoid Arthritis) was not used. This decision was made to include as many RCTs as possible (Arnett et al., 1988, Kay and Upchurch, 2012). Trials were excluded that included participants with conditions other than RA (e.g., osteoarthritis).

3.4.2.3. Types of interventions.

Strengthening exercise could involve the trial participants using equipment (e.g., free weights/machines), or their own bodyweight to provide resistance against gravity (e.g., sit-to-stand exercise). The intervention could be unsupervised (e.g., home-based), supervised (e.g., by a therapist) or both and carried out individually or in a group. The strength-based intervention could be multifactorial (e.g., used in conjunction with cointerventions like education), or multicomponent (e.g., used with other forms of exercise like aerobic or flexibility exercise).

3.5. Data collection and analysis.

3.5.1. Selection of RCTs.

Two review authors independently screened the titles and abstracts of records obtained through the database search. The title and abstract were examined and those meeting the above eligibility criteria were retrieved for further evaluation. When disagreement existed, resolution was achieved through consensus. If this was not possible, resolution was achieved using a third review author.

3.5.2. Data extraction and management.

Two review authors extracted data independently from every included RCT using a standardised data extraction form on Excel. This form was developed and piloted by both authors using two RCTs investigating knee osteoarthritis interventions prior to the searches (Loew et al., 2017, Thomas et al., 2002). The final form collected general information about the RCT (e.g., country, clinical setting, aims/objectives etc.) and participant (e.g., age, gender, ethnicity etc.). Specific information related to the intervention and control was collected using the Template for Intervention Description and Replication (TIDieR) checklist and guide (Hoffmann et al., 2014). Item 8 (When and how much) of TIDieR, taking direction from the Consensus on Exercise Reporting Template (CERT) was used to extract key information about the dose of the strengthening exercise used (Slade et al., 2016a). Key dose parameters included exercise type, equipment used, sets, repetitions, load, intensity, method of recovery, method of progression, frequency of exercise sessions and programme duration. These dose parameters were chosen because they are important for prescribing exercise interventions in both clinical research and practice (Kent et al., 2018, Slade et al., 2016a, Slade et al., 2016b, Slade and

Keating, 2012). Underpinning evidence reported to underpin the dose parameters above was also identified so that its quality, consistency, and applicability to the exercise dose used in the RCT could be evaluated. For example (Figure 3.1), should the healthcare researchers of the index RCT cite a pilot study, that study was located, and the evidence used to underpin dose parameters identified for appraisal. Alternatively, if the index RCT cited an exercise guideline, the evidence most relevant to the dose parameters used in the RCT was identified for appraisal. This approach can be likened to developing a family tree.

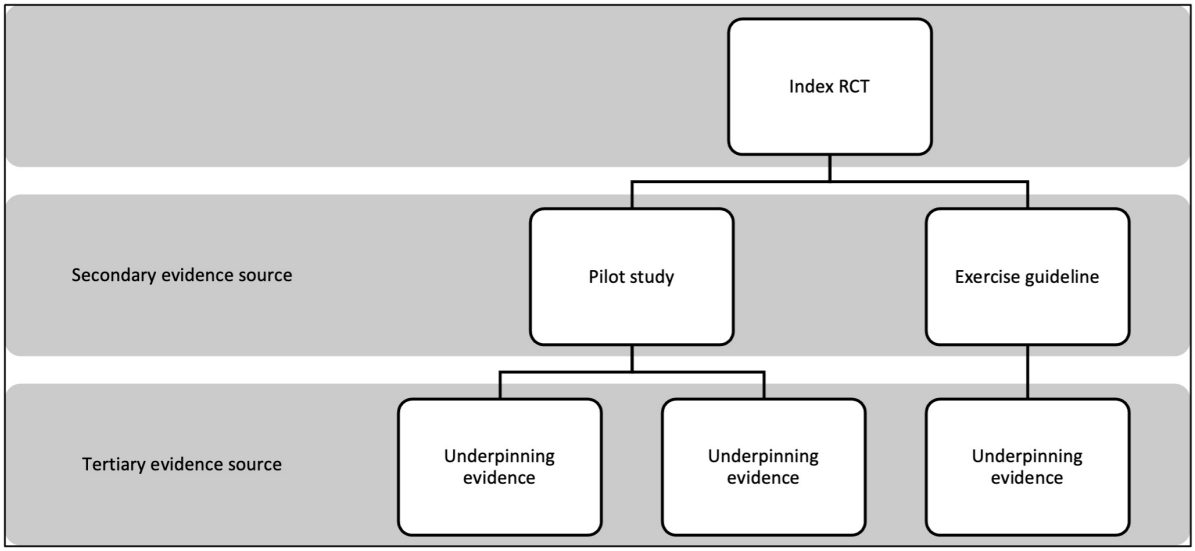

Figure 3. 1. Identifying methods used to underpin dose.

This was done by first looking in the section describing the intervention. If no underpinning evidence could be identified, the reviewers proceeded to check the rest of the manuscript. Underpinning evidence was only identified for retrieval if the trial authors explicitly stated they had been used to develop or justify the dose of strengthening exercise. If this was not clear, resolution was achieved through consensus or recourse to a third review author. Where appropriate intervention and/or protocol publications linked with the RCT were used to assist with extracting information about the intervention and to identify underpinning evidence sources. The quality, consistency and applicability of the underpinning evidence was then appraised.

3.6. Process for evaluating the underpinning evidence.

3.6.1. Assessment of quality.

For each underpinning evidence source identified, the Oxford Centre for Evidence Based Medicine (OCEBM) – levels of evidence were used to grade its quality, using the framework's question "does this treatment help?" (Howick, 2011a, Howick, 2011b, OCEBM Levels of Evidence Working Group, 2016). This tool was chosen because it offered framework that considered a range of possible evidence types and designs, assigning included evidence sources a hierarchical rating in terms of rigour. It's also a simple and standardised approach to grading evidence, something that could be easily understood by busy clinicians. The levels of evidence range from 1 to 5 where 1 = Systematic review of RCTs or n-of-1 trials, 2 = Randomised trial or observational study with dramatic effect, 3 = Non-randomised controlled cohort/follow-up study, 4 = Case-series, case-control studies, or historically controlled studies and 5 = Mechanism-based reasoning.

Grading using the above framework was relatively straightforward. However, when the evidence source cited to underpin dose was a pilot study, literature review, guideline, or book, to be more accurate with grading, the evidence used by these specific sources had to be explored. Pilot studies normally act as a pre-cursor for a more confirmatory study, therefore, to grade quality, the evidence (if any) reported by the pilot study to underpin dose was identified. For literature reviews, guidelines, and books, (where possible) the references used by these evidence sources that were most relevant to the dose parameters reported in the RCT were identified. These types of documents commonly draw on large bodies of published information to make recommendations. An example of this type of evidence source used in exercise are the ACSM position stands (Kraemer et al., 2002). Therefore, when the RCT reported using a specific part of the source to support dose, that part was located to identify the specific references which helped with grading quality of the underpinning evidence. If the RCT did not report using specific part of the cited evidence source, a pragmatic approach was adopted, and the dose parameters reported in the RCT were used to help focus the search for references. In cases where grading the level of evidence was not possible, for example, the RCT reported insufficient information about the dose parameter, or the underpinning evidence source failed reference its text clearly, the quality of the underpinning evidence was graded as 'unclear'. In cases where the underpinning evidence was judged not to support the dose parameter (e.g., not relevant to strengthening exercise or the reported evidence was cited incorrectly), the level of evidence was graded as 'incorrect citation'.

3.6.2. Assessment of consistency.

Consistency was judged by comparing the dose parameters (e.g., type of exercise used, number of sets etc.) reported by the RCT to the dose parameters reported in underpinning evidence. When dose was identical or kept within the range reported by the underpinning evidence, the RCT was judged as being 'consistent' in using the same dose. When the RCT used a different dose to that reported, the RCT was judged as being 'inconsistent'. Where the RCT and/or underpinning evidence insufficiently described the dose used, no comparison could be made and was therefore judged to be 'unclear'. Pilot studies were approached differently, assuming the characteristics of dose would be broadly similar. Therefore, any differences in dose were judged to be 'inconsistent'.

3.6.3. Assessment of applicability.

Applicability was judged by looking for areas of homogeneity/heterogeneity across three areas: 1) Whether the underpinning evidence source was applicable to RA clinical population; 2) Whether a similar gender mix was used and 3) Whether the mean age was similar (+/- 10years). These three areas were judged as 'applicable' or 'not applicable'. In cases where the underpinning evidence source was not a clinical trial (e.g., literature review, clinical guideline, or book) and there was no definitive population to assess, gender and age were judged to be 'not applicable'.

3.6.4. Assessment of risk of bias (RoB).

Two review authors assessed risk of bias for each of the RCT sources using the six key domains of the Cochrane risk of bias tool (version 1): 1) Adequate sequence generation, 2) Allocation concealment, 3) Blinding of participants and personnel, 4) Blinding of outcome assessors, 5) Incomplete outcome data, 6) Selective reporting and, 7) Other risk of bias (Higgins et al., 2011). Due to the nature of the intervention, all included RCTs were at high risk of bias for lack of blinding of participants and personnel. However, since this bias is largely unavoidable, for the purposes of contrasting studies on their overall risk of bias, this criterion was excluded. Studies characterised to be at low RoB (all categories assessed as low RoB), unclear RoB (any category rated as unclear RoB) or high RoB (one or more categories assessed as high RoB). For secondary/tertiary evidence sources, the same approach was used where the record was a RCT. If the trial was a non-randomised controlled cohort design, originally the Cochrane Risk Of Bias In Non-randomised Studies - of Interventions (ROBINS-I) tool was going to be used (Sterne et al., 2016). However, the Cochrane risk of bias tool was considered better suited to this task because the secondary/tertiary evidence sources frequently used experimental designs. Disagreement was resolved through discussion, using a third review author, when required.

3.7. Results.

The search and screening process is summarised in the PRISMA study flow diagram (Figure 3.2). A total of 4382 records were identified. Thirty-two RCTs were included (Anvar et al., 2018, Bearne et al., 2002, Breedland et al., 2011, Buljina et al., 2001, Cima et al., 2013, De Jong et al., 2003, Dogu et al., 2013, Dulgeroglu et al., 2016, Durcan et al., 2014, Eversden et al., 2007, Flint-Wagner et al., 2009, Hakkinen et al., 2001, Jahanbin et al., 2014, Lamb et al., 2015, Lange et al., 2018, Lemmey et al., 2009, Lourenzi et al., 2017, Manning et al., 2014, Mohanty et al., 2018, Neuberger et al., 2007, O'Brien et al., 2006, Piva et al., 2018, Rahnama and Mazloum, 2012, Seneca et al., 2015, Shinde and Varadharajulu, 2017, Strasser et al., 2011, Tonga et al., 2016, van den Berg et al., 2006, van den Ende et al., 2000, Van Rensburg et al., 2010, van Rensburg et al., 2012, Veitiene and Tamulaitiene, 2004). Almeida & Piva (2011) was published as a conference abstract (Almeida and Piva, 2011), however after contacting the authors, we were provided with the full-text which was published as Piva et al, 2018 (Piva et al., 2018). This RCT was included for full-text extraction. The characteristics of the included RCTs are reported in Table 3.1.

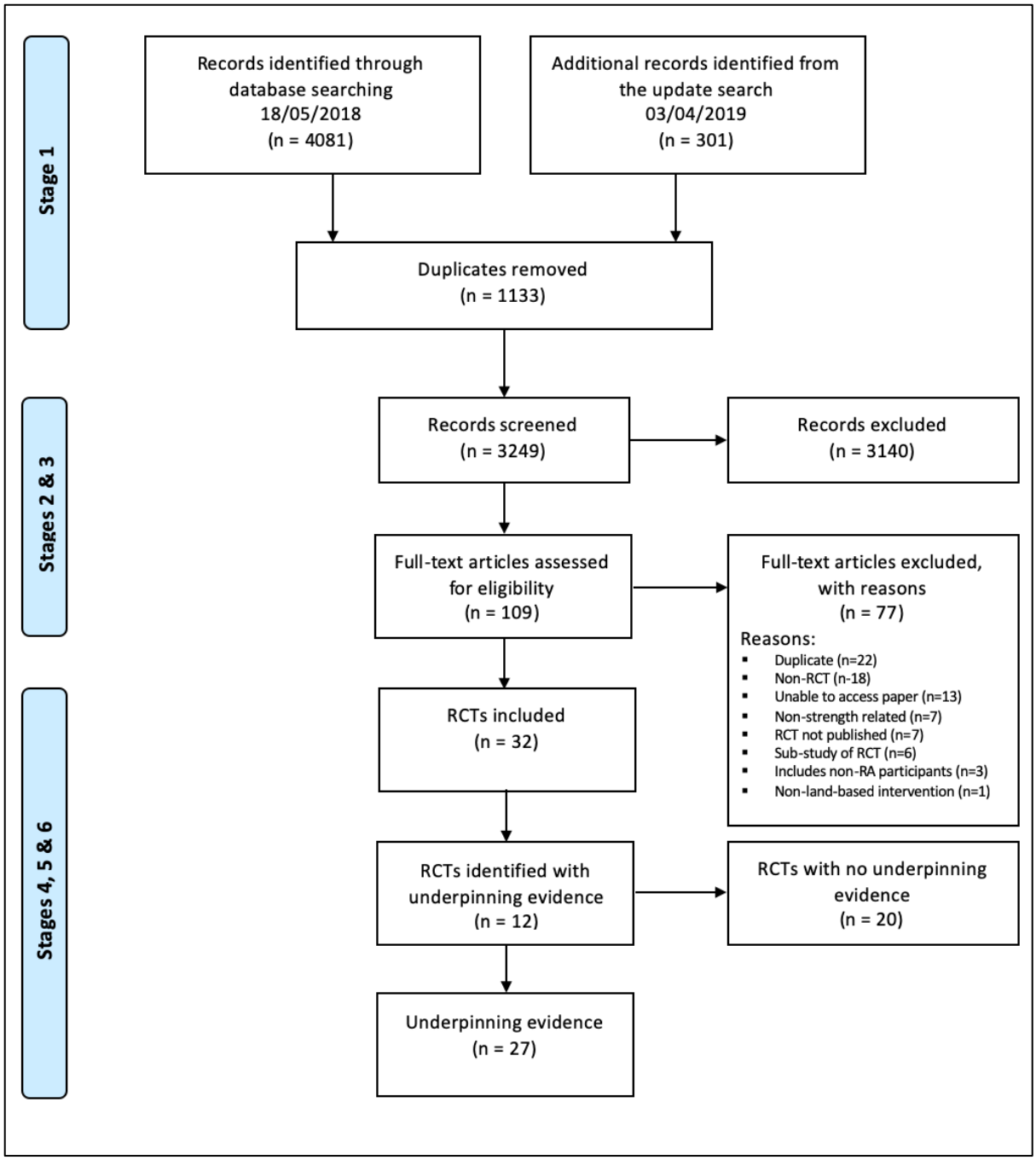

Figure 3. 2. PRISMA study flow diagram search screening process.

Table 3. 1. Characteristics of included primary evidence sources (presented in chronological order of publication).

Author and year + Country of origin	Primary aim	Sample characteristics		Intervention content	
		Control group	Intervention group	Control group	Intervention group
van den Ende et al (2000) Netherlands	To examine the consequences of an intensive exercise regimen on disease activity in active RA.	n=30 Mean age: 58 ± 14 Male/female: 41%/59%	n=34 Mean age: 62 ± 13 Male/female: 41%/59%	Conservative exercise programme that included range of movement (ROM) exercises for hands and feet and isometric exercises for the larger joints. Strength exercises used: 1. Isometric exercises of the larger joints.	Control intervention plus a dynamic, intensive exercise regime of isometric and isokinetic exercises and cycling using a home trainer. Strength exercises used: 1. Isometric shoulder girdle in prone position. 2. Isometric knee extensor/flexor. 3. Isokinetic knee extensor/flexor. Duration: Unclearly reported. Follow-up: 24 weeks
Buljina et al (2001) Bosnia and Herzegovina	To study the short-term effects of physical therapy (ice massage or wax packs, thermal baths, and faradic hand baths) and exercise therapy on the rheumatoid hand.	n=50 Mean age: 48.46 ± 10.65 Male/female: 26%/74%	n=50 Mean age: 47.94 ± 11.22 Male/female: 24%/76%	Waiting list control – participants waited 4 weeks until enrolment into physical and exercise therapy programme.	Physical and exercise therapy programme including thermal baths, therapeutic heat or cold, faradic hand baths and wax bath treatment. Strength exercises used: 1. Finger abduction. 2. Finger adduction. 3. Gross grip. Duration: 3 weeks. Follow-up: 3 weeks

Hakkinen et al (2001) Finland	To investigate whether the 24-month strength training program used to increase muscle strength and physical function in patients with early RA also produces positive effects on bone mineral density in these patients.	n=31 Mean age: 49 ± 11 Male/female: 35%/65%	n=31 Mean age: 49 ± 10 Male/female: 42%/58%	ROM and stretching exercises and free to continue recreational activities except for strength training of any kind.	Dynamic strength training. Strength exercises used: 1. Exercises for upper and lower extremities using resistance bands. 2. Abdominal and back exercises using dumbbells. Duration: 24 months. Follow-up: 24 months.
Bearne et al (2002) UK	To compare quadriceps sensorimotor function, lower limb functional performance and disability in patients with RA and healthy subjects, and to investigate the efficacy and safety of a brief rehabilitation regime.	Waiting list control group: n=46 Mean age: 59.5 (range: 30–82) Male/female: Unclear Healthy subjects (comparative group) n=25 Mean age: 65.5 (range: 50–82) Male/female: 36%/64%	n=47 Mean age: 59.5 (range: 30 - 82) Male/female: Unclear	Waiting list control - participants waited 8 weeks before being invited to take part in the progressive exercise programme.	Progressive, individually tailored exercise programme including strength, functional and balance exercise. Strength exercises used: 1. Isometric quadriceps. 2. Functional exercises (e.g. sit to stand, step-up's etc.). Duration: 10 weeks. Follow-up: 12 months.

De Jong et al (2003) Netherlands	To compare the effectiveness and safety of a long-term intensive exercise program with those of physical therapy (usual care)	n=158 Mean age: 53.5 (18) IQR Male/female: 21%/79%	n=151 Mean age: 54.0 (16) IQR Male/female: 21%/79%	Only treated by a physical therapist if this was regarded as necessary by their attending physician.	Rheumatoid Arthritis Patients In Training (RAPIT Programme). Each session included warm-up, bicycle training, exercise circuit, sport or game and cool-down. Strength exercises used: Unclear. Duration: 24 months. Follow-up: 24 months.
Veitiene and Tamulaitiene (2004) Lithuania	To compare the efficiency of home and outpatient exercise program in patients with RA.	n=21 Mean age: 59.8 ± 11.1 Male/female: 5%/95%	n=10 Mean age: 64.4 ± 9.4 Male/female: 0%/100%	ROM and isometric strength exercise programme supervised in the outpatient department. Strength exercises used: 1. Sit-up exercises on the back 2. Isometric exercises	ROM and isometric strength exercise programme conducted at home. Duration: 3 months. Follow-up: 3 months.
O'Brien et al (2006) UK	To evaluate the clinical effectiveness of three different hand therapy approaches (two of which employed different hand exercise regimes) on changes in impairment and activity limitation in patients with RA over a 6-month period.	n=103 Mean age: 65 ± 8 Male/female: 21%79%	Group 1: n=21 Group 2: n=24 Mean age: 65 ± 7 Male/female: unclear (reported 25%/75% for group 1 + 2)	Joint protection literature covering the basic principles of joint protection, energy conservation, 'top tips' relating to personal and household activities, postural advice, types of splinting and issues related to sexuality.	Group 1: Control and eight strengthening and mobilising exercises. Strength exercises used: 1. Pinch grip exercises 2. Strengthening the intrinsic/thenar eminence muscles (using a towel). 3. Wrist extension with Theratubes band. Duration: 6 months. Follow-up: 6 months. Group 2: Control and eight stretching exercises, without any specific strengthening exercises. Duration: 6 months. Follow-up: 6 months.

van den Berg et al (2006) Netherlands	To compare the effectiveness of two internet-based physical activity interventions for patients with rheumatoid arthritis.	n=78 Mean age: 49.8 (13.9) median (IQR) years (Mean age: + SD not reported) Male/female: 23%/77%	n=82 Mean Age: 49.5 (12.9) median (IQR) years (Mean Age: + SD not reported) Male/female: 24%/76%	Access to web pages where general information about aerobic, muscle strengthening, and range of movement exercises and the promotion of physical activity in patients with RA was presented.	Access to web pages where individualised training intervention consisting of muscle strengthening exercises, ROM exercise and cycling on a bicycle ergometer was presented. Strength exercises used: Not described. Duration: 12 months. Follow-up: 12 months.
Eversden et al (2007) UK	To compare individualised exercises whilst immersed in a heated pool to similar exercises on land for their effect on overall improvement in health, physical function, and quality of life in people with RA.	n=58 Age: 56.1 ± 11.9 Male/female: 32%/68%	n=57 Age: 55.2 ± 13.3 Male/female: 28%/72%	Land based exercise including mobilising and stretching, joint mobility, muscle strength and functional activities. Strength exercises used: Not described. Duration: 6 weeks. Follow-up: 3 months.	Hydrotherapy exercises including mobilising and stretching, joint mobility, muscle strength and functional activities.

Neuberger et al (2007) United States of America	To determine the effects of participation in a low-impact aerobic exercise program on fatigue, pain, and depression; to examine whether intervention groups compared with a control group differed on functional (grip strength and walk time) and disease activity (total joint count, erythrocyte sedimentation rate, and C-reactive protein) measures and aerobic fitness at the end of the intervention; and to test which factors predicted exercise participation.	n=105 Mean age: (entire sample 55.5 years (range 40–70 years)) Male/female: Unclear (entire sample 82.7% were women)	Class exercise group n=102 Mean age: Not described (Entire sample 55.5 years (range 40–70 years)) Male/female: Not described (entire sample 82.7% were women) Home exercise group n=103 Mean age: Not described (entire sample 55.5 years (range 40–70 years)) Male/female: Not described (entire sample 82.7% were women)	Asked to keep exercise levels at baseline amounts.	Class exercise group: The exercises were performed at a fitness centre and consisted of 4 phases: warm-up, low-impact aerobics, strengthening, and cool-down exercises. Strength exercises used: Unclear. Duration: 12 weeks. Follow-up: 12 weeks. Home exercise group: The exercises were performed at home using a video recording and consisted of 4 phases: warm-up, low-impact aerobics, strengthening, and cool-down exercises. Strength exercises used: Unclear. Duration: 12 weeks. Follow-up: 12 weeks.

Flint-Wagner et al (2009) United States of America	To investigate the effects of a 16-week, high-intensity, individualized, strength training program in infliximab-treated RA patients.	n=8 Mean age: 49.0 ± 12.6 Male/female: Not described	n=16 Mean age: 52.2 ± 13 Male/female: Not described	Continued with care overseen by their rheumatologists	Exercise programme: included a walking warm-up, strength training, aerobic exercise, abdominal exercises, and a cool-down period with walking and static stretching. Strength exercises used: 1. Incline press. 2. Row. 3. Hammer curl. 4. Leg press. 5. Leg curl. 6. Hip abduction. 7. Hip adduction. 8. Calf raises. Duration: 16 weeks. Follow-up: 16 weeks.
Lemmey et al (2009) UK	To confirm preliminary observations (i.e. that progressive resistance training reverses debilitating cachexia and improves function in patients with RA) and to investigate the role of the local IGF system in exercise-induced hypertrophy of skeletal muscle in patients with RA.	n=18 Mean age: 60.6 ± 11.2 Male/female: 16%/84%	n=18 Mean age: 55.6 ± 8.3 Male/female: 20%/80%	Home ROM exercises.	Progressive resistance training + low intensity ROM exercises. Strength exercises used: 1. Chest press. 2. Rowing. 3. Bicep curl. 4. Triceps extension. 5. Seated leg extension. 6. Leg press. 7. Leg curl. 8. Standing calf raises. Duration: 24 weeks. Follow-up: 24 weeks.

van Rensburg et al (2010) South Africa	To measure the effect of an endurance training programme on the fitness parameters, quality of life and disease activity of females suffering from RA.	n=12 Mean age: 49.7 ± 4.3 Male/female: 0%/100%	n=25 Mean age: 47.3 ± 9.2 Male/female: 0%/100%	Continue with their sedentary lifestyles.	Land exercise group: Warm-up phase, aerobic exercise, strength training, and flexibility training. Strength exercises used: Unclear. Duration: 12 weeks. Follow-up: 12 weeks. Aquatic exercise group: Exercise programme consisting of a warm-up phase, aerobic exercise, strength training, and flexibility training.
Breedland et al (2011) Netherlands	To evaluate the effects of a group-based exercise and educational program on the physical performance and disease self-management of people with RA.	n=15 Mean age: 51.8 ± 9.4 Male/female: 37%/63%	n=19 Mean age: 45 ± 11.9 Male/female: 20%/80%	Waiting list control	The FIT programme: 8-week, multidisciplinary group therapy program, consisting of physical exercise designed to increase aerobic capacity and muscle strength (force-generating capacity) with an educational programme to improve health status and self-efficacy for disease-self-management. Strength exercises used: 1. Chest press. 2. En Tree pulley device. 3. Rowing. 4. Leg press. 5. Leg extension. 6. Leg curl. 7. Abdominal trainer. 8. Back trainer. Duration: 8 weeks. Follow-up: 22 weeks.

Strasser et al (2011) Austria	To evaluate the effects of 6 months of combined strength and endurance training on: (1) the disease activity and functional ability in patients with RA and (2) the muscle strength, cardio-respiratory fitness, and anthropometry parameters in RA patients.	n=20 Mean age: 55.6 ± 9.7 Male/female: 15%/85%	n=20 Mean age: 59.3±7.9 Male/female: 5%/95%	Stretching exercises + normal recreational activities (except strength and endurance)	Strength training programme: Exercises for major muscle groups. Endurance training was performed on a cycle ergometer. Strength exercises used: 1. Bench press (pectoralis). 2. Chest cross (horizontal shoulder flexion). 3. Shoulder press (trapezius). 4. Pull downs (latissimus dorsi). 5. Bicep curls. 6. Triceps extension. 7. Leg press (quadriceps femoris). 8. Abdominal exercises.
Rahnama et al (2012) Iran	To investigate the effects of two types of rehabilitation techniques, including aerobic and strengthening exercises on patients with knee rheumatoid arthritis.	n=16 Mean age: 59.6 ± 8.3 Male/female: 100%/0%	Strength group n=16 Mean age: 57.0 ± 7.4 Male/female: 100%/0% Aerobic group n=16 Mean age: 59.4 ± 8.1 Male/female: 0%/100%	Beseeched to follow their ordinary lifestyle.	Strength Group: Progressive strength exercise Strength exercises used: 1. Quadriceps. 2. Hamstrings. Duration: 6 months. Follow-up: 6 months. Aerobic group: 1. Each subject ran on the treadmill for about 30 minutes, while the speed was set according to the patient ability.

van Rensburg et al (2012) South Africa	The aim of the current study was to evaluate the effect of exercise on cardiac autonomic function as measured by short-term heart rate variability in RA patients.	n=22 Mean age: 47.08 ± 7.05 Male/female: 0%/100%	n=24 Mean age: 46.81 ± 9.23 Male/female: 0%/100%	Continue with their sedentary lifestyle.	Exercise intervention: Warm-up exercises, strengthening exercises, aerobic exercises and a cool down period which included stretching. Strength exercises used: 1. Chest press. 2. Bicep curls. 3. Lateral pull-downs. 4. Hip extension. 5. Leg press. 6. Hamstring curls. 7. Hip abduction. Duration: 12 weeks. Follow-up: 12 weeks.
Cima et al (2013) Brazil	To evaluate the effects of an exercise programme aimed at improving the force of intrinsic and extrinsic hand muscles of individuals who have RA hand deformities as well as to analyse the impact of these exercises on hand functionality.	n=7 Mean age: 60.4 ±7.4 years Male/female: 0%/100%	n=13 Mean age: 53 ±10 years Male/female: 0%/100%	No exercise for wrist and hand muscles.	Rehabilitation programme: Consisted of exercises to strengthen the intrinsic and extrinsic muscles of the hands. Strength exercises used: 1. Digiflex hand exerciser. 2. Flexed fingers squeezing the modelling mass. 3. Co-ordination movement of the flexo-extension of the fingers with the modelling mass. 4. Exercises for the intrinsic muscles with the modelling mass. 5. Pulp to pulp finger pinch performed with all fingers pulling an elastic band. 6. Exercises for hand intrinsic muscles with elastic. 7. Exercises for the hand intrinsic muscles with the modelling mass. Duration: 10 weeks. Follow-up: 10 weeks.

Dogu et al (2013) Turkey	To evaluate the effect of 6-week-long isotonic and isometric hand exercises on pain, hand functions, dexterity, and quality of life in women diagnosed as RA. The secondary objective of our work was to evaluate the effects of both exercise types on handgrip strength and disease activity	n=24 Age: 50.38 ± 9.32 years Male/female: 0%/100%	n=23 Age: 54.91 ± 9.27 years Male/female: 0%/100%	Isometric hand exercises and wax bath. Strength exercises used: 1. Push hands by facing palms towards each other. 2. Ulnar deviation against pressure with fingers in flexion. 3. Pushing lid of the perfume bottle while interphalangeal (IP) joint of the thumb in flexion. 4. Abduction/adduction by placing the hands of the physician in between fingers. 5. Fingers at 90˚ metacarpophalangeal (MCP) flexion, flexion, and extension of the fingers against pressure. 6. Gripping a glass of water placed into the hand. Duration: 6 weeks. Follow-up: 6 weeks.	Isotonic hand exercises (ROM exercise) and wax bath.
Durcan et al (2014) Ireland	To evaluate the effect of an exercise program on self-reported sleep quality and fatigue in RA.	n=38 Age: 59 ± 12 years Male/female: 47%/53%	n=42 Age: 61 ± 8 years Male/female: 25%/75%	The control group was composed of patients with RA who received advice only on the benefits of exercise in RA.	12-week home exercise programme targeting deficiencies in strength, ROM and coordination and walking programme. Strength exercises used: 1. Major muscle groups. 2. Functional exercises. Duration: 12 weeks. Follow-up: 12 weeks.

Jahanbin et al (2014) Iran	To investigate the effects of conditioning exercises on the health status and pain in patients suffering from RA.	n=33 Mean age: 48.87 ± 9.24 Male/female: Not described	n=32 Mean age: 48.6 ± 10.51 Male/female: Not described	Not described	Physical training programme consisting of conditioning exercises included aerobic, isometric, and isotonic exercises. Strength exercises used: 1. Isometric exercise. 2. Isotonic exercise. Duration: 8 weeks. Follow-up: 8 weeks.
Manning et al (2014) UK	To evaluate the effectiveness of a brief supervised education, self-management, and global upper extremity exercise training program, supplementing a home exercise regimen, for people with RA; the Education, Self-Management, and Upper Extremity Exercise Training in People with Rheumatoid Arthritis (EXTRA) program).	n=56 Mean age: 57 ± 15) Male/female: 32%/68%	n=56 Mean age: 53 ± 16 Male/female: 14%/86%	Usual care - continued to be managed by their medical team.	Education, Self-Management, and Upper Extremity Exercise Training for People with Rheumatoid Arthritis (EXTRA) program (4 group sessions and home programme). Strength exercises used: (6 out 16 exercises used) 1. Putty ball squeeze. 2. Putty fingertip pinch. 3. Putty finger hook and squeeze. 4. Knife and fork putty cutting. 5. Paper clips and envelope challenge. 6. Wrist alphabet with band. 7. Back scrub. 8. Up and out of chair. 9. Arm curl with band. 10. Lift to chin with band. 11. Reach back with band. 12. Side lift with band. 13. Wall wash squares with band. 14. Door push with band. 15. Shoulder rotation with band. 16. Reach to shelf with band. Duration: 12 weeks. Follow-up: 36 weeks.

Lamb et al (2015) UK	To estimate, for people whose RA is controlled by various drug regimens, the effectiveness and cost-effectiveness of adding an individually tailored, progressive exercise programme for the hands and arms, in addition to best practice usual care.	n=244 Mean age: 63·5 ± 11 Male/female: 24%/76%	n=246 Mean age: 61·3 ± 12 Male/female: 24%/76%	Usual care (Joint protection, education and where indicated, functional splinting).	Usual care and exercise programme consisting of strengthening and ROM exercises. Strength exercises used: 1. Eccentric wrist extension. 2. Gross grip. 3. Finger adduction. 4. Pinch grip. Duration: 12 weeks. Follow-up: 12 months.
Seneca et al (2015) Denmark	To compare the effect of a partly supervised and a self-administered intensive exercise programme in patients with early RA.	n=26 Mean age: 61 (range 27-79) Male/female: 31%/69%	n=25 Mean age: 61 (range 27-79) Male/female: 32%/68%	Self-administered strength and aerobic exercise. Strength exercises used: Not described	Partly supervised strength and aerobic exercise. Strength exercises used: 1. Shoulder. 2. Legs. 3. Trunk extensors/flexors. Duration: 12 weeks. Follow-up: 12 weeks.

Dulgeroglu et al (2016) Turkey	To evaluate whether the galvanic electrotherapy can relieve rheumatic hand pain and whether conservative hand exercises increase the hand strength.	n=14 Median age: 51.5 (range 51 to 68 years) Male/female: 0%/100%	n=16 Median age: 55 (range 50 to 75 years) Male/female: 0%/100%	Home conservative exercise programme consisting of gentle exercises performed against resistance and ROM exercise. Strength exercises used: 1. Ulnar deviation of the wrist (with fingers flexed). 2. Flexing the fingers into a fist. 3. Extending the fingers. 4. Touching the tip of each finger with the thumb. 5. Rolling a 'ball' with the palm on the table with fingers extended. 6. Radial finger walking with the four ulnar fingers moving towards the thumb. 7. Abduction of the thumb with the IP joint flexed. Duration: 10 days. Follow-up: 5 weeks.	Control and galvanic electrotherapy.
Tonga et al (2016) Turkey	This study aims to examine the effectiveness of client-centred occupational therapy in patients with rheumatoid arthritis (RA). al therapy in patients with RA.	n=20 Age: 55.80±10.33 Male/female: (2 males and 38 females in trial)	n=20 Age: 51.35±11.57 Male/female: (2 males and 38 females in trial)	Ten sessions of physical therapy program were implemented on the control group consisting of pain management (hot-packs, cold-packs, and electrotherapy); exercises for stretching and strengthening; and educational therapy approaches (joint protection techniques, energy conservation techniques, splint and assistive devices use, etc.) Strength exercises used: Unclear. Duration: Unclearly reported. Follow-up: 4 weeks.	Control and 4 extra sessions delivering the Canadian Occupational Performance Measure.

Lourenzi et al (2017) Brazil	To evaluate the effectiveness of an overall progressive resistance strength program involving muscles of upper/lower limbs and trunk, regarding physical functional, pain, health-related quality of life and muscle strength.	n=27 Mean age: 50.88 ± 8.57 Male/female: 9%/91%	n=33 Mean age: 52.63 ± 7.10 Male/female: 7%/93%	The control group were contacted by the principal investigator by telephone or email at least once a week to identify complications and to improve patient compliance. After finishing all evaluations, the patient had access to the progressive resistance strength program if desired.	Progressive resistance strength programme. Strength exercises used: 1. Shoulder abductors. 2. Wrist extensors/flexors. 3. Elbow extensors/flexors. 4. Knee extensors/flexors. 5. Hip adductors/abductors. 6. Trunk extensors/flexors. Duration: 12 weeks. Follow-up: 24 weeks.
Shinde and Varadharajula (2017) India	To study the effect of therapeutic exercise programme on adults with early RA" was conducted to determine effect of Therapeutic exercise programme on functional status, maximum grip strength & perceived health in adults with early RA.	n=15 Mean age: Not described Male/female: Not described	n=15 Mean age: Not described Male/female: Not described	Conventional therapy including general patient information, pain modulating modalities and prescriptions of hospital-based training or home exercise programmes.	Group therapeutic exercise programme consisting of strength, aerobic and ROM exercises. Strength exercises used: 1. Isometric exercises. 2. Dynamic resisted exercises for the major muscle groups. Duration: 12 weeks. Follow-up: 6 months.
Anvar et al (2018) Iran	To determine the effectiveness of a self-management program amongst older women with RA.	n=40 Mean age: 69.03 ± 1.43 Male/female: 0%/100%	n=40 Mean age: Unclear Male/female: 0%/100%	Usual care	Arthritis self-management programme consisting of consisted of a stretching, endurance, and light resistance exercises. Strength exercises used: 1. Light resistance exercises. Duration: 6 weeks. Follow-up: 4 months.

Lange et al (2018) Sweden	To evaluate the effect of a person-centred, moderate -to -high intensity, aerobic and resistance exercise protocol on older adults with RA.	n=38 Mean age: 70.11 ± 2.30 Male/female: 24%/76%	n=36 Mean age: 69.14 ± 2.61 Male/female: 25%/75%	One individual meeting with the physiotherapist where they were encouraged to perform home-based exercise according to the same protocol as the intervention group, but no gym-based exercise. Strength exercises used: 1. Strength in the lower extremity.	Person-centred, supervised, exercise intervention consisting of aerobic and resistance exercise. Strength exercises used: 1. Seated row. 2. Leg press. 3. Knee extension. 4. Bicep curl. 5. Core stability. Duration: 20 weeks. Follow-up: 12 months.
Mohanty et al (2018) India	To compare the effect of Proprioceptive retraining technique over home exercise program on hand functions in RA.	Proprioceptive group n=20 Mean age: 44.85 ± 7.35 Male/female: 20%/80%	Home exercise group n=20 Mean age: 47.10 ± 6.98 Male/female: 15%/85%	Grip exercise activity, weighted pulley activity for fingers, lifting dumbbells with hand, wrist roller activity and stretch and hold of bilateral counterpart fingers. Strength exercises used: 1. Grip exercise activity. 2. Weighted pulley activity for fingers 3. Lifting dumbbells with hand.	Simple movements of wrist, and finger joints, thumb movement performed against resistance, touching the base of each finger, volar and dorsal flexion of wrist, pronation and supination of forearm, and tendon gliding exercises. Strength exercises used: 1. Simple movements of wrist, and finger joints, thumb movement performed against resistance.
Piva et al (2018) United States of America	To compare the feasibility and effectiveness of neuromuscular electrical stimulation with high-intensity volitional resistance training in improving muscle structure and function, and physical function in patients with RA.	n=31 Mean age: 61.0 ± 11.0 Male/female: 18%/82%	n=28 Mean age: 57.2 ± 8.6 Male/female: 19%/81%	Volitional exercise consisting of leg extension and leg press using machines. Strength exercises used: 1. Leg extension. 2. Leg press.	Neuromuscular electrical stimulation.

3.7.1. Risk of bias assessment.

Eight RCTs (25%) were assessed to be at overall low RoB, (Breedland et al., 2011, Lamb et al., 2015, Lange et al., 2018, Lourenzi et al., 2017, Manning et al., 2014, O'Brien et al., 2006, Piva et al., 2018, van den Berg et al., 2006) eleven RCTs (34%) to be at unclear RoB (Anvar et al., 2018, Dogu et al., 2013, Dulgeroglu et al., 2016, Durcan et al., 2014, Hakkinen et al., 2001, Lemmey et al., 2009, Mohanty et al., 2018, Neuberger et al., 2007, Strasser et al., 2011, Tonga et al., 2016, van den Ende et al., 2000) and thirteen (41%) RCTs to be at high RoB (Bearne et al., 2002, Buljina et al., 2001, Cima et al., 2013, De Jong et al., 2003, Eversden et al., 2007, Flint-Wagner et al., 2009, Jahanbin et al., 2014, Rahnama and Mazloum, 2012, Seneca et al., 2015, Shinde and Varadharajulu, 2017, Van Rensburg et al., 2010, van Rensburg et al., 2012, Veitiene and Tamulaitiene, 2004) (Table 3.2).

Table 3. 2. Results of the RoB assessment for each included study.

RCT	Sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessors for all outcomes	Incomplete outcome data for all outcomes	Selective outcome reported	Other sources of bias
van den Ende et al (2000)	✓	✓	×	✓	?	✓	✓
Buljina et al (2001)	✓	?	×	×	?	✓	✓
Häkkinen et al (2001)	?	?	×	?	✓	✓	✓
Bearne et al (2002)	?	✓	×	?	×	✓	✓
de Jong et al (2003)	✓	✓	×	×	✓	✓	✓
Veitiene & Tamulaitiene (2004)	?	?	×	?	×	✓	✓
O'Brien et al (2006)	✓	✓	×	✓	✓	✓	✓
van den Berg et al (2006)	✓	✓	×	✓	✓	✓	✓
Eversden et al (2007)	✓	✓	×	✓	×	✓	✓
Neuberger et al (2007)	✓	?	×	✓	✓	✓	✓
Flint-Wagner et al (2009)	✓	?	×	?	×	✓	×

Lemmey et al (2009)	✓	?	×	✓	?	✓	✓
van Rensburg et al (2010)	✓	?	×	?	×	✓	✓
Breedland et al (2011)	✓	✓	×	✓	✓	✓	✓
Strasser et al (2011)	✓	?	×	?	✓	✓	✓
Rahnama & Mazioum (2012)	?	?	×	?	×	✓	✓
van Rensburg et al (2012)	✓	✓	×	?	×	✓	✓
Cima et al (2013)	✓	?	×	×	✓	✓	✓
Dogu et al (2013)	✓	?	×	✓	✓	✓	✓
Durcan et al (2014)	✓	?	×	?	✓	✓	✓
Jahanbin et al (2014)	✓	?	×	?	✓	✓	×
Manning et al (2014)	✓	✓	×	✓	✓	✓	✓
Lamb et al (2015)	✓	✓	×	✓	✓	✓	✓
Seneca et al (2015)	✓	✓	×	✓	×	✓	✓
Dulgeroglu et al (2016)	✓	?	×	?	✓	✓	✓
Tonga et al (2016)	?	?	×	?	✓	✓	✓
Lourenzi et al (2017)	✓	✓	×	✓	✓	✓	✓
Shinde & Varadharajulu (2017)	✓	?	×	?	×	✓	✓
Anvar et al (2018)	?	?	×	?	✓	✓	✓
Lange et al (2018)	✓	✓	×	✓	✓	✓	✓
Mohanty et al (2018)	?	?	×	?	✓	✓	✓
Piva et al (2018)	✓	✓	×	✓	✓	✓	✓

(✓ = Low RoB, ? = Unclear RoB, × = High RoB).

3.7.2. RCTs reporting underpinning evidence.

Twenty RCTs (62.5%) did not cite evidence to underpin prescribed dose of strengthening exercise (Anvar et al., 2018, Bearne et al., 2002, Breedland et al., 2011, Buljina et al., 2001, Cima et al., 2013, De Jong et al., 2003, Dogu et al., 2013, Eversden et al., 2007, Hakkinen et al., 2001, Jahanbin et al., 2014, Lange et al., 2018, Mohanty et al., 2018, O'Brien et al., 2006, Rahnama and Mazloum, 2012, Shinde and Varadharajulu, 2017, Tonga et al., 2016, van den Berg et al., 2006, van den Ende et al., 2000, Van Rensburg et al., 2010, Veitiene and Tamulaitiene, 2004). The remaining twelve (37.5%) RCTs (Dulgeroglu et al., 2016, Durcan et al., 2014, Flint-Wagner et al., 2009, Lamb et al., 2015, Lemmey et al., 2009, Lourenzi et al., 2017, Manning et al., 2014, Neuberger et al., 2007, Piva et al., 2018, Seneca et al., 2015, Strasser et al., 2011, van Rensburg et al., 2012) cited in total, twenty-seven evidence sources to underpin the prescribed dose of strengthening exercise. This information is available as

supplementary material (Appendix 4). These included clinical trials, literature reviews, guidelines, clinical opinion, books, and a mobile phone application.

3.7.3. Completeness of intervention descriptions.

Thirty-one (97%) RCTs provided incomplete descriptions of their interventions (Table 3.3). Dose parameters with a <50% completion rate included exercise type, sets, load, and recovery.

Table 3. 3. Adapted TIDieR checklist for reporting of interventions in included primary evidence sources.

TIDieR Item	1	2	3	4	5	6	7	8		9	10	11	12
Description	**Brief Name**	**Why**	**What Materials**	**What Procedures**	**Who Provided**	**How Delivered**	**Where Delivered**	**When and How Much (Strengthening Exercise)**		**Tailoring**	**Modifications**	**How well (planned)**	**How well (actual)**
van den Ende et al (2000)	✓	✓	x	✓	✓	✓	✓	1:x 2:✓ 3:✓ 4:✓ 5:x	6:✓ 7:✓ 8:✓ 9:✓ 10:✓	✓	x	x	✓
Buljina et al (2001)	✓	✓	✓	✓	x	✓	✓	1:✓ 2:✓ 3:x 4:✓ 5:✓	6:x 7:✓ 8:x 9:✓ 10: ✓	x	x	x	x
Hakkinen et al (2001)	✓	✓	x	✓	✓	✓	✓	1:x 2:✓ 3:✓ 4:✓ 5:x	6:✓ 7:x 8:✓ 9:✓ 10:✓	✓	x	x	✓
Bearne et al (2002)	✓	✓	✓	✓	✓	✓	✓	1: x 2:✓ 3:x 4:x 5:x	6:✓ 7:x 8:✓ 9: ✓ 10:✓	✓	✓	x	✓
De Jong et al (2003)	✓	✓	x	✓	x	✓	x	1:x 2:x 3:x 4:✓ 5:x	6:x 7:✓ 8: ✓ 9:✓ 10:✓	x	x	x	✓

Veitiene & Tamulaitiene (2004)	✓	✓	x	x	x	✓	✓	1:x 2:x 3:x 4:x 5:x	6:x 7:x 8:x 9:✓ 10:✓	x	x	x	x
O'Brien et al (2006)	✓	✓	✓	✓	✓	✓	✓	1:✓ 2:✓ 3:x 4:✓ 5:x	6:x 7:x 8:✓ 9:✓ 10:✓	✓	x	x	x
van den Berg et al (2006)	✓	✓	✓	✓	✓	✓	✓	1: x 2:x 3:✓ 4:✓ 5:x	6:x 7:✓ 8:x 9:✓ 10:✓	✓	x	✓	✓
Eversden et al (2007)	✓	✓	x	✓	✓	✓	✓	1:x 2:x 3:x 4:x 5:x	6:x 7:x 8:✓ 9:✓ 10:✓	✓	✓	x	✓
Neuberger et al (2007)	✓	✓	x	✓	✓	✓	✓	1:x 2:x 3:x 4:x 5:x	6:✓ 7:x 8:✓ 9:✓ 10:✓	✓	x	x	x
Flint-Wagner et al (2009)	✓	✓	✓	✓	✓	✓	✓	1:✓ 2:✓ 3: ✓ 4:✓ 5:x	6:✓ 7:x 8:✓ 9:✓ 10:✓	✓	x	x	✓

Lemmey et al (2009)	✓	✓	✓	✓	✓	✓	✓	1:✓ 2:✓ 3:✓ 4:✓ 5:x	6:✓ 7:✓ 8:✓ 9:✓ 10:✓	✓	x	x	✓
van Rensberg et al (2010)	✓	✓	x	✓	✓	✓	x	1:x 2:x 3:x 4:x 5:x	6:✓ 7:x 8:✓ 9:✓ 10:✓	✓	x	x	✓
Breedland et al (2011)	✓	✓	✓	✓	✓	✓	✓	1:✓ 2:✓ 3:✓ 4:✓ 5:x	6:✓ 7:x 8:✓ 9:✓ 10:✓	✓	✓	x	x
Strasser et al (2011)	✓	✓	x	✓	✓	✓	x	1:✓ 2:x 3:✓ 4:✓ 5:x	6:✓ 7:x 8:✓ 9:✓ 10:✓	✓	x	x	✓
Rahnama et al (2012)	✓	✓	x	✓	✓	✓	x	1:x 2:x 3:x 4:x 5:x	6 x 7:x 8:x 9:✓ 10:✓	x	x	x	x
van Rensberg et al (2012)	✓	✓	x	✓	✓	✓	x	1:✓ 2:x 3: x 4:x 5:x	6:x 7:x 8:✓ 9:✓ 10:✓	✓	x	x	✓

Cima et al (2013)	✓	✓	✓	✓	✓	✓	✓	1:✓ 2:✓ 3:x 4:x 5:x	6:x 7:x 8:✓ 9:✓ 10:✓	✓	x	x	x
Dogu et al (2013)	✓	✓	✓	✓	✓	✓	✓	1:✓ 2:✓ 3:✓ 4:✓ 5:x	6:x 7:✓ 8:x 9:✓ 10:✓	x	x	x	x
Durcan et al (2014)	✓	✓	✓	✓	✓	✓	✓	1:x 2:✓ 3:✓ 4:✓ 5:x	6:✓ 7:✓ 8:x 9:✓ 10:✓	✓	x	x	x
Jahanbin et al (2014)	✓	✓	x	✓	✓	✓	x	1:x 2:x 3:x 4:x 5:x	6:x 7:x 8:x 9:✓ 10:✓	x	x	x	x
Manning et al (2014)	✓	✓	✓	✓	✓	✓	✓	1:✓ 2:✓ 3:✓ 4:✓ 5:x	6:✓ 7:✓ 8:✓ 9:✓ 10:✓	✓	✓	✓	✓
Lamb et al (2015)	✓	✓	✓	✓	✓	✓	✓	1:✓ 2:✓ 3:✓ 4:✓ 5:x	6:✓ 7: x 8:✓ 9:✓ 10:✓	✓	✓	✓	✓

Seneca et al (2015)	✓	✓	x	✓	✓	✓	✓	1:x 2:x 3:✓ 4:✓ 5:x	6:✓ 7:✓ 8:✓ 9:✓ 10:✓	✓	✓	x	✓
Dulgeroglu et al (2016)	✓	✓	✓	✓	x	✓	✓	1:✓ 2:✓ 3:x 4:✓ 5:✓	6:x 7:x 8:x 9:✓ 10:✓	x	x	x	x
Tonga et al (2016)	✓	✓	x	✓	x	✓	x	1:x 2:x 3:x 4:x 5:x	6:x 7:x 8:x 9: x 10:x	x	x	x	x
Lourenzi et al (2017)	✓	✓	✓	✓	✓	✓	✓	1:✓ 2:✓ 3:✓ 4:✓ 5:x	6:✓ 7:✓ 8:✓ 9:✓ 10:✓	✓	✓	x	✓
Shinde & Varadharajulu (2017)	✓	✓	x	✓	x	x	x	1:x 2:x 3:x 4:✓ 5:x	6:x 7:x 8:x 9:✓ 10:✓	x	x	x	x
Anvar et al (2018)	✓	✓	x	✓	✓	✓	✓	1:x 2:x 3:x 4:x 5:x	6:x 7:x 8:x 9:✓ 10:✓	x	x	x	x

Lange et al (2018)	✓	✓	✓	✓	✓	✓	✓	1:x 2:✓ 3:✓ 4:✓ 5:x	6:✓ 7:x 8:✓ 9:✓ 10:✓	✓	✓	x	✓
Mohanty et al (2018)	✓	✓	x	✓	x	✓	✓	1:x 2:x 3:x 4:✓ 5:x	6:x 7:✓ 8: x 9:✓ 10:✓	x	x	x	x
Piva et al (2018)	✓	✓	✓	✓	✓	✓	✓	1:✓ 2:✓ 3:✓ 4:✓ 5:x	6:✓ 7:✓ 8:✓ 9:✓ 10:✓	✓	✓	x	✓
% Completion rate	**100%**	**100%**	**50%**	**97%**	**78%**	**97%**	**75%**	**1:43% 2:54% 3:46% 4:66% 5:6%**	**6:50% 7: 37% 8: 63% 9:97% 10: 97%**	**66%**	**28%**	**9%**	**53%**

✓ = Item sufficiently described in the trial. x = Inadequately or not described. Item 8: 1 = Exercise type. 2 = Strength equipment used. 3 = Sets. 4 = Repetitions. 5 = Load = (kg/lbs.). 6 = Intensity (%1RM/Borg). 7 = Recovery.

8 = Progression. 9 = Frequency. 10 = Programme duration.

3.7.4. RCTs using pilot studies.

Four (12.5%) RCTs (Lamb et al., 2015, Lemmey et al., 2009, Manning et al., 2014, Neuberger et al., 2007) reported using a pilot study (Table 3.4). The RCT was investigated whether it used the same dose as its pilot study by comparing the individual dose parameters. Lamb et al (2015) reported using the same dose in both the pilot and main trial. There were noted inconsistencies in the dose used for Neuberger et al (2007) and Lemmey et al (2009). Neuberger and its pilot study reported insufficient information to compare most dose parameters. Only three parameters (method of progression, frequency of sessions and programme duration) were able to be judged. The method used for progression was inconsistent and the justification for it being modified was not able to be located. Lemmey et al (2009) reported progressing dose more gradually to reduce muscle soreness when compared to its pilot study. However, no evidence (e.g., adverse events) that participants experienced problems with muscle soreness during the pilot study was reported. Therefore, it is unclear why dose was modified if no problems were experienced. It was not possible to compare dose in the fourth RCT (Manning et al, 2014), owing to the pilot study being unpublished.

The evidence that the pilot studies cited to underpin dose was also explored. Neuberger et al (1997) reported that their intervention was developed by two physical therapists, an aerobics instructor hired to teach the class and the principal investigator but did not cite any evidence to underpin dose. Marcora et al (2005) cited the 2002 ACSM position stand: progression models in resistance training for healthy adults (Kraemer et al., 2002) to underpin dose sufficient for achieving optimal stimulation of muscle hypertrophy. Manning et al (2015) cited (Hurley et al., 2007), a RCT targeting chronic knee pain (ESCAPE programme) for development of their upper-limb intervention (EXTRA programme). The pilot study for Lamb et al (2015) was only described briefly (Heine et al., 2012, Williams et al., 2015) and the dose was underpinned by a variety of evidence sources. Lamb indicated the initial design of the intervention was based on an RCT conducted by O'Brien et al (2006) which also involved the rheumatoid hand and was therefore relevant. The content of the exercise programme used by O'Brien was defined by expert opinion (an unpublished survey of 60 senior hand therapists), one of the lowest levels of evidence (Evans, 2003).

Table 3. 4. Consistency in dose parameters comparing RCT against its respective pilot study.

Dose parameter > / RCT/Pilot v	Type of strength exercise	Sets	Repetitions	Load	Intensity	Method of recovery	Method of progression	Frequency of sessions	Programme duration	Consistency rating
RCT: Neuberger et al (2007)	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	60-80%1RM	Insufficiently described	Each participant was given their target HR for 60% & 80% MHR and instructed to start exercising at 60% and progress to 80% as tolerated given their subjective exertion using the talk test (being able to talk while exercising without being short of breath) and the Borg scale.	3 x week	12 weeks	Exercise type: Unclear Sets: Unclear Repetitions: Unclear Load: Unclear Intensity: Unclear Recovery: Unclear Progression: Inconsistent Frequency: Consistent Duration: Consistent
Pilot study: Neuberger et al (1997)	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	Initially warm-up and strengthening phases were longer to build muscle strength. As aerobic minutes were increased, minutes of warm-up and cool-down were reduced.	3 x week	12 weeks	

RCT: Lemmey et al (2009) (Lemmey et al., 2009)	1. Chest press 2. Seated leg extension 3. Rowing 4. Bicep curl 5. Triceps extension 6. Leg press 7. Leg curl 8. Standing calf raises	Week 1: 1 set Week 2: 2 sets Weeks 3-24 3 sets	Weeks 1-4: 15 repetitions Weeks 5-6: 12 repetitions Weeks 7-24: 8 repetitions	Insufficiently described	Weeks 1-4: 60%1RM Weeks 5-6: 70%1RM Weeks 7-24: 80%1RM	1-2 minutes between sets	1RM reassessed every 4 weeks	2 x week	24 weeks	Exercise type: Consistent Sets: Inconsistent Repetitions: Inconsistent Load: Unclear
Pilot study: Marcora et al (2005)	1. Chest press 2. Seated leg extension 3. Seated row 4. Bicep curl 5. Triceps extension 6. Leg press 7. Leg curl 8. Standing calf raises	4 sets	Set 1: 15 repetitions Sets 2-4: 8 repetitions (Repetition velocity: 1-2 seconds concentric/ Eccentric)	Insufficiently described	Set 1: 40%1RM Sets 2-4: 80%1RM	1-2 minutes between sets and exercises + 48 hours between training sessions	1RM reassessed at end of week 0 then every 2 weeks	3 x week	12 weeks	Intensity: Inconsistent Recovery: Consistent Progression: Inconsistent Frequency: Inconsistent Duration: Inconsistent

RCT: Manning et al (2014)	6 out of 16 exercises were used: 1. Putty ball squeeze 2. Putty fingertip pinch 3. Putty finger hook and squeeze 4. Knife and fork putty cutting 5. Paper clips and envelope challenge 6. Wrist alphabet with band 7. Back scrub 8. Up and out of chair 9. Arm curl with band 10. Lift to chin with band 11. Reach back with band 12. Side Lift with band 13. Wall wash squares with band 14. Door push with band 15. Shoulder rotation with band	Between 1-3 sets	8-12 repetitions	Insufficiently described	Participants were encouraged to maintain an RPE of 13–17 (equivalent to 50–80% of maximal exertion)	30 seconds between sets	Maintain Borg rating of perceived value at 13-17 (50-80% of max exertion)	Weeks 1-2 2 x week with the physio Weeks 3-12 Self-supervised 1 x daily at home	12 weeks	Exercise type: Unclear Sets: Unclear Repetitions: Unclear Load: Unclear Intensity: Unclear Recovery: Unclear Progression: Unclear Frequency: Unclear Duration: Unclear

	16. Reach to shelf with band									
Pilot study: Unpublished	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	
RCT: Lamb et al (2015)	1. Eccentric wrist extension 2. Gross grip 3. Finger adduction 4. Pinch grip	Between 1-3 sets	8-30 repetitions	Insufficiently described	3-4 to 5-6 on modified Borg scale	Insufficiently described	Permitted to progress up to 30 repetitions + increase load using RPE scale	1 x daily	12 weeks	Exercise type: Consistent Sets: Consistent Repetitions: Consistent Load: Unclear Intensity: Consistent Recovery: Unclear Progression: Consistent Frequency: Consistent Duration: Consistent
Pilot study: (reported in) (Heine et al., 2012) + (Williams et al., 2015)	1. Eccentric wrist extension 2. Gross grip 3. Finger adduction 4. Pinch grip	Between 1-3 sets	8-30 repetitions	Insufficiently described	3-4 to 5-6 on modified Borg scale	Insufficiently described	Permitted to progress up to 30 repetitions + increase load using RPE scale	1 x daily	12 weeks	

3.7.5. RCTs using dose escalation methodology.

Across the thirty-two trials (Table 3.1), no evidence of dose-escalation methodology, described in chapter two, was reported. There was also no evidence of the dose-escalation methodology being used in the four pilot studies identified above (Table 3.4).

3.7.6. Quality, consistency, and applicability of the underpinning evidence.

3.7.6.1. Quality.

The quality of the twenty-seven underpinning evidence sources was rated using the OCEBM level of evidence framework (Table 3.5). Eight (29.6%) were judged to be level 2 evidence (Bearne et al., 2002, Hakkinen et al., 2001, Hoenig et al., 1993, Hurley et al., 2007, McGuigan et al., 2004, O'Brien et al., 2006, Rall et al., 1996, van den Ende et al., 2000), three (11.1%) judged to be level 3 evidence (Marcora et al., 2005, Neuberger et al., 1997, Rønningen and Kjeken, 2008) and one (3.7%) judged to be level 5 evidence (Borg, 1982). Several of the underpinning evidence sources were guidelines, literature reviews or books. Exploring the references these sources used, a level of evidence rating that best described their quality was assigned. Five (18.5%) were judged to range between 2-5 (Garber et al., 2011, Hicks, 1994, Kraemer et al., Marcora et al., 2005). ACSM (2002) (Kraemer et al.) was cited twice. The pilot study (Marcora et al., 2005) of Lemmey et al (2009) cited the ACSM position stand (Kraemer et al.) to underpin dose. In this instance, we explored the evidence used by the position stand to assign the pilot study a level of evidence rating of 2-5. For the remaining two (7.4%), a rating of 2-4 (Ratamess et al., 2009) and 3-5 (Baechle and Earle, 2000) was assigned respectively. Sometimes assigning a level of evidence wasn't straightforward. Six (22.2%) were rated as 'unclear'. (American College of Sports Medicine, 1991, Borg, 1998, Dept of PT & OT Aarhus University Hospital, 2015, Durstine et al., 2009, Iversen, 2002, Williams et al., 2007) Two (7.4%) evidence sources were assigned an 'incorrect' rating. One source used by Dulgeroglu et al, 2016 was not relevant to volitional strengthening exercise and focused on electrostimulation (Pelland et al., 2002). The second, the source appeared to be incorrectly referenced by the RCT (van Rensburg et al., 2012). Consequently, it was not possible to retrieve it for investigation.

3.7.6.2. Consistency.

The RCT was explored to identify if it used the same dose as described/recommended by the underpinning evidence (Table 3.5). Twenty-two examples across nine RCTs (Dulgeroglu et al., 2016, Durcan et al., 2014, Lamb et al., 2015, Lemmey et al., 2009, Lourenzi et al., 2017, Neuberger et al., 2007, Piva et al., 2018, Seneca et al., 2015, Strasser et al., 2011)where the dose used was the same as the dose used/recommended by the underpinning evidence source. There were forty-nine examples

across eight RCTs where the dose used was different (Dulgeroglu et al., 2016, Lamb et al., 2015, Lemmey et al., 2009, Lourenzi et al., 2017, Manning et al., 2014, Neuberger et al., 2007, Piva et al., 2018, van Rensburg et al., 2012). In forty-six examples across nine RCTs (Durcan et al., 2014, Flint-Wagner et al., 2009, Lamb et al., 2015, Lemmey et al., 2009, Lourenzi et al., 2017, Manning et al., 2014, Neuberger et al., 2007, Piva et al., 2018, van Rensburg et al., 2012), it was not possible to compare dose used due to insufficient detail and across six RCTs (Dulgeroglu et al., 2016, Flint-Wagner et al., 2009, Lemmey et al., 2009, Seneca et al., 2015, Strasser et al., 2011, van Rensburg et al., 2012), there were thirty-seven examples where individual dose parameters were unsupported with evidence.

3.7.6.3. Applicability.

The applicability of the twenty-seven underpinning evidence sources in relation to RA, gender and age varied (Table 3.5). Fourteen (51.8%) were judged not applicable to RA (American College of Sports Medicine, 1991, Baechle and Earle, 2000, Borg, 1982, Borg, 1998, Dept of PT & OT Aarhus University Hospital, 2015, Durstine et al., 2009, Garber et al., 2011, Hurley et al., 2007, Kraemer et al., McGuigan et al., 2004, Ratamess et al., 2009, Williams et al., 2007) + (ACSM, 2006), seventeen (62.9%) to gender (American College of Sports Medicine, 1991, Baechle and Earle, 2000, Bearne et al., 2002, Borg, 1982, Borg, 1998, Dept of PT & OT Aarhus University Hospital, 2015, Durstine et al., 2009, Garber et al., 2011, Hicks, 1994, Iversen, 2002, Kraemer et al., Pelland et al., 2002, Ratamess et al., 2009, Williams et al., 2007) + (ACSM, 2006) and eighteen (66.6%) to age (American College of Sports Medicine, 1991, Baechle and Earle, 2000, Borg, 1982, Borg, 1998, Dept of PT & OT Aarhus University Hospital, 2015, Durstine et al., 2009, Garber et al., 2011, Hakkinen et al., 2001, Hicks, 1994, Iversen, 2002, Kraemer et al., McGuigan et al., 2004, Pelland et al., 2002, Rall et al., 1996, Ratamess et al., 2009, Rønningen and Kjeken, 2008, Williams et al., 2007) + ACSM (2006).

Table 3. 5. Quality, consistency, and applicability of the underpinning evidence.

RCT	Underpinning evidence	Quality	Consistency									Applicability		
		OCEBM level	Exercise	Sets	Reps	Load	Intensity	Recovery	Progress	Frequency	Duration	RA	Gender	Age
(Neuberger et al., 2007)	(American College of Sports Medicine, 1991)	'Unclear'	Nil	Nil	Nil	Nil	✓	Nil	?	Nil	Nil	×	×	×
	(Neuberger et al., 1997)	'3'	?	?	?	?	?	?	×	✓	✓	✓	✓	✓
(Flint-Wagner et al., 2009)	(Baechle and Earle, 2000)	'3-5'	Nil	Nil	Nil	Nil	?	Nil	Nil	Nil	Nil	×	×	×
	(Borg, 1998)	'Unclear'	Nil	Nil	Nil	Nil	Nil	Nil	?	Nil	Nil	×	×	×
(Lemmey et al., 2009)	(Kraemer et al., 2002)	'2-5'	Nil	✓	×		×	Nil	Nil	Nil	Nil	×	×	×
	(Marcora et al., 2005)	'2-5'	Nil	×	×	?	×	✓	×	×	×	✓	✓	✓
(Strasser et al., 2011)	(Williams et al., 2007)	'Unclear'	Nil	Nil	✓	Nil	✓	Nil	Nil	Nil	Nil	×	×	×
(van Rensburg et al., 2012)	(Iversen, 2002)	'Unclear'	Nil	Nil	Nil	Nil	Nil	Nil	×	Nil	Nil	✓	×	×
	ACSM (2006)	'Incorrect citation'	Nil	Nil	Nil	Nil	Nil	Nil	?	Nil	Nil	×	×	×
(Durcan et al., 2014)	(Durstine et al., 2009)	'Unclear'	?	?	?	?	?	?	?	?	?	×	×	×
	(Garber et al., 2011)	'2-5'	✓	✓	✓	?	✓	✓	✓	✓	?	×	×	×
(Manning et al., 2014)	(Hurley et al., 2007)	'2'	×	?	×	?	?	?	×	×	×	×	✓	✓
(Lamb et al., 2015)	(Borg, 1982)	'5'	Nil	Nil	Nil	Nil	?	Nil	Nil	Nil	Nil	×	×	×
	(Hoenig et al., 1993)	'2'	Nil	Nil	Nil	?	Nil	Nil	Nil	Nil	Nil	✓	✓	✓
	(Kraemer et al., 2002)	'2-5'	Nil	✓	✓	?	Nil	?	Nil	×	Nil	×	×	×
	(McGuigan et al., 2004)	'2'	Nil	Nil	Nil	Nil	?	Nil	Nil	Nil	Nil	×	✓	×
	(Marcora et al., 2005)	'3'	Nil	×	×	Nil	×	Nil	Nil	Nil	Nil	✓	✓	✓
	(O'Brien et al., 2006)	'2'	✓	?	×	?	?	?	×	×	×	✓	✓	✓
(Seneca et al., 2015)	(Dept of PT & OT Aarhus University Hospital, 2015)	'Unclear'	Nil	Nil	Nil	Nil	✓	Nil	Nil	Nil	Nil	×	×	×
(Dulgeroglu et al., 2016)	(Pelland et al., 2002)	'Incorrect citation'	Nil	Nil	×	Nil	Nil	Nil	Nil	Nil	Nil	✓	×	×
	(Rønningen and Kjeken, 2008)	'3'	Nil	Nil	✓	Nil	Nil	Nil	Nil	×	×	✓	✓	×

(Lourenzi et al., 2017)	(Hicks, 1994)	‘2-5’	?	?	×	?	?	×	×	×	✓	✓	×	×
	(Bearne et al., 2002)	‘2’	Nil	Nil	Nil	Nil	×	Nil	Nil	Nil	Nil	✓	×	✓
	(Ratamess et al., 2009)	‘2-4’	Nil	Nil	Nil	Nil	Nil	Nil	Nil	✓	?	×	×	×
(Piva et al., 2018)	(Rall et al., 1996)	‘2’	✓	✓	×	?	×	×	×	×	×	✓	✓	×
	(van den Ende et al., 2000)	‘2’	×	✓	×	?	×	×	×	×	×	✓	✓	✓
	(Hakkinen et al., 2001)	‘2’	?	×	×	?	?	?	×	×	×	✓	✓	×

× = Inconsistent/not applicable.? = Unclear as insufficiently described/not described. ✓ = Consistent/applicable. Nil = Source not used to underpin dose parameter.

3.7.7. Relationship between RoB and underpinning evidence:

Exploration of a relationship between the RoB for the twelve RCTs and the judged quality (OCEBM level of evidence) of the underpinning evidence (Table 3.6) was made. Relating to RoB, four (33.3%) were assessed to be at low RoB,(Lamb et al., 2015, Lourenzi et al., 2017, Manning et al., 2014, Piva et al., 2018) five (41.6%) were assessed to be at unclear RoB (Dulgeroglu et al., 2016, Durcan et al., 2014, Lemmey et al., 2009, Neuberger et al., 2007, Strasser et al., 2011) and three (25%) were assessed to be at high RoB (Flint-Wagner et al., 2009, Seneca et al., 2015, van Rensburg et al., 2012). While there were too few studies for reliable statistical evaluation, of the eight RCTs assessed as unclear, or at high risk of bias, seven (87.5%) had evidence rated as incorrect or unclear (Dulgeroglu et al., 2016, Durcan et al., 2014, Flint-Wagner et al., 2009, Neuberger et al., 2007, Seneca et al., 2015, Strasser et al., 2011, van Rensburg et al., 2012). Of the four assessed at low RoB, none of the underpinning evidence sources were rated as incorrect or unclear.

Table 3. 6. RoB and level of underpinning secondary evidence for primary evidence sources.

RCT	Sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessors for all outcomes	Incomplete outcome data for all outcomes	Selective outcome reported	Other sources of bias	Overall RoB rating	No of underpinning evidence sources	Source 1 - OCEBM level of evidence	Source 2 - OCEBM level of evidence	Source 3 - OCEBM level of evidence	Source 4 - OCEBM level of evidence	Source 5 - OCEBM level of evidence	Source 6 - OCEBM level of evidence
Neuberger et al (2007)	✓	?	×	✓	✓	✓	✓	?	2	Unclear (American College of Sports Medicine, 1991)	3 (Neuberger et al., 2007)				
Flint-Wagner et al (2009)	✓	?	×	?	×	✓	×	×	2	3-5 (Baechle and Earle, 2000)	Unclear (Borg, 1998)				
Lemmey et al (2009)	✓	?	×	?	✓	✓	✓	?	2	2-5 (Kraemer et al.)	2-5 (Marcora et al., 2005)				
Strasser et al (2011)	✓	?	×	?	✓	✓	✓	?	1	Unclear (Williams et al., 2007)					
Van Rensburg et al (2012)	✓	✓	×	?	×	✓	✓	×	2	Unclear (Iversen, 2002)	Incorrect				
Durcan et al (2014)	✓	?	×	?	✓	✓	✓	?	2	Unclear (Ratamess et al., 2009)	2-5 (Garber et al., 2011)				

Manning et al (2014)	✓	✓	×	✓	✓	✓	✓	✓	1	2 (Hurley et al., 2007)					
Lamb et al (2015)	✓	✓	×	✓	✓	✓	✓	✓	6	5 (Borg, 1982)	2 (Hoenig et al., 1993)	2-5 (Kraemer et al., 2002)	2 (McGuigan et al., 2004)	3 (Marcora et al., 2005)	2 (O'Brien et al., 2006)
Seneca et al (2015)	✓	✓	×	✓	×	✓	✓	×	1	Unclear (Dept of PT & OT Aarhus University Hospital, 2015)					
Dulgeroglu et al (2016)	✓	?	×	?	✓	✓	✓	?	2	Incorrect (Pelland et al., 2002)	3 (Rønningen and Kjeken, 2008)				
Lourenzi et al (2017)	✓	✓	×	✓	✓	✓	✓	✓	3	2-5 (Hicks, 1994)	2 (Bearne et al., 2002)	2-4 (Ratamess et al., 2009)			
Piva et al (2018)	✓	✓	×	✓	✓	✓	✓	✓	3	2 (Rall et al., 1996)	2 (van den Ende et al., 2000)	2 (Hakkinen et al., 2001)			

✓ = Low RoB.? = Unclear RoB. × = High RoB

3.8. Discussion.

3.8.1. Summary of main results.

This systematic review identified 32 published clinical trials spanning almost 20 years of research. It explored in detail the underpinning evidence used by healthcare researchers to justify the prescribed dose of strengthening exercise used in clinical trials of RA. Most clinical trials involving exercise in RA do not report the use of evidence to underpin exercise dose. Only four trials formally piloted the intervention and its dose prior to evaluation. None of the pilot studies used dose-escalation designs to optimise dose-response, something which is more commonly seen in the evaluation of new drugs. In the absence of formal piloting, the underpinning evidence cited to justify dose parameters (when used) varied in quality and applicability and sometimes did not support the reported dose parameters.

3.8.2. Piloting interventions and dose prior to evaluation by clinical trial.

The lack of formal testing highlighted by this review suggests that current practice in the field of RCTs using exercise-based interventions in RA does not align with the MRC framework for the development and evaluation of complex interventions (Medical Research Council, 2000, medical Research Council, 2006, Skivington et al., 2021). Potential reasons for not piloting may include lack of time, research culture, funding, conflicting priorities, policy focus etc, though in some cases may simply reflect a lack of reporting (Swan et al., 2009). For the minority of RCTs who piloted their interventions, dose-escalation methods were not used. In the absence of such methods, how the dose of strengthening exercise was developed was explored. The underpinning evidence sources used by the pilot studies (where published) supported that development was often based on expert opinion (Lamb et al., 2015, Neuberger et al., 1997) and/or evidence that was not applicable to the clinical population (Lamb et al., 2015, Lemmey et al., 2009, Manning et al., 2014). In the absence of robust empirical data for dose of strengthening exercise, such approaches to development may be a reasonable attempt in deciding what dose is best to prescribe. However, when researchers have used similar methods to those seen in drugs trials (Dite et al., 2015, Wallis et al., 2015), they discovered discrepancies between the dose that patients could tolerate, and the dose recommended in the literature. Whilst the number of early phase trials using these methods in exercise is low, these findings suggest that relying on expert opinion and consensus alone, may be inaccurate and illustrates the potential value of pilot studies using dose escalation methodology for tailoring dose (Bajuaifer et al., 2023, Bultijnck et al., 2021, Colucci et al., 2017, Dite et al., 2015, Galloway et al., 2023, Kramer et al., 2020, Mackie et al., 2021a, Mackie et al., 2021b, Peiris et al., 2017, Wallis et al., 2015).

3.8.3. Overall completeness of the underpinning evidence.

In the absence of piloting, the judicious use of evidence to underpin all aspects of dose development should be expected (Cathain et al., 2019), yet only a small proportion of RCTs reported the evidence underpinning the dose of strengthening exercise. This finding is consistent with insufficient reporting of physiotherapy interventions (Yamato et al., 2016) and complex interventions seen more broadly (Hoffmann et al., 2013), and is a cause for methodological concern. In many cases, dose parameters were insufficiently described.

3.8.4. Quality of the underpinning evidence.

Only four of the twelve RCTs that reported underpinning evidence had a low overall RoB rating. When exploring if a relationship existed between RoB and the level of underpinning evidence used, seven of the eight RCTs with an overall RoB rating of unclear/high also had underpinning evidence that was rated unclear or incorrect. Whilst not enough trials for statistical evaluation, these trials appeared to be using underpinning evidence that was less robust in terms of quality. Overall, the findings of this review indicate the development and testing of exercise dose in clinical trials is an area that should be improved.

3.8.5. Applicability of the underpinning evidence.

Where reported, most of the underpinning evidence was not applicable to individuals living with RA. The results also indicated the evidence used was also not applicable to either the age or genders of participants contained in the main clinical trial.

3.9. Potential strengths and limitations in the review process.

This review offers new insight into clinical trials using exercise interventions. A comprehensive search strategy without language limitations and methodological approach was used to explore in detail, the evidence used to underpin dose of strengthening exercise. This review does have some limitations. Firstly, without a complete published description of the intervention, incomplete reporting by both RCTs and the underpinning evidence, limited the amount of information available to conduct the review, though this highlights a challenge for this field. Secondly, owing to the number of clinical trials involving strengthening exercise in musculoskeletal disorders, the review only includes people living with RA. It is possible that the underpinning evidence for exercise dose in other conditions may be more robust. However, given the broad issues identified in the current review, this is unlikely and may not be limited strengthening exercise in RA (Gallois et al., 2017, Holden and Barton, 2019). Thirdly, the novel and exploratory nature of this review meant it was not possible to anticipate all of the challenges

for grading the quality of the underpinning evidence. Judging the quality was not always easy in practice. The grading process was more complicated for pilot studies, literature reviews, clinical guidelines, and books as it necessitated going back a further generation of underpinning evidence. Often with literature reviews, guidelines, and books, it was not always clear where in the text support existed. Whilst these types of evidence source may be useful for assimilating large bodies of evidence on a particular topic, using these to underpin dose has potential drawbacks for assessing quality, consistency, and applicability. Some RCTs did not stipulate what part of the underpinning evidence they used. This meant that to grade quality, sometimes a pragmatic approach was needed to be able to reach a consensus. Similarly, the factors (RA, gender, and age) used to assess applicability of the underpinning evidence in terms of homogeneity/heterogeneity were chosen intuitively. It is possible that other factors could also be used to assess applicability.

3.10. Conclusions.

This systematic review identified that the majority of included RCTs did not report pilot studies or evidence to underpin exercise dose. When evidence is cited, the different types used vary in quality, consistency, and applicability. The findings of this review question whether dose is optimised for use with the clinical populations, which is a cause for methodological concern. There are clear scientific imperatives to improve practice in this area of clinical research, including to maximise the potential for exercise interventions to deliver benefit. Addressing these weaknesses may contribute to better quality research being conducted and reducing research waste in exercise interventions.

3.11. Future implications of this review.

In the context of patient centred care, the prescription of an effective exercise intervention should be tailored to meet the needs of the individual (Brody, 2011), for strengthening exercise this should be done within a broader framework that is underpinned by evidence. The results of this review indicate researchers need to improve not only the standard of reporting related to their interventions, but also the evidence they use to justify their decisions about what dose to prescribe. Reporting guidelines like TIDieR and CERT (Hoffmann et al., 2014, Slade et al., 2016a) should be used to raise standards going forward and as these evolve (Holden and Barton, 2019), could recommend researchers be explicit with type, quality, consistency and applicability of evidence they have used to support each dose parameter and. Funders and peer reviewers should take a careful and critical approach when considering how exercise dose has been formulated. Those interventions that fail to offer evidence supporting dose, or use evidence of low quality and applicability, may not in the future be funded or published. The absence of clear robust evidence supporting dose identified by this review indicates pilot testing using

dose escalation methodology may help answer uncertainties about what dose works best (Chartered Society of Physiotherapy, 2018). The implication of such would necessitate funders considering more funding and time to support researchers generate the preliminary data before conducting a definitive RCT. As such there was a case for exploring dose of strengthening exercise using data from one of the included RCTs included in the review. The SARCH RCT explored tailored hand exercise in addition to usual care and was central to the 2015 update of the NICE recommendations (Lamb et al., 2015, National Institute for Health and Care Excellence, 2015). Therefore, for the second study in this thesis, a prospective analysis of the exercise data from the SARCH RCT was planned to investigate factors influencing its prescription and the effect overall dose prescribed had on key pre-selected outcomes. The following chapter describes that study and its findings.

3.12. Addendum.

3.12.1. Background.

This addendum provides an update of the original search described in section 3.4.1.

3.12.2. Methods.

A search of the MEDLINE database was run (10/10/2024) to identify RCTs that had been published since the last search was conducted (03/04/2019). The same search strategy eligibility criteria was applied. One reviewer independently screened the titles and abstracts of records obtained through the database search. The title and abstract were examined and those meeting the above eligibility criteria were retrieved for further evaluation. An identical process was employed for data extraction and evaluating RoB and underpinning evidence.

3.12.3. Results.

A total of 499 records were identified, with four duplicates removed. After screening titles and abstracts, 468 records were excluded. Twenty-seven full texts were assessed, and 18 were excluded (n=11: Non-strength related, n=3: Unable to access paper, n=2: Includes non-RA participants, n=1: Non-RCT, n=1: Sub-study of RCT). Nine RCTs were included (Azeez et al., 2020, Ellegaard et al., 2019, Garcia-Morales et al., 2020, Khan et al., 2022, Rodrigues et al., 2020, Rodriguez Sanchez-Laulhe et al., 2022, Somers et al., 2022, Teuwen et al., 2024, Yun et al., 2023). The characteristics of the included RCTs are reported in Table 3.7.

Table 3. 7. Characteristics of included primary evidence sources from Medline update search (presented in chronological order of publication).

Author and year + Country of origin	Primary aim	Sample characteristics		Intervention content	
		Control group	Intervention group	Control group	Intervention group
Ellegaard et al (2019) Denmark	To examine whether hand exercise as add on to compensatory intervention (CIP) will improve observed ADL ability in RA.	n=27 Mean age: 62.6 ± 12.0 Male/female: 0%/100%	n=27 Mean age: 64.8 ± 13.5 Male/female: 0%/100%	The CIP consisted of an introduction to compensatory strategies including joint protection, assistive devices, and alternative methods of performing ADL.	8-week hand exercise programme consisting of three parts: (1) warm-up/mobility (10 min), (2) muscle strength training (20 min), and (3) cool-down (5 min) in addition to CIP. Strength exercises used: 1. Gross grip with exercise putty. 2. Finger pinch with exercise putty. 3. Finger adduction with exercise putty. 4. Wrist extension with exercise band. 5. Wrist flexions with resistance from a table. 6. Biceps curls with exercise band. 7. Triceps extensions with exercise band. Duration: 8 weeks. Follow-up: 8 weeks (i.e. post-intervention).
Azeez et al (2020) Ireland	To investigate the effects of a specifically designed exercise programme on body composition, aerobic capacity, muscle strength and cognition in RA.	n=24 Median age: 63 (36-74 years) Male/female: 17%/83%	n=28 Median age: 58.5 (34-73 years) Male/female: 14%/86%	Standard care (e.g., advice on benefits of exercise in RA and outlining recommendations by ACSM and American Heart Association guidelines for physical activity in older adults (men and women age ≥ 65 years) and adults aged 50 to 64 years with clinically significant chronic conditions and/or functional limitation.	Personalised exercise programme prescribed by the study physiotherapist (CC) and had three sessions with the physio- therapist during the period of study. Strength exercises used: 1. Biceps curls. 2. Triceps extensions. 3. Shoulder press. 4. Grip strength using resistance bands and balls. 5. Leg squats. Duration: 12 weeks. Follow-up: 12 weeks (i.e. post-intervention).

Garcia-Morales et al (2020) Mexico	To assess the individual and combined effects of a mediterranean diet (MD) plus, a dynamic exercise program (DEP) on health-related quality of life in women with RA.	n=31 Mean age: 49.1 ± 12.1 Male/female: 0%/100%	MD + DEP n=36 Mean age: 51.4 ± 12.4 Male/female: 0%/100% DEP n=36 Mean age: 49.7 ± 11.4 Male/female: 0%/100% MD n=40 Mean age: 46.3 ± 13.1 Male/female: 0%/100%	Patients randomised to the DEP and control groups received general nutritional recommendations.	DEP Twice-a-week training sessions lasting 80 to 90 minutes comprising a warm-up (10 minutes), aerobic exercise using a static bike (20 minutes) using a static bicycle, anaerobic exercise including 8 to 10 exercises aiming to improve articular movement (to tolerance), muscular component, and activities of daily living (20 minutes), including 8 to 10 exercises aiming to improve articular movement (to tolerance), muscular component, and activities of daily living, recreational games such as basketball, soccer, and volleyball (20 minutes) and cool-down applying dynamic, static stretches for muscular and articular recovery. MD Individualised diet prescribed according to basal energy expenditure. Strength exercises used: Unclear Duration: 24 weeks. Follow-up: 24 weeks (i.e. post-intervention).

Rodrigues et al (2020) Brazil	To evaluate the effects of a low-load resistance training program associated with partial blood-flow restriction in patients with RA.	n=16 Mean age: 58.1 ± 5.9 Male/female: 0%/100%	High-load resistance training group n=16 Mean age: 58.0 ± 6.6 Male/female: 0%/100% Low-load resistance training with partial blood-flow restriction group n=16 Mean age: 59.6 ± 3.9 Male/female: 0%/100%	The control group was instructed to maintain their habitual daily living activities.	High-load resistance training group Strength exercises used: 1. Bilateral leg press. 2. Knee extension. Low-load resistance training with partial blood-flow restriction group Strength exercises used: 1. Bilateral leg press. 2. Knee extension. Duration: 12 weeks. Follow-up: 12 weeks (i.e. post-intervention).
Khan et al (2022) Republic of Korea	To assess the synergistic effects of curcumin with and without strengthening exercises in RA.	n=45 Mean age: Unclear Male/female: Unclear	n=45 Mean age: Unclear Male/female: Unclear	Curcumin.	Strengthening exercises and curcumin. Strength exercises used: 1. Upper extremity resistive exercises, resistive hand training with the medicine ball, and elbow and shoulder resistive training with dumbbells. 2. Lower extremity exercises, resistive knee training by pressing soft rollers and ankle weights, 3. Upper extremity TheraBand strengthening exercises and lower extremity TheraBand strengthening exercises. Duration: 8 months. Follow-up: 12 and 24 weeks.

Rodrigues Sanchez-Laulhe et al (2022) Spain	To assess the short- and medium-term efficacy of a digital app (CareHand) that includes a tailored home exercise program, together with educational and self-management recommendations, compared with usual care, for people with RA of the hands.	n=22 Mean age: 61.8 ± 10.7 Male/female: 41%/59%	n=14 Mean age: 57.6 ± 7.2 Male/female: 36%/64%	Hand exercise programme delivered in primary care. Strength exercises used: 1. This consisted of providing a written exercise program and recommendations on a paper sheet, together with pictures and written explanations of upper limb strengthening and stretching exercises focusing on the hands, wrist, and finger joints.	Hand exercise programme delivered using the CareHand app. Strength exercises used: 1. Unclear (unable to access app) Duration: 12 weeks. Follow-up: 12 weeks and 6 months.
Somers et al (2022) United States	To examine the feasibility of an enhanced lifestyle behavioural weight management protocol in a sample of RA patients with obesity.	n=29 Mean age: 55.6 ± 12.9 Male/female: 9.9%/90.1%	n=21 Mean age: 56.4 ± 9.7 Male/female: 6.9%/93.1%	Standard care, with patients assigned to this condition continued to receive their routine RA care, including regular appointments with their rheumatologist and appointments as needed for symptom flares or other RA-related problems	Enhanced Lifestyle Behavioural Weight Management Group where patients received instruction in pain coping skills and traditional behavioural weight management strategies and exercise. Strength exercises used: 1. Isometric strengthening of postural muscles. Duration: 12 weeks. Follow-up: 12 weeks (i.e. post-intervention).
Yun et al (2023) South Korea	To develop and evaluate the effects of a self-determination theory-based, nurse-led, physical activity programme for postmenopausal women with RA.	n=31 Mean age: 63.3 ± 7.4 Male/female: 0%/100%	n=31 Mean age: 63.1 ± 6.8 Male/female: 0%/100%	Instructed to continue their usual daily activities and were provided with routine care at the rheumatology outpatient clinic.	Tai Chi-based physical activity, a supportive psychosocial strategy based on the SDT constructs, and interactive counselling using the telephone/social networking service. Strength exercises used: 1. Eleven motions.
Teuwen et al (2024) Netherlands	To compare the effectiveness of longstanding (>52 weeks), supervised exercise therapy with usual care in adults with RA and severe functional limitations.	n=106 Mean age: 58.1 ± 13.6 Male/female: 8.5%/91.5%	n=109 Mean age: 59.4 ± 12.1 Male/female: 11%/89%	Usual care, with the content and delivery determined by the treating clinician(s) and participants themselves. The use of regular physical therapy, accessible through referral by a physician or self- referral (direct access), was neither encouraged nor discouraged.	Personalised, supervised and longstanding (≥52 weeks) active exercise therapy according to a standardised treatment protocol delivered by a trained primary care physical therapist. Strength exercises used: 1. Muscle strengthening exercises (using own weight or devices) Duration: 16 weeks. Follow-up: 8 weeks and 16 weeks.

3.12.3.1. Risk of bias assessment.

One RCT (12%) was assessed to be at overall low RoB (Ellegaard et al., 2019), four RCTs (44%) to be at unclear RoB (Khan et al., 2022, Rodrigues et al., 2020, Teuwen et al., 2024, Yun et al., 2023) and four (44%) RCTs to be at high RoB (Azeez et al., 2020, Garcia-Morales et al., 2020, Rodriguez Sanchez-Laulhe et al., 2022, Somers et al., 2022) (Table 3.8).

Table 3. 8. Results of the RoB assessment for each included study.

RCT	Sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessors for all outcomes	Incomplete outcome data for all outcomes	Selective outcome reported	Other sources of bias
Ellegaard et al (2019)	✓	✓	×	✓	✓	✓	✓
Azeez et al (2020)	✓	?	×	×	×	✓	×
Garcia-Morales et al (2020)	✓	?	×	✓	✓	✓	×
Rodrigues et al (2020)	✓	?	×	✓	✓	✓	✓
Khan et al (2022)	✓	?	×	?	✓	✓	✓
Rodrigues Sanchez-Laulhe et al (2022)	✓	✓	×	?	×	✓	✓
Somers et al (2022)	✓	✓	×	✓	×	✓	✓
Yun et al (2020)	✓	?	×	?	✓	✓	✓
Teuwen et al (2024)	✓	✓	×	?	✓	✓	✓

3.12.3.2. Completeness of intervention descriptions.

Eight RCTs (89%) provided incomplete descriptions of their interventions. Key dose parameters were also incomplete (Table 3.9).

Table 3. 9. Adapted TIDieR checklist for reporting of interventions in included primary evidence sources.

TIDieR Item	1 Brief Name	2 Why	3 What Materials	4 What Procedures	5 Who Provided	6 How Delivered	7 Where Delivered	8 When and How Much (Strengthening Exercise)		9 Tailoring	10 Modifications	11 How well (planned)	12 How well (actual)
Ellegaard et al (2019)	✓	✓	✓	✓	✓	✓	✓	1: ✓ 2: ✓ 3: ✓ 4: ✓ 5: ×	6: ✓ 7: × 8: ✓ 9: ✓ 10: ✓	✓	✓	✓	✓
Azeez et al (2020)	✓	✓	×	×	✓	×	×	1: × 2: × 3: × 4: × 5: ×	6: × 7: × 8: ✓ 9: ✓ 10: ✓	✓	×	×	×
Garcia-Morales et al (2020)	✓	✓	×	✓	✓	✓	×	1: × 2: × 3: ✓ 4: ✓ 5: ×	6: ✓ 7: × 8: × 9: ✓ 10: ✓	×	×	✓	×
Rodrigues et al (2020)	✓	✓	✓	✓	✓	✓	✓	1: ✓ 2: ✓ 3: ✓ 4: ✓ 5: ×	6: ✓ 7: × 8: ✓ 9: ✓ 10: ✓	✓	×	×	×
Khan et al (2022)	✓	✓	✓	✓	×	×	×	1: × 2: ✓ 3: × 4: × 5: ×	6: × 7: × 8: × 9: ✓ 10: ✓	×	×	×	×

Rodrigues Sanchez-Laulhe et al (2022)	✓	✓	✓	✓	✓	✓	✓	1: × 2: × 3: × 4: × 5: ×	6: × 7: × 8: × 9: ✓ 10: ✓	✓	×	✓	×
Somers et al (2023)	✓	✓	×	✓	✓	✓	✓	1: × 2: × 3: × 4: × 5: ×	6: × 7: × 8: × 9: ✓ 10: ✓	×	×	✓	✓
Yun et al (2023)	✓	✓	×	✓	✓	✓	✓	1: × 2: × 3: ✓ 4: ✓ 5: ×	6: ✓ 7: × 8: × 9: ✓ 10: ✓	✓	×	✓	✓
Teuwen et al (2024)	✓	✓	✓	✓	✓	✓	✓	1: × 2: × 3: × 4: × 5: ×	6: × 7: × 8: × 9: ✓ 10: ✓	✓	✓	✓	✓
% Completion	100%	100%	56%	89%	89%	78%	67%	1: 22% 2: 33% 3: 33% 4: 44% 5: 0%	6: 44% 7: 0% 8: 33% 9: 100% 10: 100%	67%	22%	67%	44%

✓ = Item sufficiently described in the trial. × = Inadequately or not described.

Item 8

1 = Exercise type	6 = Intensity (%1RM/Borg)
2 = Strength equipment used	7 = Recovery
3 = Sets	8 = Progression
4 = Repetitions	9 = Frequency
5 = Load (kg/lbs)	10 = Programme duration

3.12.3.3. RCTs using pilot studies.

None of the nine identified RCTs reported conducting a pilot study.

3.12.3.4. RCTs using dose escalation methodology.

Across the nine trials, no evidence of dose-escalation methodology was reported.

3.12.3.5. RCTs reporting underpinning evidence.

Four RCTs (44.4%) did not cite evidence to underpin prescribed dose of strengthening exercise (Azeez et al., 2020, Khan et al., 2022, Rodrigues et al., 2020, Somers et al., 2022). The remaining five RCTs (55.6%) cited in total 15 evidence sources to underpin prescribed dose of strengthening exercise. This information is available as supplementary material (Appendix 5).These included clinical trials (n=3), literature reviews (n=4), clinical guidelines (n=3), books (n=2), publications describing intervention development (n=2) and a publication about a reporting tool (n=1).

3.12.3.6. Quality, consistency and applicability of the underpinning evidence.

Quality: We rated the quality of the 15 underpinning evidence sources using the OCEBM level of evidence framework (Table 3.10). We judged two (13.3%) to be level 2 evidence (Osthoff et al., 2018a, Williams et al., 2015) and two (13.3%) to be level 3 evidence (Brorsson et al., 2009, Moritani and DeVries, 1979). One (6.8%) of the underpinning evidence sources was an intervention development paper for the SARAH RCT by Lamb et al (2015). Exploring the references this source used, we assigned a level of evidence rating that best described their quality. Its level of evidence ranged between 2-5 (Heine et al., 2012). Sometimes, assigning the level of evidence wasn't straightforward. We rated eight (53.3%) as 'unclear' (Borg, 1998, Gabriel et al., 2006, Garber et al., 2011, Haskell et al., 2007, Osthoff et al., 2018a, Williams et al., 2012). Two of the eight underpinning evidence sources (Garber et al., 2011, Osthoff et al., 2018a) were used by two different RCTs (Teuwen et al., 2024, Yun et al., 2023). One evidence source (6.7%) we assigned an 'incorrect' rating owing to the evidence source being a tool for assessing therapeutic quality of exercise programmes (Hoogeboom et al., 2021).

Consistency: Trials were explored to see whether they explored to identify if it used the same dose as described/recommended by the underpinning evidence (Table 3.10). We found nine examples across two RCTs (Ellegaard et al., 2019, Teuwen et al., 2024) where the dose used was the same as the dose used/recommended by the underpinning evidence source. There were twenty-one examples across three RCTs where the dose used was different (Ellegaard et al., 2019, Rodriguez Sanchez-Laulhe et al., 2022, Teuwen et al., 2024). We found seventy-nine examples across five RCTs where we were unable

to compare dose used due to insufficient detail (Ellegaard et al., 2019, Garcia-Morales et al., 2020, Rodriguez Sanchez-Laulhe et al., 2022, Teuwen et al., 2024, Yun et al., 2023) and across five RCTs (Ellegaard et al., 2019, Garcia-Morales et al., 2020, Rodriguez Sanchez-Laulhe et al., 2022, Teuwen et al., 2024, Yun et al., 2023), we found no examples where dose parameters were unsupported with evidence. However, four of the five RCTs cited an evidence source to underpin programme design, making it unclear how well each parameter was supported by evidence (Ellegaard et al., 2019, Rodriguez Sanchez-Laulhe et al., 2022, Teuwen et al., 2024, Yun et al., 2023).

Applicability: The applicability of the 15 underpinning evidence sources in relation to RA, gender and age varied (Table 3.10). Eight (55.3%) were judged not applicable to RA (Borg, 1982, Borg, 1998, Gabriel et al., 2006, Garber et al., 2011, Haskell et al., 2007, Hoogeboom et al., 2021, Moritani and DeVries, 1979). Garber et al (2011) was cited twice (Teuwen et al., 2024, Yun et al., 2023). Thirteen (86.6%) were judged not applicable to gender or age (Adams et al., 2012, Borg, 1982, Borg, 1998, Gabriel et al., 2006, Garber et al., 2011, Haskell et al., 2007, Heine et al., 2012, Hoogeboom et al., 2021, Moritani and DeVries, 1979, Osthoff et al., 2018a, Williams et al., 2012). Garber et al (2011) and Osthoff et al (2018a) were cited twice (Teuwen et al., 2024, Yun et al., 2023).

Table 3. 10. Quality, consistency, and applicability of the underpinning evidence.

RCT	Underpinning evidence	Quality	Consistency									Applicability		
		OCEBM level	Exercise	Sets	Reps	Load	Intensity	Recovery	Progress	Frequency	Duration	RA	Gender	Age
Ellegaard et al, 2019	Brorsson et al, 2009	'3'	×	×	×	✓	✓	?	×	×	×	✓	✓	✓
	Adams et al, 2012	'5'	?	?	?	?	?	?	?	×	×	✓	×	×
	Heine et al, 2012	'2-5'	×	✓	✓	?	✓	?	×	×	×	✓	×	×
	Moritani & DeVries, 1979	'3'	×	×	×	×	×	?	×	×	✓	×	×	×
	Gabriel et al, 2006	'Unclear"	?	?	?	?	?	?	?	?	?	×	×	×
	Borg, 1982	'5'	Nil	Nil	Nil	Nil	?	Nil	Nil	Nil	Nil	×	×	×
Garcia-Morales et al (2020)	Haskell et al, 2007	'Unclear	Nil	Nil	Nil	Nil	?	Nil	Nil	Nil	Nil	×	×	×
Rodrigues Sanchez-Laulhe (2022)	Williams et al, 2015	'2'	?	?	?	?	?	?	?	×	✓	✓	✓	✓
	Williams et al, 2012	'Unclear'	?	?	?	?	?	?	?	?	?	✓	×	×
Yun et al (2023)	Osthoff et al, 2018a	'Unclear'	?	?	?	?	?	?	?	?	?	✓	×	×
	Borg, 1998	'Unclear'	Nil	Nil	Nil	Nil	?	Nil	Nil	Nil	Nil	×	×	×
	Garber et al, 2011	'Unclear	?	?	?	?	?	?	?	?	?	×	×	×
Teuwen et al (2023)	Osthoff et al, 2018a	'Unclear	?	?	?	?	?	?	?	?	?	✓	×	×
	Hoogeboom, 2021	'Incorrect citation'	?	?	?	?	?	?	?	?	?	×	×	×
	Garber et al, 2011	'Unclear	?	?	?	?	✓	?	✓	×	?	×	×	×

× = Inconsistent/not applicable.? = Unclear as insufficiently described/not described. ✓ = Consistent/applicable. Nil = Source not used to underpin dose parameter.

3.12.3.7. Relationship between RoB and underpinning evidence.

Exploration of a relationship between the RoB for the five RCTs and the judged quality (OCEBM level of evidence) of the underpinning evidence (Table 3.11) was made. Relating to RoB, one RCT (20%) was assessed to be at overall low RoB (Ellegaard et al., 2019), two RCTs (40%) to be at unclear RoB (Teuwen et al., 2024, Yun et al., 2023) and two (40%) RCTs to be at high RoB (Garcia-Morales et al., 2020, Rodriguez Sanchez-Laulhe et al., 2022). While there were too few studies for reliable statistical evaluation, of the four RCTs assessed as unclear, or at high risk of bias, seven (100%) had evidence rated as incorrect or unclear (Garcia-Morales et al., 2020, Rodriguez Sanchez-Laulhe et al., 2022, Teuwen et al., 2024, Yun et al., 2023). Of the one assessed at low RoB, one of the six underpinning evidence sources were rated as incorrect or unclear (Ellegaard et al., 2019).

Table 3. 11. RoB and level of underpinning secondary evidence for primary evidence sources.

RCT	Sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessors for all outcomes	Incomplete outcome data for all outcomes	Selective outcome reported	Other sources of bias	Overall RoB rating	No of underpinning evidence sources	Source 1 - OCEBM level of evidence	Source 2 - OCEBM level of evidence	Source 3 - OCEBM level of evidence	Source 4 - OCEBM level of evidence	Source 5 - OCEBM level of evidence	Source 6 - OCEBM level of evidence
Ellegaard et al (2019)	✓	✓	×	✓	✓	✓	✓	✓	6	3 Brorsson et al, 2009	5 Adams et al, 2012	2-5 Heine et al, 2012	3 Moritani & DeVries, 1979	Unclear Gabriel et al, 2006	5 Borg, 1982
Garcia-Morales et al (2020)	✓	?	×	✓	✓	✓	×	×	1	Unclear Haskell et al, 2007					
Rodrigues Sanchez-Laulhe et al (2022)	✓	✓	×	?	×	✓	✓	×	2	2 Williams et al, 2015	Unclear Williams et al, 2012				
Yun et al (2023)	✓	?	×	?	✓	✓	✓	?	3	Unclear Osthoff et al, 2018a	Unclear Borg, 1998	Unclear Garber et al, 2011			

Teuwen et al (2024)	✓	✓	×	?	✓	✓	✓	?	3	Osthoff et al, 2018a	Incorrect citation Hoogeboom, 2021	Unclear Garber et al, 2011			

✓ = Low RoB.? = Unclear RoB. × = High RoB

3.12.4. Discussion.

3.12.4. Summary of main results.

The update to the systematic review identified nine published clinical trials. It explored in detail the underpinning evidence used by healthcare researchers to justify the prescribed dose of strengthening exercise used in clinical trials of RA. Similar to the results presented in published review, reporting of the intervention characteristics was broadly poor with the exception of Ellegaard et al (2019). None of the nine trials reported piloting the intervention or used dose-escalation designs to optimise dose-response. Previously, four clinical trials reported conducting a pilot study. In keeping with the previous results, almost half of the clinical trials employing a strength exercise component do not report evidence underpinning dose choices. Furthermore, similar to previous results, the underpinning evidence cited by healthcare researchers to justify dose parameters varied in quality and applicability and sometimes, no support existed the reported dose parameters such as sets, repetitions, load or progression.

3.12.5. Conclusion.

The results of the updated search do not change the overall conclusions of the review published in 2020.

CHAPTER FOUR. STUDY TWO. UNDERSTANDING PRESCRIBED DOSE IN HAND STRENGTHENING EXERCISE FOR RA: A SECONDARY ANALYSIS OF THE STRENGTHENING AND STRETCHING FOR RHEUMATOID ARTHRITIS OF THE HAND (SARAH) MULTICENTRE RCT.

4.1. Study overview.

The second study in this thesis, this chapter provides a rationale for selecting the study methodology, a description of the study objectives, the methods used, results and discussion. A protocol was developed prior to the study but was not registered or published. The study was published in Musculoskeletal Care (Boniface et al., 2022) (Appendix 6), presented in poster format at the virtual NHS Scotland Allied Health Professionals Research event and reported via social media (i.e. Twitter/X).

4.2. Introduction.

The SARCH RCT instigated NICE to recommend tailored strengthening and stretching hand exercise (Lamb et al., 2015, National Institute for Health and Care Excellence, 2018). NICE offer no information for HCPs about what dose to prescribe. Determining optimal dosage of hand exercise in RA is indicated (Hammond and Prior, 2016, Williams et al., 2018). The results of study one questioned whether dose is optimised for individuals living with RA. Considering that identifying what dose works best in interventions shown to be effective is a research priority for patients, carers, and HCPs (Chartered Society of Physiotherapy, 2018), in this chapter we used to data from the SARAH RCT to answer the following objectives:

4.3. Study objectives.

1. To explore the therapist and participant characteristics at baseline associated with the overall dose of hand strengthening exercise prescribed to participants in the SARAH RCT (Analysis 1).
2. To explore the association between overall dose of hand strengthening exercise prescribed during the programme and hand function and grip strength at 4-month follow-up (Analyses 2 and 3).

4.4. Background to the SARAH RCT.

The SARAH multicentre RCT was a pragmatic parallel-group trial conducted at 17 National Health Service sites across the UK. It found that providing a tailored hand exercise programme in addition to usual care, is a clinically and cost-effective adjunct to the various drug regimens presently recommended (Lamb et al., 2015). The complete methods of the SARAH RCT are described in full elsewhere (Williams et al., 2015). The outcomes of the SARAH RCT resulted in NICE recommending

tailored hand exercise for individuals with pain and dysfunction of the hands and wrists caused by RA (National Institute for Health and Care Excellence, 2018).

4.4.1. SARAH hand exercise programme.

The programme comprised six sessions of face-to-face contact (one assessment and five supervised exercise sessions) with an occupational therapist or physiotherapist. Seven mobility and four strengthening exercises were used. The four strengthening exercises (eccentric wrist extension, gross grip, pinch grip, finger adduction) used load (resistance) provided by bands, balls, or therapeutic putty. Therapists followed a predefined protocol for prescribing the dose (sets, repetitions, and load) of each strengthening exercise. Intensity was set using the Borg rating of perceived exertion scale (Borg, 1982) and each exercise was progressed or regressed according to both participant capability and therapist judgement. The goal was for the participant to perform each exercise, where possible at a volume and load that was achievable while still providing a stimulus for physiological change (Heine et al., 2012).

4.4.2. Post-hoc analysis of the SARAH hand exercise programme.

Hall et al (2017) conducted a causal mediation analysis of the SARAH RCT to determine whether overall hand function measured by the Michigan Hand Outcomes Questionnaire (MHQ) for the treatment outcome (Chung et al., 1998) was mediated by changes in strength (full hand and tripod pinch grip strength) and mobility (wrist and finger flexion and extension, thumb opposition and dexterity). Each proposed mediating variable was tested to determine if they had a significant effect on overall hand function at the four-month trial timepoint. Only grip strength was identified as a significant mediator, and a single mediator model was chosen to test grip strength individually. Grip strength was found to mediate 19.4% (95% CI: 0.9% to 37.8%) of the change in overall hand function. Although, the authors conclude that improved grip strength partially mediated the improvement in overall hand function, they also acknowledged that other factors may also contribute to this improvement (Hall et al., 2017).

4.5. Methods.

4.5.1. Ethical approval.

Ethical approval for this study was granted by Brunel University London Research Ethics Committee (13763-LR-Jan/2019- 17357-1) (Appendix 7). This study was a post-hoc exploratory analysis of the data from the SARAH RCT. Original ethical approval for the SARAH RCT (ISRCTN registration number: 89936343) was gained from the Oxford C Multi-Centre Research Ethics Committee (MREC 08/H0606/47).

4.5.2. Data collection.

This study used data provided by participants at baseline and 4-month follow-up. Data describing the prescribed hand strengthening exercise was extracted from the exercise treatment logs that were completed by therapists at each exercise session (Williams et al., 2015), including dose parameters (sets, repetitions and load). Where exercise treatment logs contained insufficient/ambiguous information about dose, we utilised the personal exercise diaries completed by the therapist and participant to assist with completion.

4.5.3. Participants.

Between 05/10/2009 and 10/05/2011, the SARAH RCT recruited 490 participants with a RA diagnosis according to the American College of Rheumatology clinical and immunological criteria (American College of Rheumatology Subcommittee on Rheumatoid Arthritis, 2002), with pain and dysfunction of the hands and/or wrist joints, who were not on a disease-modifying antirheumatic drugs (DMARD) regime, or had been stable on a DMARD regime (including biological agents if used) for 3 months or more were recruited. 244 participants were randomly assigned to usual care and 246 to the tailored exercise programme. Usual care included information published by Arthritis Research UK, joint-protection education and, where indicated, functional splinting.

4.5.4. Prescribed dose of hand strengthening exercise.

The overall dose of hand strengthening exercise that participants were prescribed at the five supervised exercise sessions was calculated using the area under the curve (AUC) method. This approach has previously been used for identifying response to an intervention and considers the change in the value of a parameter over time (Matthews et al., 1990, Pruessner et al., 2003).

4.5.4.1. Calculating overall dose using area under the curve.

To calculate overall dose of strengthening exercise, first the dose of strengthening exercise was calculated for each individual exercise (wrist extension, gross-grip, finger adduction and pinch-grip) for both left and right hands. To calculate the area under the curve (AUC), Microsoft Excel was used. To calculate AUC, we theoretically mapped (e.g. didn't physically draw the graph) the trendline for dose of strengthening exercise and then determined the four integrals underneath the trendline. Participant five from the SARAH RCT is used as an example to describe the step-by-step approach:

4.5.4.2. Step by step example for calculating overall dose.

Participant five attended four out of the five supervised exercise sessions with a SARAH trained therapist. They missed one exercise session (session 4) due to being unwell. Each of the four strengthening exercises (wrist extension, gross-grip, finger adduction and pinch-grip) used had the following dose parameters (sets, repetitions, and load) recorded in the exercise treatment logs (Table 4.1) by the SARAH therapist. This represents the therapist prescribed dose of strengthening exercise completed by the participant at the face-to-face session across all four exercises.

Table 4. 1. Participant five documented strength exercise data.

Exercise session	Eccentric wrist extension			Gross grip			Finger adduction			Finger pinch		
	Sets	Reps	Load	Sets	Reps	Load	Sets	Reps	Load	Sets	Reps	Load
1	1	10	Red	1	10	Yellow	1	10	Yellow	1	10	Yellow
2	1	10	Red	1	10	Yellow	1	10	Yellow	1	10	Yellow
3	1	10	Red	1	10	Red	1	10	Yellow	1	10	Yellow
4	-	-	-	-	-	-	-	-	-	-	-	-
5	1	10	Red	1	10	Yellow	1	10	Yellow	1	10	Yellow

To calculate the overall cumulative dose prescribed by the therapist and completed by the participant we completed the following steps in Microsoft Excel.

Step 1:

For each exercise across the five-exercise sessions, we completed the following three steps:

1) Sets were multiplied by repetitions to calculate the volume (e.g. 1x10=10).

2) Load (denoted by colour) was replaced with a corresponding load value (Table 4.2) (e.g. red=5).

3) Volume was multiplied by the load value to calculate dose (Table 4.3). Graphically, dose for each exercise across the five exercise sessions is shown below (Figure 4.1).

Table 4. 2. Corresponding load value.

Resistance colour	Load value	Resistance colour	Load value
Nil load used	1	**Green**	6
White	2	**Blue**	7
Cream/Flesh/Pink/Tan	3	**Black**	8
Yellow	4	**Silver†**	9
Red	5	**Gold†**	10

†Silver and gold are colours used to denote the strongest TheraBands

Table 4. 3. Participant five strength exercise data.

Exercise session	Eccentric wrist extension	Gross grip	Finger adduction	Finger pinch
	Dose	Dose	Dose	Dose
1	50	40	40	40
2	50	40	40	40
3	50	50	40	40
4	0	0	0	0
5	50	40	40	40

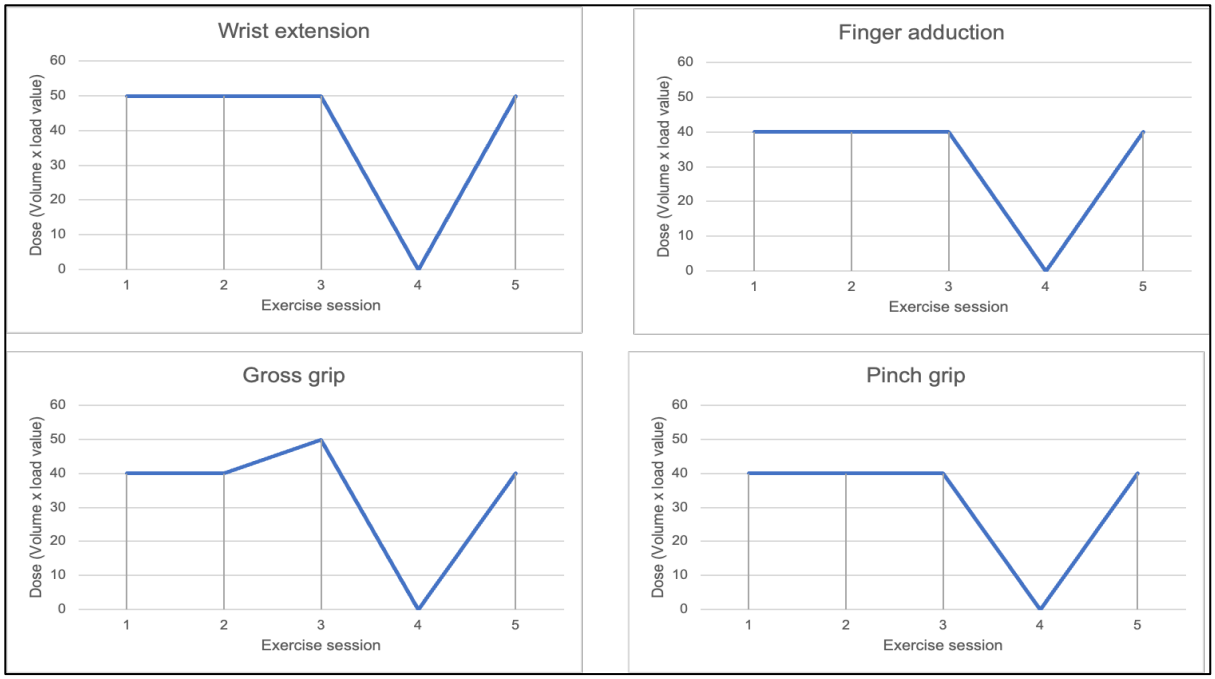

Figure 4. 1. Dose trendlines for each strengthening exercise.

Step 2:

To calculate overall AUC for each strengthening exercise, the four integral areas (i.e. exercise sessions 1-2, exercise sessions 2-3, exercise sessions 3-4 and exercise sessions 4-5) under the trendlines (Figure 5.2) were added together using Microsoft Excel (Table 4.4). Using wrist extension as an example, the following formula =SUM(B1+B2)/2*(A2-A1) was used to calculate the four integral AUC (Column C). For example, to calculate the integral AUC between session 1 and 2, the equation would be: Integral AUC=SUM (50+50)/2*(2-1). We repeated this equation for calculating integrals between exercise sessions 2 and 3, 3 and 4 and 4 and 5. Note there is no value recorded in Column C, Row 5. This is because, in Excel, the value in the cell is deleted as it references nothing in what would be Row 6. The process was repeated for the other three strengthening exercises. Overall AUC (Cell D, Row 4) was calculated by adding together the four integral AUC values. To calculate the overall cumulative dose prescribed by the therapist and completed by the participant across the five face-to-face exercise

sessions, the overall AUC values (i.e. 150+130+120+120=520) were added together. This process was repeated for both hands to consider any differences in dose between left and right sides. In participant 5's case, the dose used for both hands were identical, therefore the overall dose of strengthening exercise prescribed by the therapist and completed by the participant was 1040 AUC.

Table 4. 4. Calculating integral AUC and overall AUC in Microsoft Excel.

Row	Column												
	Cell A	**Cell B**	**Cell C**	**Cell D**	**Cell E**	**Cell F**	**Cell G**	**Cell H**	**Cell I**	**Cell J**	**Cell K**	**Cell L**	**Cell M**
	Exercise session	**Eccentric wrist extension**			**Gross grip**			**Finger adduction**			**Finger pinch**		
		Dose	**Integral AUC**	**Overall AUC**	**Dose**	**Integral AUC**	**Overall AUC**	**Dose**	**Integral AUC**	**Overall AUC**	**Dose**	**Integral AUC**	**Overall AUC**
Row 1	1	50	50		40	40		40	40		40	40	
Row 2	2	50	50		40	45		40	40		40	40	
Row 3	3	50	25		50	25		40	20		40	20	
Row 4	4	0	25	150	0	20	130	0	20	120	0	20	120
Row 5	5	50			40			40			40		

The study focused exclusively on the dose prescribed and completed at the five supervised exercise sessions due to well recognised problems with recording exercise adherence to home exercise (Nicolson et al., 2018). Table 4.5 provides a guide for a participant attending all five supervised exercise sessions. For example, if the participant was prescribed 1x10 repetitions using yellow band, ball, or therapeutic putty for each of the four strengthening exercises used in the SARAH programme, the prescribed overall dose would be 640 AUC.

Table 4. 5. A guide to interpreting dose calculated using AUC.

Volume	**Load (Resistance used)** [†]							
Sets x Repetitions	*Nil load*	*White*	*Tan*	*Yellow*	*Red*	*Green*	*Blue*	*Black*
1x10	160	320	440	640	800	960	1120	1280
2x10	320	640	880	1280	1600	1920	2240	2560
3x10	480	960	1320	1920	2400	2880	3360	3840

[†]White = Lowest resistance. Black = Highest resistance of band, ball, or therapeutic putty.

4.5.5. Candidate predictors for prescribed dose.

Based on theoretical knowledge and the clinical experience of physiotherapists within the research team, the following candidate predictors potentially associated with the overall dose prescribed were selected (Table 4.6).

Table 4. 6. Selected candidate predictors of overall dose prescribed.

Candidate predictors	How measured
Age	Measured in years
Gender	Female Male
Therapist profession	Occupational therapist Physiotherapist
Therapist grade (Agenda for Change†)	Band 5 Band 6 Band 7
Active wrist extension	Measured in degrees by goniometer
Hand and wrist swelling count	0-22 (0 = No swollen joints)
Hand and wrist tenderness count	0-22 (0 = No tender joints)
Mean combined finger flexion	Measured in millimetres by ruler
Metacarpophalangeal (MCP) joint deformity	Deformity present (Radial/ulnar) No deformity
Thumb opposition‡	Measured using the Kapandji scale (0-10, 10 = best opposition)
Full-hand grip strength	Newtons (Measured by dynometer)
Tripod grip strength	Newtons (Measured by dynometer)
Confidence to perform exercise without making symptoms worse	0 - 10 (10 = Totally confident)
Michigan hand outcomes questionnaire (MHQ) overall hand function subscale score§	0 - 100 (100 = Greater function)
Pain frequency	Rarely/never Sometimes Always/often
Pain severity	Very mild/mild Moderate Severe/very severe
Short-Form Survey (SF-12) question¶ - Have you accomplished less than you would like?	A little/most of the time Some of the time All/most of the time
Short-Form Survey (SF-12) question¶ - Have you felt downhearted and low?	A little/most of the time Some of the time All/most of the time
Years diagnosed with RA	Measured in years

†(National Health Service, 2021); ‡(Kapandji, 1992); §(Chung et al., 1998), ¶(Jenkinson and Layte, 1997)

4.5.6. Hand function and grip strength.

Hand function and grip strength at 4-month follow-up (closest to the supervised exercise sessions ending) were the outcomes used in the model to evaluate association with exercise dose. MHQ overall hand function was the primary outcome in the SARAH RCT, and hand grip strength is known to partially mediate overall hand function (Hall et al., 2017).

4.6. Statistical Analysis.

Data was analysed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, N.Y., USA). The unit of analysis was the hand. Distribution of the outcome and each candidate variable was described using mean and standard deviation, median (interquartile range), as well as tabulations of frequency and percentage.

4.6.1. Analysis 1 (To identify the therapist and participant characteristics at baseline associated with the overall dose of hand strengthening exercise prescribed to participants in the SARAH RCT).

Steps:

1. Distribution of continuous independent and dependent variables were checked for normality using histograms. Possible errors were also checked within the data.
2. Generalised estimating equation (GEE) univariate analysis: Variables with a ($p<0.10$) were included from the multivariate analysis. For each participant, an exchangeable correlation matrix was used to adjust for correlation between each hand.
3. Multivariate analysis: To select factors associated with prescribed overall dose, backward stepwise regression was used with a $p<0.05$ used as a cut off. Only complete cases were used.
4. Generalised estimating equations (GEE) linear regression. Coefficients (β) with 95% confidence intervals (CIs) were calculated.

4.6.2. Analyses 2 and 3 (To identify the association between overall dose of hand strengthening exercise prescribed during the programme and hand function and grip strength at 4-month follow-up).

Steps:

1. Each predictor variable identified in analysis 1 with a $p<0.10$ was included in the univariate analysis.
2. GEE Univariate analysis: Along with prescribed overall dose (independent variable), we evaluated whether each predictor variable was associated with the dependent variable of outcome (4-month overall hand function or full-hand grip strength). Adjustment was made for baseline overall hand function and full-hand grip strength respectively. Only complete cases were used.
3. Variables associated with both prescribed overall dose and outcome (p-value <0.05) were included in the multivariate analysis.
4. GEE linear regression. Coefficients (β) with 95% confidence intervals (CIs) were calculated.

4.7. Results.

4.7.1. Characteristics of participants included.

Of the 246 participants randomised to the tailored exercise programme, 24 (9.7%) were excluded: 19 because no hand strengthening exercise was prescribed (e.g., withdrew from treatment) and 5 because their exercise treatment logs were recorded as missing (e.g., unable to calculate dose).

Participants who had no hand strengthening exercise prescribed were younger (mean (SD; standard deviation) 56.4 (15.5) vs. 61.6 (11.9)), had a longer diagnosis of RA (mean (SD; standard deviation) 14.0 (10.3) vs. 12.4 (10.1)) and more frequently (always/often) reported pain (73.7% vs. 61.7%). Participant characteristics are described in more detail in and are available in table 4.7.

Table 4. 7. Characteristics of non-hand specific study sample variables (N=246)

Indicator variable	Participants with dose	Participants with no dose	Participants with missing dose
	n=222 (444 hands)	**n=19 (38 hands)**	**n=5 (10 hands)**
Participant age, mean (SD):	61.6 (11.9)	56.4 (15.5)	62.4 (13.0)
Participant age, n (%):			
Less than 45 years	22.0 (9.9)	6.0 (31.6)	0.0 (0.0)
45-54 years	35.0 (15.8)	3.0 (15.8)	2.0 (40.0)
55-64 years	73.0 (32.9)	2.0 (10.5)	1.0 (20.0)
65 and over	92.0 (41.4)	8.0 (42.1)	2.0 (40.0)
Missing data	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
Sex, n (%):			
Male	54.0 (24.3)	3.0 (15.8)	1.0 (20.0)
Female	168.0 (75.7)	16.0 (84.2)	4.0 (80.0)
Missing data	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
Years diagnosed with RA, mean (SD):	12.4 (10.1)	14.0 (10.3)	5.8 (3.8)
Missing data	1.0 (0.5)	0.0 (0.0)	0.0 (0.0)
Type of therapist treating, n (%):			
Physiotherapist	79.0 (35.6)	0.0 (0.0)	1.0 (20.0)
Occupational therapist	143.0 (64.4)	4.0 (21.1)	4.0 (80.0)
Missing data	0.0 (0.0)	15.0 (78.9)	0.0 (0.0)
Treating therapist grade, n (%):			
Job band 5	10.0 (4.5)	1.0 (5.3)	0.0 (0.0)
Job band 6	133.0 (59.9)	3.0 (15.8)	2.0 (40.0)
Job band 7	70.0 (31.5)	0.0 (0.0)	2.0 (40.0)
Missing data	9.0 (4.1)	15.0 (78.9)	1.0 (20.0)
Pain frequency, n (%):			
Always/often	137.0 (61.7)	14.0 (73.7)	3.0 (60.0)
Sometimes	59.0 (26.6)	4.0 (21.1)	2.0 (40.0)
Rarely/never	26.0 (11.7)	1.0 (5.3)	0.0 (0.0)
Missing data	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
Pain severity, n (%):			
Very mild/mild	55.0 (24.8)	4.0 (21.1)	1.0 (20.0)

Moderate	116.0 (52.3)	7.0 (36.8)	4.0 (80.0)
Severe/very severe	45 (20.3)	8.0 (42.1)	0.0 (0.0)
Missing data	6.0 (2.7)	0.0 (0.0)	0.0 (0.0)
Accomplished less than liked (SF-12), n (%):			
All/most of the time	38.0 (17.1)	5.0 (26.3)	1.0 (20.0)
Some of the time	52.0 (23.4)	5.0 (26.3)	2.0 (40.0)
A little/none of the time	132.0 (59.5)	9.0 (47.4)	2.0 (40.0)
Missing data	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
Feeling downhearted or low (SF-12), n (%):			
All/Most of the time	17.0 (7.7)	4.0 (21.1)	1.0 (20.0)
Some of the time	52.0 (23.4)	4.0 (21.1)	2.0 (40.0)
A little/none of the time	140.0 (63.1)	11.0 (57.9)	2.0 (40.0)
Missing data	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
Confidence to perform exercise, median (IQR):	7.0 (5.0, 9.0)	6.0 (3.0, 8.0)	6.0 (4.5, 9.2)
Missing data, n (%)	1.0 (0.5)	0.0 (0.0)	0.0 (0.0)
Hand/wrist swollen joint count, median (IQR):	2.0 (1.0, 7.0)	3.0 (2.0, 7.0)	1.0 (0.0, 3.2)
Missing data, n (%)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
Hand/wrist joint tenderness count, median (IQR):	3.0 (1.0, 8.0)	5.0 (1.0, 9.0)	2.0 (2.0. 3.7)
Missing data, n (%)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)

4.7.2. Prescribed Overall Dose.

Overall dose of hand strengthening exercise was calculated for 222/246 (90.2%) participants (Table 4.8). Of the 4 exercises, gross grip had the highest overall dose prescribed compared to eccentric wrist extension, finger adduction and finger pinch.

Table 4. 8. Summary statistics of prescribed overall dose (AUC) (n=222)

Strengthening exercise	**Hand side**	**Median (IQR)**
Eccentric wrist extension:	Left:	160.0 (80.7, 205.0)
	Right:	160.0 (80.7, 205.0)
Gross grip:	Left:	260.0 (195.8, 391.2)
	Right:	260.0 (200.0, 382.5)
Finger adduction:	Left:	138.7 (74.6, 195.0)
	Right:	137.5 (75.7, 195.0)
Finger pinch:	Left:	162.5 (104.2, 220.0)
	Right:	165.0 (108, 217.0)
Prescribed overall dose:	**Left:**	**725.0 (501.8, 1017.0)**
	Right:	**731.5 (529.3, 1025.0)**

4.7.3. Analysis 1 (Factors associated with prescribed overall dose).

Following univariate analysis (Table 4.9), therapist type, therapist grade, metacarpophalangeal (MCP) joint deformity, thumb opposition, full-hand grip strength, tripod grip strength, overall hand function, hand and wrist swollen joint count, hand and wrist tender joint count, pain severity, accomplishing less than you would like, feel down hearted or low, confidence to perform exercise without fear of making symptoms worse, age, gender, years since diagnosed with RA were included in the backward stepwise multivariate regression. In this model a mix of therapist, participant physical and psychological factors were predictive of the prescribed overall dose. These are reported below:

Table 4. 9. Analysis 1: Univariate analysis of candidate predictors.

Predicting factors	No. participants /No. hands	Coef. (β)	95% CI	p-value
Therapist factors:				
Type of therapist (Reference category: physiotherapist):	222/444			
Occupational therapist		-272.0	-378.0; -166.0	0.00†
Therapist grade (Reference category: job band 7):	213/426			
Job band 5		-129.6	-352.8, 93.4	0.25
Job band 6		97.6	-3.1, 198.4	0.05†
Participant physical factors:				
MCP joint deformity (Reference category: No deformity):	221/442	-22.1	-39.3; -4.9	0.01†
Active wrist extension:	222/444	0.1	-0.2, 0.6	0.41
Composite finger flexion:	222/443	-0.3	-0.8, 0.1	0.13
Thumb opposition:	222/444	2.3	-0.1, 4.7	0.06†
Full-hand grip strength:	221/441	0.1	0.03, 0.2	0.01†
Tripod grip strength:	219/436	0.7	0.3, 1.1	0.00†
Overall hand function:	222/444	0.3	-0.05, 0.6	0.05†
Hand/wrist tender joint count:	222/444	-10.2	-18.9, -1.5	0.02†
Hand/wrist swollen joint count:	222/444	-11.3	-21.8, -0.9	0.03†
Participant reported factors:				
Age into 4 categories (Reference category: 55-64 years old):	222/444			
Less than 45		-171.1	-352.6; 10.4	0.06†
45-54		-86.9	-263.3; 89.5	0.33
65 and over		-80.1	-202.2; 42.0	0.19
Sex (Reference category: male):	222/444			

Female		-21.7	-49.8; 6.3	0.12†
Years since diagnosed with RA:	221/442	-4.9	-9.66, -0.19	0.04†
Pain frequency (Reference category: rarely/never):	222/444			
Always/often		-36.2	-186.7, 114.3	0.63
Sometimes		12.2	-161.8, 186.4	0.89
Pain severity (Reference category: Very mild/mild):	216/432			
Moderate		-49.7	-169.9; 70.4	0.41
Severe/very severe		-151.1	-292.2; -10.1	0.03†
Accomplished less than you would like (Reference category: A little/none of the time):	222/444			
All/Most of the time		-209.9	-333.2, -86.5	0.00†
Some of the time		-92.8	-224.1, 38.4	0.16
Feeling downhearted or low (Reference category: A little/none of the time):	222/444			
All/most of the time		-364.4	-532.0, -196.8	0.00†
Some of the time		-86.1	-203.5, 31.8	0.15
Confidence to perform exercise:	221/442	21.3	2.7, 39.9	0.02†

†Variables with a (p<0.10).

4.7.4. Therapist factors.

When the prescribing therapist was an occupational therapist, participants received (β= -297.0 AUC, 95% CI -398.6, -195.4, p=<0.001) less overall dose compared to when the clinician was a physiotherapist. Participants were prescribed greater overall dose of strengthening exercise (β= +159.1 AUC, 95% CI 65.7, 252.5, p=<0.001) when their therapist was a grade 6 compared to when their therapist was a grade 5 or grade 7.

4.7.5. Participant physical factors.

Participants with MCP joint deformity (radial or ulnar drift) were prescribed (β= -24.1 AUC, 95% CI -42.3, -5.9, p=<0.009) less overall dose compared to those participants with no deformity. Swollen joints count was also associated with less overall dose being prescribed. For each swollen joint recorded, overall dose reduced by (β= -11.4 AUC, 95% CI -21.6, -1.2, p=<0.028). In contrast, for each one Newton increase in full-hand grip strength recorded at baseline, the prescribed overall dose increased by (β= +0.15 AUC, 95% CI 0.02, 0.2, p=<0.016).

4.7.6. Participant psychological factors.

Participants who reported feeling downhearted or low all the time were prescribed (β= -293.6 AUC 95% CI -436.1, -151.1, p=<0.001) less overall dose when compared to those feeling downhearted less often. Conversely, participants who reported a greater confidence to exercise on a scale of 1-10 (10 = most confident) were associated with being prescribed a greater overall dose of hand strengthening exercise (β= +18.9 AUC, 95% CI 1.5, 36.3).

4.7.7. Association between prescribed overall dose and outcome.

4.7.7.1. Analysis 2 (Overall hand function).

Of the 246 participants, 29 (11.7%) were excluded: 24 where the outcome (overall hand function) was missing at baseline and/or 4-month follow up and 5 because their exercise treatment logs were recorded as missing (e.g., unable to calculate dose). Potential confounders (thumb opposition, full-hand grip strength, participant age, years diagnosed with RA, therapist grade, pain severity and confidence to perform exercise without making symptoms worse) were included in the multivariate analysis. Higher overall exercise dose was associated with better outcomes in function at 4-months. For every 1 AUC, overall hand function increased by β= 0.005 points (95% CI 0.001, 0.010, p=0.027).

4.7.7.2. Analysis 3 (Full-hand grip strength).

Of the 246 participants, we excluded 55 (22.3%), 50 where the outcome (full-hand grip strength) was missing at baseline and/or 4-month follow up and 5 participants because their exercise treatment logs were recorded as missing (e.g., unable to calculate dose). Potential confounders (thumb opposition, years diagnosed with RA, and therapist type) were included in the multivariate analysis. Higher overall exercise dose was associated with better outcomes in function at 4 months. For every 1 AUC, full-hand grip strength increased by β= 0.014 Newtons (95% CI 0.00, 0.02, p=0.045).

4.8. Discussion.

This study provides evidence that being prescribed a higher overall dose of hand strengthening exercise is associated with better clinical outcomes. It indicates that the prescription of hand strengthening exercise is a complex multi-factorial process, associated with both therapist and participant characteristics. Greater full-hand grip strength at baseline, having strengthening exercise prescribed by a grade 6 therapist and the participant being more confident to exercise without fear of making symptoms worse was associated with a higher overall dose. Conversely MCP joint deformity, having hand strengthening exercise prescribed by an occupational therapist as opposed to a

physiotherapist, the participant reporting feeling downhearted all the time and a higher number of swollen wrist/hand joints was associated with a lower overall dose.

Limited evidence exists to ascertain the most effective dose of hand exercise in RA. Higher intensities of exercise is tentatively recommended over lower intensities (Bergstra et al., 2014, Hammond and Prior, 2016). This study supports clinicians aiming to prescribe higher overall dose with their patients to achieve better outcomes. What is less well understood from our results, is whether volume (i.e. sets and repetitions) is more or less important than load (i.e. resistance) used. Exercise-based clinical trials may better inform the development of future guidelines if more detailed dose-response information is offered as part of the dissemination process.

Both therapist professional background and job grade (as a proxy for clinical experience) were associated with dose. Clinician professional background, years of experience, knowledge, beliefs, attitudes, and behaviour towards exercise have previously been associated with how exercise is prescribed in rehabilitation settings (Bennell et al., 2014, Eulenburg et al., 2015, Hansen et al., 2018). Healthcare professions such as occupational therapy and physiotherapy have evolved and possess their own distinct culture, encompassing unique values, beliefs, attitudes, customs, and behaviours (Hall, 2005). Both professions brought their culture associated with their profession when they participated in the SARAH trial. Differences in professional culture may be one possible reason for the difference in overall prescribed dose between professions. Physiotherapy as a profession appears to place a stronger emphasis on movement, exercise and optimising human performance (Aguilar et al., 2014, The Chartered Society of Physiotherapy, 2018). Consequently, physiotherapists may have prioritised prescribing higher initial dosages of hand strengthening exercise or progressed participants dosages more quickly over the five face to face exercise sessions. In contrast, occupational therapy as a profession place greater emphasis on improving an individual's ability to perform daily occupations (i.e. activities and valued life roles at work, in the home, at leisure and socially), facilitating successful adaptations to disruptions in lifestyle, prevent losses of function and improve or maintain psychological status (Hammond, 2004, Royal College of Occupational Therapists, 2024). Consequently, occupational therapists may have approached strength exercise prescription differently to physiotherapists, framing dose in terms of occupational outcomes, with less emphasis on individual dose parameters and more on qualitative, functional improvements that support independence and quality of life.

Outlined in chapter two, frameworks suited to prescribing interventions have evolved and moved away from the traditional medical model, where interventions and their dose are typically prescribed based on professional authority to a more collaborative approach to prescribing, where shared decision making (SDM) emphasises autonomy, giving individuals seeking help an active role in decisions and requires that their preferences, values, and concerns be considered (Elwyn et al., 2012, National Institute for Health and Care Excellence, 2021c). Although HCPs are encouraged to embed SDM in their prescribing decisions (Couët et al., 2015, National Institute for Health and Care Excellence, 2021c), applying SDM in clinical practice may be challenging. Lack of time and SDM being at odds with HCP training (i.e. the physician knows best) have been suggested as some of the potential reasons (Ankolekar et al., 2021). Focus on HCPs providing evidence-based care over the communication and negotiation skills required for SDM, may leave many HCPs less confident in implementing SDM effectively. Addressing the balance between prescribing evidence-based exercise dosage and prioritising shared decision-making (SDM) may help explain the dosage differences observed in the SARAH trial between occupational therapists and physiotherapists. Further research is needed to explore this relationship in depth.

Two indices of disease activity (MCP joint deformity and joint swelling) were associated with dose. MCP joint deformity has been reported as a reliable indicator of impaired hand function and grip strength in RA (Dias et al., 2012, Vliet Vlieland et al., 1996). Joint swelling is commonly associated clinical feature with RA (National Health Service, 2019). Swelling has been proposed to influence the range of joint movement and grip strength (Fraser et al., 1999, Scott and Houssien, 1996). Participants with greater grip strength measured at baseline had a higher dose. Previous research suggests grip strength has been identified as an important marker for hand function (Higgins et al., 2018). Two participant psychological factors (mood and confidence) were found to be associated with dose. Exercise and its positive effects on mood are well known (Cooney et al., 2013). Less understood are the effects of mood on dose prescribed in exercise-based clinical trials. Depression is considerably higher amongst individuals with RA (Katon and Schulberg, 1992). Participant reporting of feeling downhearted or low all the time was associated with lower dose being prescribed. Higher participant confidence to exercise without fear of making their symptoms worse was associated with higher prescribed dose In a qualitative study that interviewed SARAH RCT participants, confidence was identified as a facilitator for performing and adhering to the exercises (Nichols et al., 2017). Those participants with lower confidence levels may need more support to engage and progress the exercises. Evaluating these factors may help therapists to work with participants to achieve greater doses of hand strengthening exercise.

4.9. Potential strengths and limitations of this study.

This study utilised a relatively large trial data set and the analyses controlled for a range of variables relating to baseline function, condition severity and participant characteristics. However, this study does have some important limitations. First, these findings are based on observational data from within an RCT and the analyses were not pre-planned as part of that trial. Second, the study recruited participants who were not on a disease-modifying antirheumatic drugs (DMARD) regime or had been on a stable on a DMARD regime (including biological agents if used) for three months or more. Indeed, the mean disease duration of the participants who received the tailored hand exercise programme was ten years. The results may not be generalisable to individuals with more recent diagnoses, where symptoms may be less well controlled. Third, whilst the overall dose calculated for the five supervised sessions acts as a reasonable proxy for dose completed over the twelve-week programme, it may not fully reflect changes in the participants ability to perform the strengthening exercises (for example during symptom flare-up, injury, or illness). Fourth, a numerical rating was assigned to each level of resistance to help with calculating dose as it was not possible to obtain information on resistance level for exercise balls and putty (i.e. colour equating to kg). This approach may have influenced the overall dose calculated. However, this issue is not isolated to the SARAH RCT. A systematic review with meta-analysis investigating the effect of resistance exercise dose components for tendinopathy management identified one challenge investigating resistance intensity was the lack of reporting actual intensities used when using exercise resistance bands (Pavlova et al., 2023). Finally, as discussed in chapter two, the prescribed dose of exercise-based interventions may be influenced by many important factors, some that were not collected during the SARAH RCT. These may include therapist knowledge/training, therapist or participant beliefs about the prescribed intervention, or access to equipment such as exercise band/putty which may determine what load is ultimately prescribed.

4.10. Conclusions.

There was an observed association between higher overall dose of strengthening exercise and both overall hand function and gross grip strength. HCPs using the SARAH hand exercise intervention shoulder consider this when prescribing the recommended strengthening component of the programme. Further research into understanding about how therapists select, weight, and combine information gathered during the healthcare consultation when prescribing dose may be useful for informing future clinical practice.

4.11. Future implications of this study.

In the context of patients, carers and HCPs wanting to know what dose works best, greater overall dose of hand exercise is associated with better overall hand function and grip strength. Considering some of the difficulties in calculating overall dose, future trials using strength-based exercise should explicitly report load/resistance in metric terms (e.g., kilograms). In addition, considering the poor reporting of evidence underpinning dose of strengthening exercise and that exercise prescription was controlled using a pre-determined protocol, it is useful to examine how hand strengthening exercise and its dose is prescribed without such restrictions. Therefore, the third study in this thesis, investigates dose of hand strengthening exercise outside of directed RCTs where HCPs are required to align their prescribing with a pre-defined protocol. The following chapter describes that study and its findings.

CHAPTER FIVE. STUDY THREE. PRESCRIBING HAND STRENGTHENING EXERCISES FOR PATIENTS WITH RHEUMATOID ARTHRITIS; CLINICAL CUES INFLUENCING OCCUPATIONAL THERAPISTS' AND PHYSIOTHERAPISTS' JUDGEMENTS.

5.1. Study overview.

The third and final study in this thesis, this chapter provides a rationale for the study, a description of the study objectives, the methods used, results and discussion. A protocol was developed prior to the study but wasn't registered or published. The study was published in Musculoskeletal Care (Boniface et al., 2024) (Appendix 8) and reported via social media (i.e. Twitter/X).

5.2. Introduction.

In chapter two, it was established that occupational therapists and physiotherapists are the two most likely professions to prescribe hand strengthening exercise in RA. Both professions are encouraged to align their clinical practice with the evidence-base when making decisions about patient care. However, in chapter two, it was shown that for both professions, engaging with the evidence base was difficult due to lack of time in clinical practice. Instead, many reported relying on their own experiences or asking colleagues for advice. Clinical practice guidelines such as NICE are meant to aid HCPs improve the quality of their care. In the management of pain and dysfunction of the hands and wrists associated with the RA, NICE recommends tailored hand exercise. However, it offers no specific information about how to implement and tailor its prescription (National Institute for Health and Care Excellence, 2018). This has been identified as an issue across other RA guidelines (Hurkmans et al., 2011). There is a recognised need for the producers of clinical practice guidelines to provide better implementation support (Gagliardi and Brouwers, 2015). One potential reason for the lack of information around exercise dosage in RA identified in chapter two surrounds the methods employed by healthcare researchers for optimising dose of strength-based exercise prior to evaluation by RCT. Additionally, dose parameters are rarely reported in full detail needed for HCPs to replicate in clinical practice. In the absence of clear clinical guidance for prescribing hand strengthening exercise in RA, the results of study two (chapter four) and the causal mediation analysis (Hall et al., 2017) suggest dose matters for clinical outcomes. Investigating how occupational therapists and physiotherapists (referred to from this point as "therapists") decide what intensity of hand strengthening exercise to prescribe is valuable for understanding how these judgements are made in the clinical setting, away from the tightly controlled protocols required by RCTs.

5.3. Judgement Analysis.

To understand how therapists prescribe dose of strengthening exercise, an approach is needed that can explore their judgements. As previously mentioned in chapter two, NICE recommendations stipulate the use of tailored hand exercise programmes in RA. Tailoring exercise prescription relies on clinical reasoning (Brody, 2011, Higgs et al., 2019, Wessel, 2004). Clinical reasoning is central to clinical practice (Kirwan et al., 1990) and is defined as: *"the cognitive and non-cognitive process by which a healthcare professional consciously and unconsciously interacts with the patient and environment to collect and interpret patient data, weigh the benefits and risks of actions, and understand patient preferences to determine a working diagnostic and therapeutic management plan whose purpose is to improve a patient's well-being"* (Page xvii) (Trowbridge et al., 2015). A critical part of the clinical reasoning process as defined above centres on the healthcare consultation (i.e. the interaction and collecting and interpreting of data whilst considering benefits vs risks as well as patient preference). A comprehensive healthcare consultation is considered important for making appropriate recommendations balanced against possible risks (American College of Sports Medicine, 2020, Royal Pharmaceutical Society, 2016). Broadly speaking a consultation may be defined as an two-way encounter between the HCP and the patient (Pawlikowska et al., 2007), although others may be involved such as a family member, direct support worker or interpreter (Fatahi et al., 2008, Iacono and Johnson, 2004). Most consultations occur face to face (Hobbs et al., 2016), but may also occur via telephone or video conference (Brant et al., 2016, Donaghy et al., 2019, Wherton and Greenhalgh, 2020). The information gathered during the encounter is considered important for making a diagnosis and helping guide subsequent prescribing decisions (Japp et al., 2018, Peterson et al., 1992). A consultation may be broken down into two key domains, the subjective and objective examination (Atkins et al., 2010, Innes et al., 2018, Petty and Moore, 2011). The subjective examination involves taking a concise history about why patient has presented for help. This information gathering is traditional across most consultation models proposed in general practice (Denness, 2013, Pawlikowska et al., 2007). Often the subjective examination may be further broken down into the following sub-domains: 1) Presenting complaint, 2) History of presenting complaint, 3) Past medical history, 4) Family history 5) Social history and 6) Lifestyle (Innes et al., 2018, Petty and Moore, 2011). Additionally, further questioning may also be used to identify possible sinister pathology (red flags) (Greenhalgh and Selfe, 2010). Whilst a comprehensive history is important, conducting an objective examination is often used to supplement the healthcare professional's understanding about what may be responsible/contribute towards patients symptoms and/or impairments (Atkins et al., 2010, Petty and Moore, 2011). Most diagnoses often require information from a physical examination (Peterson et al., 1992).

Various theoretical models have been proposed to explain the clinical reasoning process (Higgs et al., 2019). Some key models include: 1) Hypothetico-deductive reasoning which involves the healthcare professional generating hypotheses based on clinical information and their knowledge and testing these through further investigation (Elstein et al., 1978) and 2) Pattern recognition or inductive reasoning, where the healthcare professional is able to identify patterns (effectively diagnose) based on past knowledge (Gorry, 1970, Groen and Patel, 1985). Identifying the information HCPs use when judging what dose of strengthening exercise to prescribe a patient with RA is important considering the lack of guidance in the current NICE guideline and uncertainty around dose in the current evidence base. Using hypothetical patient case scenarios to explore judgements was identified as an appropriate method as information normally gathered during the consultation could be combined into a hypothetical patient case scenario which an HCP then has to judge what dose to prescribe. The association between dose prescribed and the clinical information contained in the case scenario can be statistically modelled using linear regression analysis.

One theoretical approach capable of exploring this is judgement analysis (JA). JA is based on social judgement theory, a derivative of Brunswik's 1952 original lens model (Brunswik, 1952, Cooksey, 1996, Denig et al., 2002, Hammond, 1996). In the context of a therapist deciding what intensity of hand strengthening exercise to prescribe a patient (Figure 5.1), JA allows the researcher to link the judgement process (i.e. how the therapist uses the clinical information collected during the patient-therapist consultation) to the outcome (i.e. what intensity of hand strengthening exercise to prescribe the patient). This is done by asking a therapist to assess a series of hypothetical patient case scenarios, in which several clinical cues (e.g., pain) with varying levels of severity (e.g., no pain, mild pain, moderate pain, severe pain) are presented. The process allows the association between the cues and the therapist's judgement to be statistically modelled. The relative importance given to each cue by the therapist is referred to as the therapist's judgement policy. Therefore, the third study in this thesis aimed to investigate the judgements of therapists prescribing hand strengthening exercise.

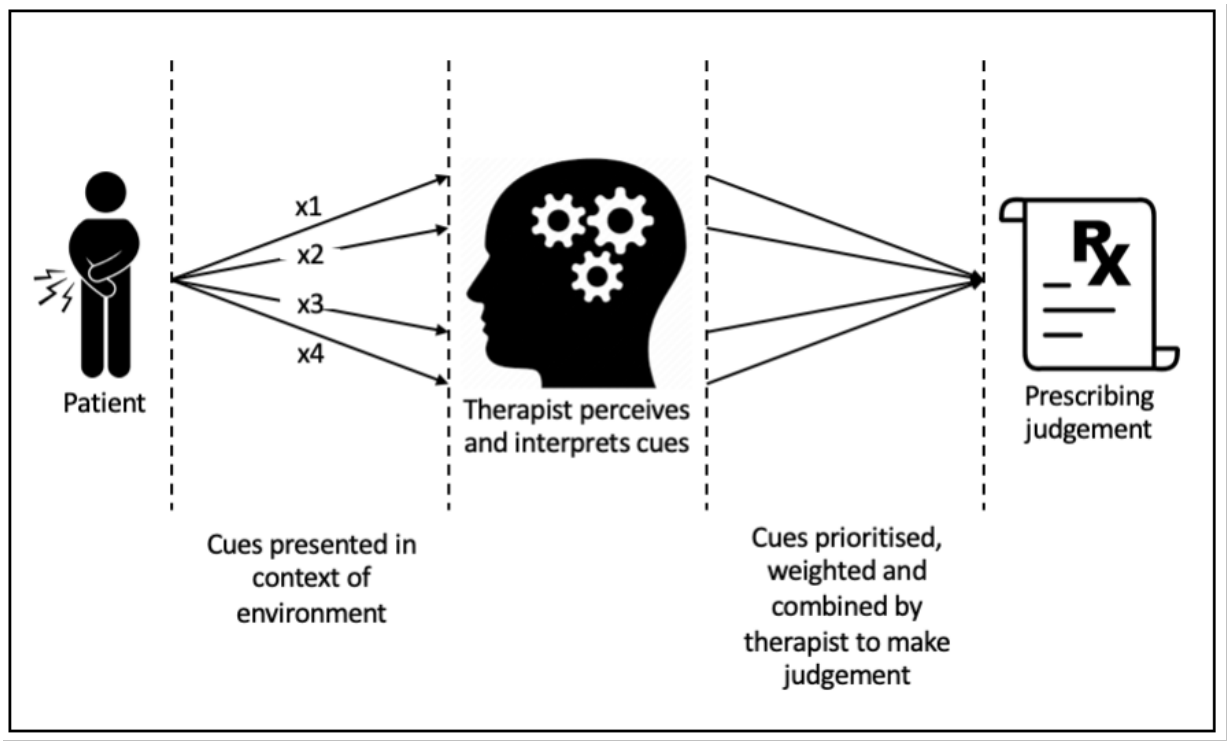

Figure 5. 1. Adaptation of the Brunswik lens model (Brunswik, 1952, Waghorn et al., 2021).

5.3. Objectives.

The objectives of this study were:

1. To explore how therapists' judge the intensity of hand strengthening exercise to prescribe a patient with RA based on the clinical information gathered during the patient-therapist consultation.
2. To identify those therapists' who are more consistent in their prescribing judgements and compare their policy to those therapists identified less consistent.

5.4. Overall study design.

There were two distinct phases to this study. Phase I informed the content and design of the hypothetical patient case scenarios and involved a modified Delphi process based on Nominal Group Technique (NGT) with two rounds and a final consensus. Phase II used an online experiment involving the hypothetical patient case scenarios developed in phase I. The methods and results of each phase will be described separately, starting with phase I.

5.5. Methods – Phase I.

5.5.1 Ethical approval.

Ethical approval was granted by Brunel University London Research Ethics Committee (Phase I: 36607-LR-May/2022- 39386-2 & 36607-A-Jun/2022- 40324-1) (Appendix 9).

5.5.2. Participants.

UK-based occupational therapists and physiotherapists with expertise in treating RA of the hand. No consensus existed on what constitutes an expert therapist. Previous research investigating clinical reasoning in novice and expert occupational therapists and physiotherapists (Barton et al., 2015, Doody and McAteer, 2002, Dunford et al., 2011, Unsworth, 2001) suggests expertise is a therapist with ≥ 5 years clinical experience and who possesses a higher level of formal or specialised training since graduation. This knowledge was combined with information collected during the implementation work following on from the SARAH RCT (Williamson et al., 2020). Using the demographic characteristics of the 790 UK-based therapists who enrolled in the online training for the study, an extra eligibility criterion was added: treating ≥5 RA patients per month. The rationale for using this criteria was aimed at ensuring participants taking part in phase I were: (1) Clinically active, (2) Regularly treating individuals with RA and (3) Possessed sufficient post-registration experience and training. The eligibility criteria are described below.

5.5.3. Eligibility criteria.

Table 5.1 describes the eligibility criteria for phase I of the study three. Recruitment was slow in the first month with three participants consenting to take part. The decision to amend the eligibility criteria to be more inclusive was made on the 24/06/2022 and gained ethical approval on the 28$^{th\ of}$ June 2022 (Appendix 9). If participants did not meet these criteria, they were excluded.

Table 5. 1. Eligibility criteria for phase I.

Original eligibility criteria	Amended eligibility criteria
Health and Care Professions Council (HCPC) registered.	Health and Care Professions Council (HCPC) registered.
≥ 5 years post-registration experience.	≥ 5 years post-registration experience.
Treat >5 patients with pain and dysfunction of the hands and wrists caused by rheumatoid arthritis per month.	Have current or recent experience in treating patients with pain and dysfunction of the hands and wrists caused by RA

Possess either postgraduate level training (e.g., Master's/PhD) and/or specialist hand therapy training (e.g., British Association of Hand Therapy accreditation).	Have undertaken some form of post-graduate training. Examples of post-graduate training include modules from a master's degree, a full Master's degree or undertaking a PhD/completed a PhD. Alternatively, the participant may have undertaken specialist hand therapy training (e.g., CPD course (e.g. iSARAH or BAHT), attended a recognised conference related to hand therapy/treatment or may be accredited with BAHT).

CPD = Continuing professional development. iSARAH = Online training related to the SARAH hand exercise programme. BAHT = British Association of Hand Therapists.

5.5.4. Participant sample size.

In keeping with nominal group technique (NGT), a consensus gathering approach, the aim was to recruit up to 12 participants (McMillan et al., 2016, Potter et al., 2004).

5.5.5. Recruitment strategy.

Participants were recruited between 17/05/2022 and 03/08/2022 using known contacts of the research team, advertising in the British Association of Hand Therapists (BAHT) July 2022 ebulletin and using social media (Twitter/X).

5.5.6. Procedure.

Prospective participants were sent participant information leaflet and consent form (Appendix 10). Upon return of the consent form, participants were sent an email (Appendix 11) along with a data collection form (Appendix 12) asking them to identify all the cues they subjectively considered when prescribing hand strengthening exercise for a patient with pain and dysfunction of the hands caused by RA. These forms were returned via email. Participants were sent a maximum of two reminders to complete and return the data extraction form. The responses were coded using a short descriptor (e.g., pain, joint deformity). The cues were ranked by the number of times they were reported across participants. These were then combined with a list of cues identified from study two (Boniface et al., 2022). These included both physical (joint deformity, swollen wrist/hand joints, grip strength) and psychological factors (participant mood and confidence to exercise). Participants were sent an email (Appendix 13) with the updated list of cues and had the opportunity to (1) Add more cues and (2) Comment on the short descriptions for each cue. No further cues were added by participants, and no comments offered. Finally, a 2.5-hour virtual consensus meeting was held on the 27/09/2022 using Microsoft TEAMS. Participants met to agree and rank the final set of cues and to discuss how the cues could be presented in Phase II. Figure 5.2 provides an overview of phase I.

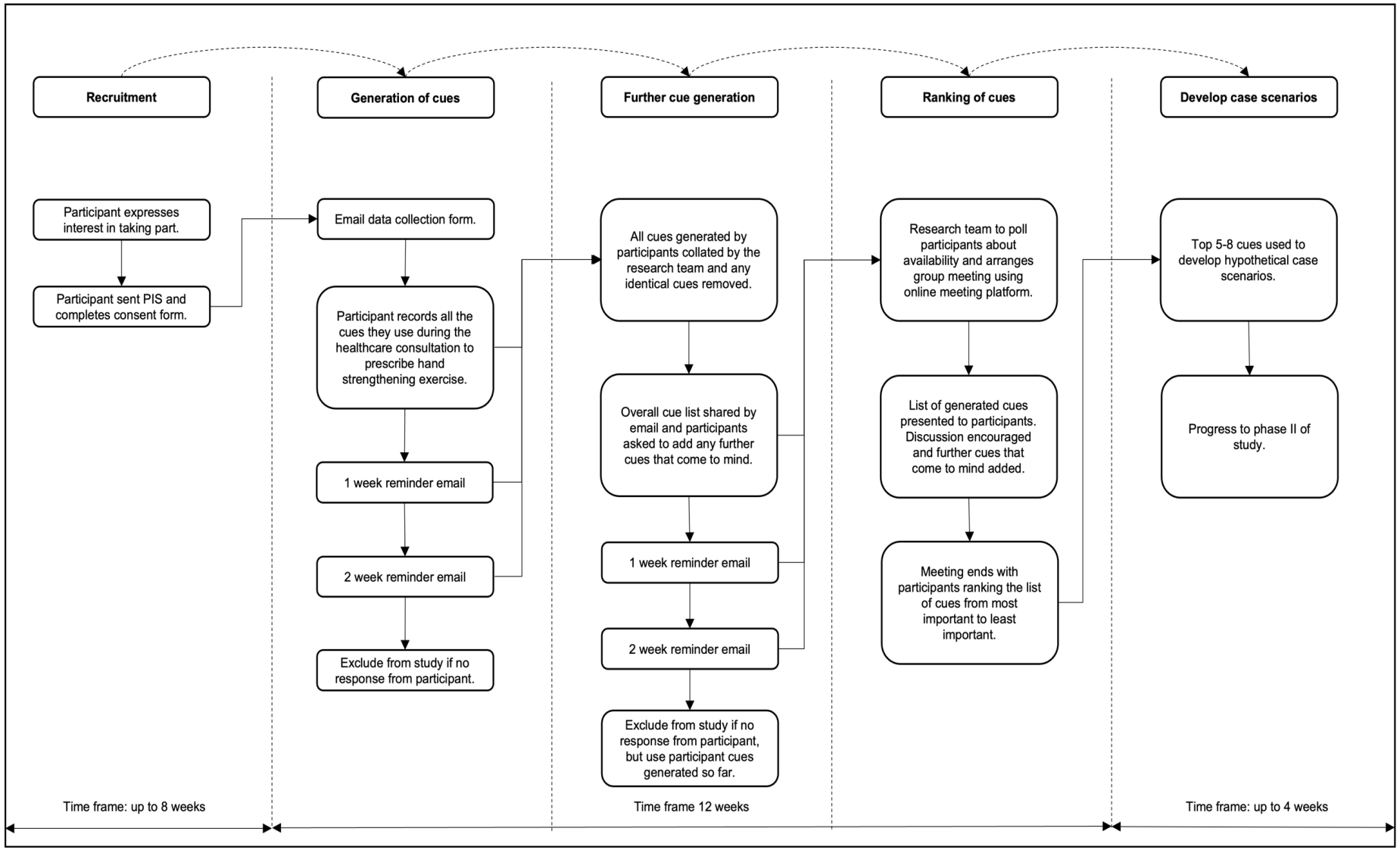

Figure 5. 2. Phase I process.

5.5.7. Selecting number of cues and case scenarios for phase II.

In keeping with the method, each cue used in a hypothetical patient case scenario requires between five and ten scenarios to determine the judgement policy of the individual (Cooksey, 1996). Therefore, if ten clinical cues were investigated, 50 to 100 case scenarios would be required in the JA task. To reduce participant burden and thereby minimise risk of withdrawal from the study, the total number of cues was limited to seven. Each cue was reviewed, and a final selection made by study authors (GB, PH). Including all possible combinations was not feasible as seven cues with different levels (e.g., (5x4x4x4x4x4x3) would have meant presenting participants 15360 possible case scenarios. Therefore, fractional factorial design (using IBM SPSS V.26.0 orthogonal design function) was used to create a representative subset that could be assessed whilst at the same time, reduce burden on therapists This resulted in 54 original case scenarios. For judging inconsistency (Cooksey, 1996), 15 duplicate case scenarios were included, resulting in a total of 69 case scenarios.

5.6. Results – Phase I.

5.6.1. Participants.

Eleven participants were recruited overall (Table 5.2). Eleven (100%) completed and returned information about the cues they considered when prescribing hand strengthening exercise for a patient with pain and dysfunction of the hands caused by RA. Six (54.5%) participants attended the group online meeting. The five therapists who did not attend, three gave their apologies before the meeting (e.g., holiday or clinical commitments) and two provided no explanation, although one therapist later emailed citing a family bereavement.

Table 5. 2. Phase I therapist characteristics (Mean (Standard Deviation) or n (%)).

Variables	**Overall (n=11)**
Participant profession:	
Occupational therapist	9 (81.8%)
Physiotherapist	2 (18.2%)
Age (years) on consent to study:	46.4 (10.6)
Gender:	
Female	11 (100%)
UK location:	
England	9 (81.8%)
Scotland	2 (18.2%)
Work environment:	
NHS	6 (54.5%)
NHS and private sector	4 (36.4%)
Other[†]	1 (9.1%)
Job grade (Agenda For Change):	
Band 6	5 (45.5%)
Band 7	4 (36.4%)
Band 8a	1 (9.1%)
Other	1 (9.1%)

Years qualified (since graduation):	23 (9.6)
Highest level of qualification:	
Diploma in Occupational therapy (DIPCOT)	1 (10%)
Undergraduate degree plus postgraduate hand therapy training (BAHT course, PG cert in hand therapy, SARAH training programme)	5 (45%)
Postgraduate degree (Masters module, Masters, MPhil, PGDip)	5 (45%)
Approximate number of RA patients treated per month:	
5-10	4 (36.4%)
11-15	3 (27.3%)
More than 15	3 (27.3%)
Other‡	1 (9.1%)

† = Academia. ‡ = Non-clinical, but possessed significant research experience involving hand exercise in RA.

5.6.2. Cue identification.

During the email stages from phase I, 124 responses were generated by the 11 therapists. Summarising these responses, 33 clinical cues were identified. These were ranked by number of times the clinical cue was reported. The clinical cues including the top-10 are described in Appendix 14. During the group online meeting, no further cues were generated and therapists in attendance agreed that the top-10 clinical cues were the most important for judging what intensity of hand strengthening exercise to prescribe. The finalised seven clinical cues (independent variables) with differing severity levels used in the case scenarios are presented in Table 5.3. Clinical cues were coded so that higher scores indicated greater severity (e.g., 1=no pain, 2=mild pain, 3=moderate pain, 4=severe pain).

Table 5. 3. Final list of agreed cues with their corresponding levels.

Clinical Cue	**Coding of clinical cue levels**
Average pain in right hand over the last week:	1 = no pain (0 on NRS†) in her right hand over the last week 2 = mild pain (≤5 on NRS) in her right hand over the last week 3 = moderate pain (6-7 on NRS)in her right hand over the last week 4 = severe pain(≥8 on NRS) in her right hand over the last week
Current functional level:	1 = has no problems doing her usual activities 2 = has slight problems doing her usual activities 3 = has moderate problems doing her usual activities 4 = has severe problems doing her usual activities 5 = is unable to do her usual activities
Disease activity score (DAS-28):	1 = <2.6 = disease remission 2 = 2.6 - <3.2 = low disease activity 3 = 3.2 - 5.1 = moderate disease activity 4 = >5.1 = high disease activity

Ulnar drift at metacarpophalangeal joints:	1 = No drift noted 2 = Actively correctable 3 = Passively correctable 4 = Fixed
Hand range of movement:	1 = Able to make a full fist 2 = Partially able to make full fist 3 = Not able to make a full fist
Power grip strength using JAMAR:	1 = Grip strength is comparable to someone of similar age and gender with no abnormalities or pain in upper limb (no weakness) 2 = Grip strength is slightly reduced compared to someone of similar age and gender with no abnormalities or pain in upper limb (mild weakness) 3 = Grip strength is moderately reduced compared to someone of similar age and gender with no abnormalities or pain in upper limb (moderate weakness) 4 = Grip strength is severely reduced compared to someone of similar age and gender with no abnormalities or pain in upper limb (severe weakness)
Hand pain while performing the exercise:	1 = no pain (0 on NRS) 2 = mild pain (≤5 on NRS) 3 = moderate pain (6-7 on NRS) 4 = severe pain (≥8 on NRS)

† = NRS (Numerical rating scale).

5.6.3. Case scenario presentation.

After discussion in the group meeting, the group agreed that the best way to present the clinical information in phase II was in the SOAP (Subjective, Objective, Analysis, Plan) note format. This format is commonly used by therapists in clinical practice to record patient consultations (Petty and Moore, 2011). An example case scenario and the web page set-up can be seen in Figure 5.3.

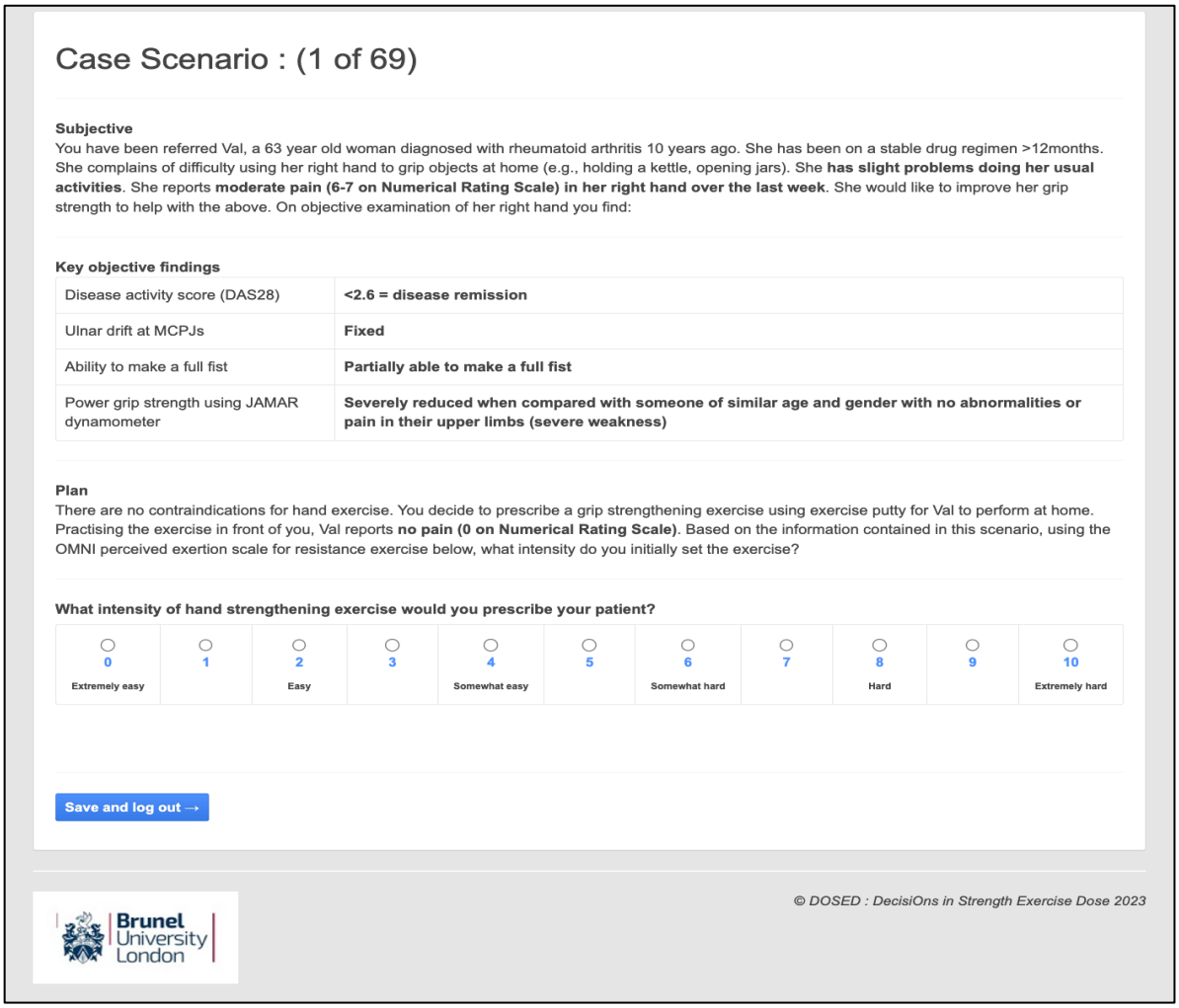

Figure 5. 3. Example of hypothetical patient case scenario.

5.7. Methods – Phase II.

5.7.1. Ethical approval.

Ethical approval was granted by Brunel University London Research Ethics Committee (Phase II: 37041-LR-Jul/2022- 40789-1 & 37041-A-Feb/2023- 43653-1) (Appendix 9).

5.7.2. Participants.

UK-based occupational therapists and physiotherapists with experience in treating RA of the hand. The eligibility criteria are described below.

5.7.3. Eligibility criteria.

Table 5.4 describes the eligibility criteria for phase II of study three.

Table 5. 4. Eligibility criteria for phase II.

Eligibility criteria
Health and Care Professions Council (HCPC) registered.
≥ 2 years post-registration experience.
Have current or recent experience in treating patients with pain and dysfunction of the hands and wrists caused by RA

5.7.4. Participant sample size.

In previous JA studies involving healthcare professionals (e.g., community nurses, pharmacists, doctors), sample sizes have ranged between four to 109 participants (Adderley and Thompson, 2015, Dwyer et al., 2018, Hancock et al., 2012, Jenkins et al., 2007, Waghorn et al., 2021, Wigton, 1996, Wigton et al., 2008). Owing to the range of sample sizes previously used, phase II aimed to recruit a minimum of 40 participants.

5.7.5. Recruitment strategy.

Participants were recruited between 15/01/2023 and 31/05/2023 using known contacts of the research team, advertising in the BAHT March 2023 ebulletin and using social media (Twitter).

5.7.6. Primary outcome of phase II.

Intensity (i.e. how hard) is one of the key exercise dose parameters therapists should consider when prescribing hand exercise (Hammond and Prior, 2016). Therefore, the CR-10 Borg Rating of Perceived Exertion (RPE) scale (Table 5.5) was initially selected to determine therapist's judgements (Borg, 1998). However, following feedback from the supervisory team that participants may not find the text anchors used to describe points along the scale easy to use, the decision was made to change to the OMNI-Resistance Exercise Scale (OMNI-RES) where the text anchors (Table 5.5) were more clearly described (Robertson et al., 2003). This amendment gained ethical approval on 10th February 2023 (Appendix 9).

Table 5. 5. CR-10 Borg and OMNI-RES RPE scales.

Rating	BORG CR-10 Text Anchors	OMNI- RES Text Anchors
0		Extremely Easy
1	Very, Very Easy	
2	Easy	Easy
3	Moderate	
4	Somewhat Hard	Somewhat Easy
5	Hard	
6	*	Somewhat Hard
7	Very Hard	
8	*	Hard

9	*	
10	Maximal	Extremely Hard

5.7.7. Procedure.

Participants interested in taking part were directed to the study website (www.dosed.brunel.ac.uk) where they answered questions to check if they met the eligibility criteria. Those eligible could view and download the participant information sheet about the study (Appendix 10). Participants completed the online consent form and provided demographic (Age and gender), clinical career and training information (Profession, UK location, working environment, agenda for change job band (National Health Service, 2021), graduation date, highest professional qualification and approximate number of RA patients treated per month). On-screen instructions for completing the study were provided and participants were able to complete two practice case scenarios before completing the main set. For each case scenario, participants were asked to review the information and provide a response to what intensity of exercise they would prescribe for this patient (the primary outcome). The case scenarios were randomised to prevent order effects. Participants were able to log out and return to the same place if they needed to. Email reminders to complete the study were sent when a participant logged out and did not return to the website after one week. Figure 5.4 provides an overview of phase II.

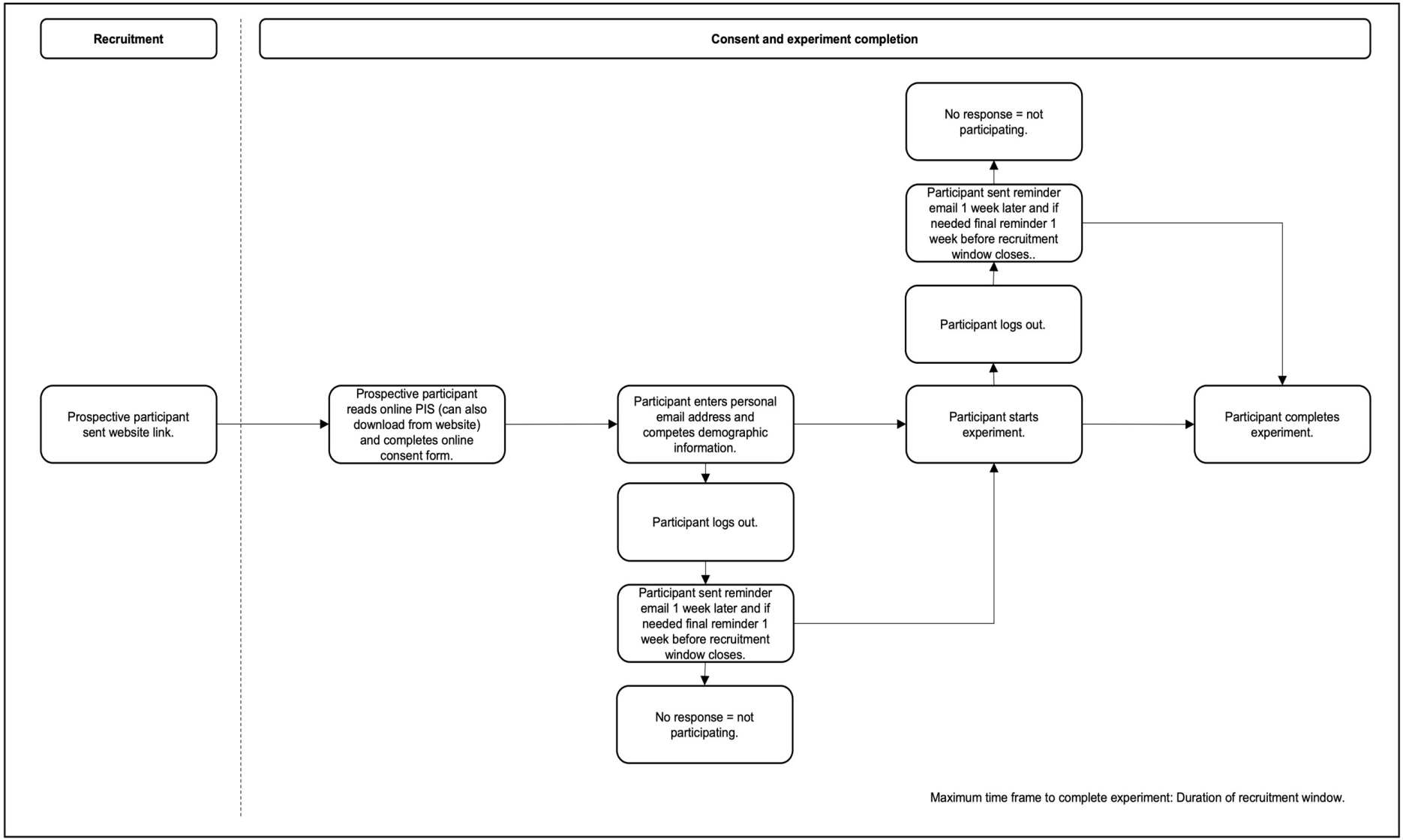

Figure 5. 4. Phase II process.

5.7.8. Statistical analysis.

Participant characteristics were presented in table format using descriptive statistics (mean, standard deviations, counts/percentages as appropriate). Participants who did not complete all case scenarios were removed from the analysis as they would not have completed the 15 repeat case scenarios required to assess consistency. Data was analysed using IBM SPSS Statistics for Windows, version 29.0 (IBM Corp., Armonk, N.Y., USA). The analysis comprised of three steps:

5.7.8.1. Analysis 1.

Step 1:

To assess the level of agreement between the therapists for each scenario, a two-way mixed effects intraclass correlation coefficient (ICC) was calculated.

Step 2:

Using the repeat case scenarios, the Cochran-Weiss-Shanteau (CWS) index of expertise was calculated to identify participants who were more consistent in their scores (Rassafiani et al., 2009, Weiss and Shanteau, 2003, Weiss and Shanteau, 2014, Weiss et al., 2006). The CWS index of expertise is a quantitative measure that assesses the level of expertise demonstrated in a set of responses. The index assumes an expert should meet two necessary criteria. The first is the expert's ability to discriminate between different stimuli (i.e. clinical cues) within the domain they operate. The second is demonstrating internal consistency with their judgements.

We used a software programme (CWS calculator V1.0.4) to calculate the CWS index score for each participant (Shanteau, 2023). Discrimination was determined by calculating the average response for each repeated case scenario (resulting in 15 average responses for the 15 case scenarios) and then calculating the variance of the values. Inconsistency was determined according to the mean of variances of the responses to the same case scenario. A larger CWS index score suggests better performance in discrimination and consistency. We reviewed the index scores for participants in the form of a bar chart (Appendix 15) to identify a relevant cut point. For the purposes of analysis, a CWS index score ≥5 was used to classify participants more consistent in their prescribing judgements. Those with a CWS index score <5 was deemed inconsistent for the purposes of the analysis in step 3.

Step 3:

To determine the overall group judgement policy of the included cues, the mean OMNI-RES score was calculated for each case scenario. This method has been used previously in JA studies to understand

the influence of the cues at a group level (Weiss et al., 2006, Williams et al., 2008). A linear regression analysis was conducted using the mean-OMNI score as the outcome and the clinical cues as the predictors.

5.7.8.2. Analysis 2.

A sub-analysis using linear regression was completed for participants identified as consistent (e.g., CWS index score = ≥5) versus those participants identified as inconsistent (e.g., CWS index score <5).

5.8. Results – Phase II.

5.8.1. Participants.

A total of 53 UK-based therapists were recruited, 30 (56.6%) of which completed all 69 hypothetical case scenarios (Table 5.6). The other 23 therapists did not 100% complete the study and were excluded from the analysis (Table 5.6). Based on CWS score ≥5, 12 (40%) therapists were categorised as the most consistent prescribers (Table 5.6). The remaining 18 (60%) therapists (CWS score <5) were considered less consistent in their prescribing judgements (Table 5.6). The mean (SD) completion time per case scenario was 31 (154) seconds.

Table 5. 6. Phase II therapist characteristics (n=30) (Mean (Standard Deviation) or n (%))

Variables	**Total number of completing therapists (n=30)**	**Therapists with CWS index score ≥ 5 (n=12)**	**Therapists with CWS index score < 5 (n=18)**	**Therapists not completing study (n=23)**
Participant profession:				
Occupational therapist	19 (63.3%)	7 (58.3%)	12 (66.7%)	14 (60.9%)
Physiotherapist	11 (36.7%)	5 (41.7%)	6 (33.3%)	9 (39.1%)
Age (years) on consent to study:	44.4 (9.3)	41.1 (8.9)	46.6 (9.1)	41.4 (11.6)
Gender:				
Female	26 (86.7%)	9 (75.0%)	17 (94.4%)	19 (82.6%)
Male	4 (13.3%)	3 (25.0%)	1 (5.6%)	3 (13.0%)
Prefer not to say	0 (0.0%)	0.0 (0.0%)	0 (0.0%)	1 (4.3%)
Therapist location:				
England	27 (90.0%)	11 (91.7%)	16 (88.9%)	19 (82.6%)
Northern Ireland	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (8.7%)
Scotland	1 (3.3%)	1 (8.3%)	0 (0.0%)	2 (8.7%)
Wales	2 (6.7%)	0 (0.0%)	2 (11.1%)	0 (0.0%)

Therapist work environment:				
NHS	25 (83.3.%)	10 (83.3%)	15 (83.3%)	20 (87.0%)
NHS and private sector	5 (16.7%)	2 (16.7%)	3 (16.7%)	3 (13.0%)
Other	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Therapist grade (Agenda For Change):				
Band 5	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (17.4%)
Band 6	12 (40.0%)	3 (25.0%)	9 (50.0%)	6 (26.1%)
Band 7	13 (43.3%)	8 (66.7%)	5 (27.8%)	7 (30.4%)
Band 8a	4 (13.3%)	0 (0.0%)	4 (22.2%)	6 (26.1%)
Band 8b	1 (3.3%)	1 (8.3%)	0 (0.0%)	0 (0.0%)
Years qualified (since graduation):	21.0 (11.2)	17.6 (8.2)	23.2 (12.6)	18.5 (10.3)
Highest level of qualification:				
Undergraduate degree (e.g., BSc)	16 (53.3%)	7 (58.3%)	9 (50.0%)	16 (69.6%)
Postgraduate degree (e.g., Masters)	12 (40.0%)	5 (41.7%)	7 (38.9%)	7 (30.4%)
Other:	2 (6.7%)‡	0 (0.0%)	2 (11.1%)†	0 (0.0%)
Approximate number of RA patients treated per month:				
Less than 5	5 (16.7%)	4 (33.3%)	1 (5.6%)	5 (21.7%)
5-10	6 (20.0%)	3 (25.0%)	3 (16.7%)	5 (21.7%)
11-15	8 (26.7%)	0 (0.0%)	8 (44.4%)	4 (17.4%)
More than 15	11 (36.7%)	5 (41.7%)	6 (33.3%)	9 (39.1%)

† = Undergraduate degree + Masters module and Diploma College of Occupational Therapy

5.8.2. Level of agreement between therapists.

There was a high level of agreement between therapists overall about the intensity of hand strengthening exercise prescribed in the 54 hypothetical patient case scenarios (ICC= 0.891, 95% CI 0.837 to 0.931).

5.8.3. Level of consistency.

The CWS index score was calculated for therapists who completed 100% of the case scenarios using 15 repeated cases (Appendix 16). CWS index scores ranged between 0.70 and 22.48. The mean (SD) of all therapists' scores was 5.65 (5.20). The higher the score, the better the therapist was at discriminating between the clinical cues whilst at the same time was consistent in their judgement when presented with the identical case.

5.8.4. Clinical cues influencing the prescribed intensity of exercise across all therapists.

For all therapists, six out of the seven cues influenced judgements about what intensity of hand strengthening exercise to prescribe (Table 5.7). All cues had an inverse relationship, meaning as cue severity level increased, the intensity of hand exercise prescribed decreased. The most influential cue was patient-reported pain when practising the exercise (β=-.804, p<0.001). To put this result into context, a patient reporting severe pain when performing the exercise in front of the therapist was prescribed approximately 1/3rd (2.4 points less on the OMNI-RES scale) less intensive hand strengthening exercise compared to a patient reporting no pain. The second most influential cue was disease activity (β=-.439, p<0.001). A patient scoring >5.1 (i.e., high disease activity) using the DAS-28 was prescribed 1.317 points less intensive exercise on the OMNI-RES scale compared to a patient whose disease activity was judged to be in remission. This was followed by average hand pain reported during the previous week (β=-.420, p<0.001), hand range of movement (β=-.149, p<0.001), ulnar drift (β=-.090, p<0.05) and patient grip strength (β=-.083, p<0.05). Only one cue ('patient current functional level') was identified as not significantly influential.

5.8.5. Comparing therapists (CWS index score ≥5 versus <5).

Twelve (40%) therapists were identified as consistent prescribers, meaning they had a CWS index score ≥5. Across the consistent prescribers, three cues were identified as influential (Table 5.7). These were patient-reported pain when practising the exercise in the front of the therapist (β=-1.150, p<0.001), disease activity (β=-0.425, p<0.001) and average hand pain reported during the previous week (β=-0.353, p<0.001). For the 18 (60%) therapists with a CWS index score <5, all cues influenced the intensity of hand strengthening exercise prescribed to varying degrees (Table 5.7). For both groups, patient-reported pain when practising the exercise, disease activity and average hand pain reported during the previous week were identified as the most influential. Consistent therapists (i.e. CWS index score ≥5) prescribed lower intensities of hand exercise when the patient reported greater pain practising the exercise. For the cues 'disease activity' and 'patient's average hand pain for the week', inconsistent therapists prescribed less intense exercise as severity of the cue changes increased.

Table 5. 7. Judgement policy by therapist group (Overall, CWS≥5 and CWS<5).

Analysis	R^2	Adj. R^2	AvPain	DAS	ExPain	Function	GripStr	ROM	UlnarDr	Constant
Overall Group (n=30)	.964	.959	-.420**	-.439**	-.804**	-.076	-.083*	-.149**	-.090*	8.646
Group CWS≥5 (n=12)	.957	.951	-.353**	-.425**	-1.150**	-.036	-.080	-.078	-.062	8.890
Group CWS<5 (n=18)	.915	.903	-.483**	-.456**	-.601**	-.102*	-.096*	-.224**	-.122*	8.646

AvPain = Average pain in hand over last week. DAS = Disease activity score. ExPain = Hand pain practising exercise. Function = Current functional level. GripStr = Grip strength. ROM = Ability to make a fist. UlnarDr = Ulnar drift at metacarpophalangeal joints. *Sig <0.05. **<.005.

5.9. Discussion.

This study identified six clinical cues that influenced therapists when prescribing intensity of hand strengthening exercise. In order of magnitude (i.e. greatest effect on the intensity of exercise prescribed), these were (1) Patient-reported hand pain when practising the exercise in front of the therapist, (2) Disease activity, (3) Average hand pain reported by the patient during the previous week, (4) Ability to make a fist, (5) Ulnar drift at the metacarpophalangeal joints, and (6) Grip strength. Current functional level was not significantly associated. Therapists categorised as consistent prescribers (i.e. CWS index score ≥5) used fewer clinical cues (three vs. seven) when compared to therapists categorised as less consistent (CWS index score <5). Again, in order of magnitude, these were (1) Patient-reported hand pain when practising the exercise in front of the therapist, (2) Disease activity and average (3) Hand pain reported by the patient during the previous week.

Comparing the above results to study two, a key difference centred on patient reported pain. In our post-hoc analysis of the SARAH RCT, both pain frequency and severity were not identified to be associated with the dose prescribed. Yet in the current study, pain whilst practising the exercise in front of the therapist and average hand pain reported by the patient during the previous week both significantly influenced therapists to prescribe lower intensity hand strengthening exercise. One possible reason for this difference may be related to when the participants from the SARCH RCT had their outcome measures taken. In our current study, the patient in the case scenario is reporting their pain during the patient-therapist consultation (i.e. at the point of the exercise being prescribed). In the SARCH RCT, pain was rated on the participant joining the trial, which could have been several weeks before the hand exercise programme commenced. A second reason may have been the therapists from the SARCH RCT were following a study protocol for prescribing the hand exercise programme, thus influencing their judgements.

Whilst our two studies differed regarding pain, there were also similarities. In our earlier study, we identified the presence of metacarpophalangeal joint deformity and swollen joint count were associated with prescribed overall dose of strengthening exercise. In the current study, both ulnar drift at the metacarpophalangeal joints and disease activity influenced judgements about what intensity of hand strengthening exercise to prescribe. The greater the severity, the lower the intensity of exercise prescribed. Whilst swollen joint count was not identified as a stand-alone clinical cue in the current study, swollen joint count is an integral part of calculating the disease activity score (DAS-28) (Van Riel, 2014).

Our study also identified those therapists who were categorised as being more consistent in their prescribing judgements relied on fewer cues (e.g., pain and disease activity). This finding indicates this group may have possessed a better sense of what is relevant and irrelevant and prioritised what to pay attention to during the patient-therapist consultation. Pattern recognition is a recognised trait that has been associated with expertise previously (Jensen et al., 2019).

In terms of using the CWS index score to compare therapist prescribing performance, 18 (60%) therapists were categorised as being less consistent in their prescribing judgements. As previously stated, a lower CWS index score demonstrates inconsistency. To put this in context, two identical patients could be prescribed different exercise intensities when seen by the same therapist. It is unknown if such variation has potential consequences for patient outcomes. In a study unrelated to healthcare, the performance of air traffic controllers managing their airspace was assessed. Researchers identified a larger CWS index score was associated with better air traffic control performance and outcomes (Thomas et al., 2001). Whilst different professions and markedly different contexts for making judgements, greater discrimination between clinical cues and better internal consistency with prescribing decisions may be important factors for generating better patient outcomes.

5.10. Potential strengths and limitations of this study.

This is the first study to have investigated judgement policies of UK-based therapists related to hand strengthening exercise prescription in RA. A comprehensive approach was used to identify the cues and to construct the hypothetical case scenarios used in phase II of the study. It is recognised this study has some important limitations. Firstly, these are statistically modelled policies and not those necessarily used in clinical practice. However, there is no clear standard for prescribing hand exercise in RA and guidance is needed. The statistical approach used in this study has been shown to be more

predictive of decision making than other research approaches. For example, policies calculated using linear regression analysis were more successful in predicting rheumatologists' judgements for measuring disease severity in rheumatoid arthritis compared to detailed interview (Kirwan et al., 1986). Secondly, in our approach, hypothetical case scenarios cannot include all the variables that influence decision making. Nevertheless, phase I of this study involved therapists experienced in prescribing hand exercise in RA and utilised a structured consensus technique to systematically identify and select the most important cues used in phase II. Thirdly, using hypothetical case scenarios may have lacked ecological validity (i.e. non-real world) and therapists would prefer making judgements on what intensity to prescribe face-to-face. This limitation we believe is somewhat compensated by the ability to compare numerous therapists' judgements on the same set of hypothetical case scenarios. Fourth, therapists were asked to judge what intensity of hand strengthening exercise they would prescribe a hypothetical patient. Intensity is just one parameter making up dose and, therapist judgement policy may differ for other parameters.

5.11. Conclusion.

The results of this study illustrate that patient-reported pain and disease activity influence therapists the most when judging what intensity of hand strengthening exercise to prescribe a patient with pain and dysfunction of the hand associated with RA. Focusing on these cues may streamline hand exercise prescription and improve patient outcome but needs further evaluation.

5.12. Future implications of this study.

JA was a novel approach for understanding the complexities of hand exercise prescription in RA. Statistical analysis of therapist judgements suggest JA be used to provide insight related to the clinical decision-making process during the healthcare consultation. Whilst all therapists relied to varying degrees on the same clinical cues, those more consistent, relied on less. This has implications for practice, such as offering novices prescribers of hand strengthening exercise in RA guidance based on decisions of therapists more expert. This requires further investigation.

CHAPTER SIX. SUMMARY OF STUDIES, IMPLICATIONS OF FINDINGS, STRENGTHS AND LIMITATIONS, FUTURE RESEARCH RECOMMENDATIONS AND CONCLUSION.

6.1. Overview.

The overall objective of this thesis was to explore how dose of strengthening exercise in RA is prescribed in both research and clinical practice. This was accomplished through three studies employing multiple methodological approaches. All three studies are peer reviewed, published and contribute new knowledge in the field of exercise prescription and RA. Interpretation of the findings specific to each study have been presented chapters three, four, and five. This chapter aims to synthesise the work of this thesis and provide broader context to the findings.

6.2. Brief summary of each study.

Study one (Chapter three) explored how healthcare researchers determine the dosage of strength-based exercise interventions in RA before subjecting them to evaluation by RCT. Interventions were seldomly piloted and no evidence of healthcare researchers using dose escalation methodology to optimise dose was identified. In the majority of RCTs, healthcare researchers failed to report the underpinning evidence guiding their dose choices. Where evidence was cited, it's quality varied and it was often not directly applicable to individuals living with RA. Furthermore, there was often inconsistency in applying the recommended dosage from the underlying evidence to the strength exercise component used in the intervention being evaluated. The innovative approach to examining the literature identified significant methodological concerns regarding whether dosages of therapeutic strengthening exercises are adequately optimised for individuals living with RA prior to evaluation by RCT.

Study two (Chapter four) re-examined a landmark RCT that prompted NICE to recommend tailored hand strengthening exercise in the non-pharmacological management of RA. This study examined the relationship between dose of strengthening exercise prescribed in the SARCH RCT with both overall hand function and full-hand grip strength. Furthermore, it examined how therapist and participant factors influenced the overall dosage prescribed and completed at the five face-to-face exercise sessions. A higher dosage was associated with improved overall hand function and full-hand grip strength. Factors such as being treated by an occupational therapist, the presence of metacarpophalangeal joint deformity, a higher number of swollen wrist/hand joints and the participant feeling downhearted and low all the time were all associated with a lower prescribed dosage. Conversely, being treated by a grade six therapist, higher baseline grip strength and greater participant confidence to exercise without fear of making symptoms worse were associated with

higher prescribed dosage. This study is the first to specifically provide evidence indicating that multiple factors (both therapist and participant) were associated with the prescribed dose of strengthening exercise used in the SARAH RCT. HCPs implementing the SARAH hand exercise programme in clinical practice should where appropriate, consider prescribing higher overall dosages across the four hand strengthening exercises.

Study three (Chapter five) investigated how therapists judge the intensity of hand strengthening exercise to prescribe to individuals with physical impairments of the hand associated with RA. Employing a modified Delphi approach, therapists experienced in prescribing hand exercise in RA, prioritised clinical cues thought important for guiding prescription of hand strengthening exercise. The clinical cues were used in hypothetical patient case scenarios which UK-based therapists evaluated online. Using judgement analysis (JA), a methodological approach not used in the area of hand exercise prescription before, linear regression analysis examined the association between pre-selected clinical cues and the prescribed intensity of hand strengthening exercise. Increasing severity across all the clinical cues, including patient-reported hand pain when practising the exercise in front of the therapist, disease activity reported in the form of a DAS28 score, average hand pain reported by the patient during the previous week prior to the healthcare consultation, the patient's ability to make a fist, ulnar drift at the metacarpophalangeal joints (i.e. joint deformity) and gross grip strength significantly influenced therapists to prescribe lower intensity hand strengthening exercise. Sub-group analysis identified that therapists who exhibited greater consistency with their prescribing judgements tended to rely on fewer clinical cues. Results may offer therapists less experienced in hand exercise prescription for RA a starting point on how to tailor hand strengthening exercise as recommended by NICE.

In bringing together the findings from the three studies, four issues worthy of acknowledgement emerged. First, the findings of study one indicate that healthcare researchers do not optimise dose of strengthening exercise using preliminary studies employing dose-escalation methodology. Second, in the absence of objectively determining optimal therapeutic dose, an assumption would be healthcare researchers default to employing previous research evidence that is both relevant to the intervention and clinical population to optimise dose. Study one challenges this assumption that critical decisions around dose are effectively underpinned by high quality, applicable research and suggests dose may not optimised prior to evaluation by RCT. Third, study two identified that dose of hand strengthening exercise had an association with key clinical outcomes measured during the SARAH RCT. Fourth, studies two and three support that prescribed dose is influenced by a range of factors and indicates

how challenging tailoring dose can be. If optimising dose is a research priority and tailoring the intervention an important clinical recommendation (Chartered Society of Physiotherapy, 2018, National Institute for Health and Care Excellence, 2018), improving how dose is chosen by healthcare researchers prior to evaluation by RCT and subsequently prescribed at the point of clinical contact is urgently needed.

6.3. Implications of findings within this thesis.

The current research findings generated by this thesis have implications for a range stakeholders including healthcare researchers developing rehabilitation interventions, HCPs prescribing exercise-based interventions, individuals receiving exercise-based interventions, peer reviewers and publishing houses evaluating the quality, validity, and relevance of research manuscripts involving rehabilitation interventions, policy makers in healthcare responsible for shaping the healthcare system and research funding bodies who provide financial support for research involving rehabilitation interventions.

6.3.1. Reporting how dose is developed in exercise-based RCTs.

Considering selecting safe and effective dose (i.e. optimal therapeutic dose) is an essential part of prescribing therapeutic exercise-based rehabilitation interventions (Jette, 2017). Study one should alert the above stakeholders that in RA, dose of strengthening exercises may not be optimised and appears to be a poorly considered step in the research process from a methodological standpoint. If dose is not being optimised at the development stage of the research process, there is potential for the wrong dose being prescribed, increasing the risk of therapeutic failure and/or the risk of harm on the basis of inadequate or inappropriate dose.

A notable finding from study one was the lack of reporting around the evidence used to underpin dose choices. Furthermore, the majority dose parameters were poorly reported. These issues are not confined to RA. Research has identified that in 44% of RCTs evaluating exercise-based rehabilitation interventions, healthcare researchers do not cite any evidence underpinning their dose choices (Gallois et al., 2017) and in research involving strengthening exercise, dose parameters are frequently missing (Holden and Barton, 2019, Holden et al., 2018, Pavlova et al., 2023). Missing information in published non-pharmacological interventions is not a new issue (Glasziou et al., 2008, Hariohm et al., 2017, Hoffmann et al., 2013, Yamato et al., 2016). While missing information prevents healthcare researchers and HCPs from reliably building on or implementing these interventions, the lack of information provided by healthcare researchers underpinning their dose choices means any of the

above stakeholders cannot reliably appraise whether dose has been sufficiently optimised for the clinical population it was intended.

Furthermore, while poor reporting of underpinning evidence identified by study one aligns with the findings of the review by Gallois et al (2017), the results also raises further concerns. Where healthcare researchers cited evidence, it was often low in quality and not directly applicable to those living with RA. In many cases where books or exercise guidelines were cited, it was not clear where the information informing dose parameters had come from. Improvement will require healthcare researchers to explicitly stipulate (i.e. disclose) where in the cited evidence, the information supporting a choice has come from (e.g., cite the page number and paragraph). Additionally, where healthcare researchers choose to deviate from the recommended dose contained within the supporting evidence, a clear rationale for the change should also be provided. This would allow the research consumer (i.e. stakeholder) to evaluate if this was appropriate or not in relation to intended aims of the intervention.

Adopting the above recommendations would provide an auditable trail for each dose parameter. Checklists like CERT (Consensus of Exercise Reporting Template), CONSORT (Consolidated Standards of Reporting Trials Statement) and TIDieR (Template for Intervention Description and Replication) have been developed to improve the critical appraisal of the validity and applicability of the results and to describe interventions in sufficient detail to allow their replication in clinical practice (Boutron et al., 2017, Boutron et al., 2008, Hoffmann et al., 2013, Hoffmann et al., 2014, Slade et al., 2016a). However, none require the healthcare researcher to explicitly link underpinning evidence to the chosen dose parameter level (e.g., frequency, intensity, volume etc.). Therefore, reporting checklists such as TIDieR should add an extension to ensure that healthcare researchers clearly and transparently provide the evidence justifying each dose parameter. Furthermore, peer reviewers, publishing houses and research funding bodies evaluating the quality, validity, and relevance of research manuscripts and proposals should be cautioned on accepting and publishing exercise-based rehabilitation interventions where dose has not been formally evaluated or adequately underpinned with high quality and appropriate evidence. It is imperative that all stakeholders consider how dose has been developed before adopting the evidence and implementing the intervention in clinical practice, research and policy recommendations.

6.3.2. Optimising dose using dose escalation methodology prior to RCT.

It has been shown that addressing key uncertainties, such as the dose of complex exercise interventions, is a crucial step for ensuring the safety, feasibility, and effectiveness of rehabilitation

interventions (El-Kotob and Giangregorio, 2018, Skivington et al., 2021). Considering the issues presented above, healthcare researchers should consider alternative approaches for developing dose of therapeutic exercise-based rehabilitation interventions. Study one identified healthcare researchers do not employ dose escalation methodology as an approach to safeguard participants and optimise potential for efficacy prior to evaluating the intervention by RCT. However, in other rehabilitation specialities (e.g., mainly stroke), dose escalation methodology has been employed successfully and offers healthcare researchers developing exercise-based rehabilitation interventions both in RA and more broadly (e.g., other exercise types for other healthcare conditions) a feasible alternative to relying on previous low quality, poor applicable research (Bajuaifer et al., 2023, Bultijnck et al., 2021, Colucci et al., 2017, Dite et al., 2015, Galloway et al., 2023, Kramer et al., 2020, Mackie et al., 2021a, Mackie et al., 2021b, Peiris et al., 2017, Taylor et al., 2023, Wallis et al., 2015). However, a consequence of adopting dose escalation methodology would be more time to conduct the research. Consequently, this would require additional funding. This may not be feasible as research projects are typically tied to public funding streams (Swan et al., 2009). For example, the SARAH RCT was funded by the UK National Institute of Health Research Health Technology Assessment Programme (Lamb et al., 2015). However, the potential implication of dose is not being optimised at the development stage of the research process, means there is potential for the wrong dose being prescribed, increasing the risk of therapeutic failure and/or the risk of harm on the basis of inadequate or inappropriate dose. These harms may have far greater personal and financial ramifications for individual and society than the cost of funding preliminary studies using dose escalation methods in the first instance.

6.3.3. Determining prescribed dose at point of contact and implications for clinical practice.

Studies two and three focused on therapeutic hand strengthening exercise in RA, a key therapeutic exercise recommended by NICE (National Institute for Health and Care Excellence, 2018). The results from study two allign with a past systematic review that prescribing high intensity home hand exercise programmes are associated with better short-term clinical outcomes when compared to low intensity programmes (Hammond and Prior, 2016). The implications of study two are where appropriate, HCPs implementing the SARAH hand exercise programme should consider prescribing higher dosages across the four strengthening exercises (i.e. greater volume, intensity or both) over the course of the programme. However, in prescribing hand strengthening exercise at the point of contact, both studies two and three indicated HCPs should consider a range of clinical cues when selecting what dose to prescribe, in particular, tailoring intensity according to current levels of pain and disease activity. Therefore, simply prescribing higher overall dosage may not in itself be appropriate to all individuals.

Adopting a framework around which to base exercise prescription on may help HCPs more clearly consider those individuals with additional physical and psychological barriers to regular exercise.

Chapter two introduced two frameworks, the RPS 'Competency Framework for all Prescribers' and the WHO 'International Classification of Functioning, Disability and Health' as valuable tools for HCPs aiming to achieve a holistic, engaging approach to exercise prescription in RA (Royal Pharmaceutical Society, 2021, World Health Organization, 2024). Optimising engagement, adherence, and outcomes associated with therapeutic exercise depends on activating trust, motivation, and confidence (Wood et al., 2024). Employing a framework by which to prescribe may contribute to building a therapeutic alliance with individuals living with RA seeking help from HCPs.

An unexpected finding from study two indicated that occupational therapists and physiotherapists prescribed different overall doses of strengthening exercise during the SARAH trial. This may reflect how each profession brings their own unique approaches to RA management beyond exercise prescription (Hall, 2005). Adopting a framework may bring unity of approach to exercise prescription in RA, offering a shared language across different health professions (Moran et al., 2020, World Health Organization, 2024).

Healthcare professionals working with RA-related hand impairments should prioritise prescribing higher initial dosages of strengthening exercises, with the goal of gradually increasing the dosage over time. The clinical cues identified in studies two and three can help tailor exercise prescriptions to each individual's needs and disease characteristics. However, broader factors should also be considered. Achieving optimal outcomes for RA patients likely requires supportive frameworks alongside adequate exercise doses (National Institute for Health and Care Excellence, 2021c, Wood et al., 2024).

6.4. Strengths and limitations of this thesis.

The methodological strengths and limitations of each study included within this thesis have been reported in their respective chapters (three, four and five). This section provides only an overview of the major strengths and limitations of the research as a whole.

6.4.1. Strengths.

The key strength of this work is the range of methodologies employed across the three studies. Study one used a novel systematic review methodology to forensically identify the evidence healthcare researchers used to underpin dose of therapeutic strength-based exercise interventions in RA. This

approach provided a detailed understanding about how dose is determined prior to the intervention being evaluated by RCT. Study two utilised data from a well-conducted multicentre RCT conducted within the UK and used AUC technique in the absence of metric data for load (e.g., kg/lbs) provided by hand exercise equipment. This approach provided greater detail about what dose of therapeutic hand strengthening exercise should be prescribed when following NICE's recommendation to use tailored hand exercise programmes in RA. Study three was grounded in real world practice. The clinical cues used in the hypothetical patient case scenarios were informed by the results from study two and clinical knowledge and experience of UK-based therapists prescribing hand strengthening exercise in RA. This was also the first study to use JA and CWS index of expertise to explore how therapists judge what intensity of hand strengthening exercise to prescribe in RA.

6.4.2. Limitations.

A significant limitation of this work is the absence of patient and public involvement (PPI). PPI is an important part of the research process, and while study two used the SARAH RCT (which included PPI) and study three involved therapists selecting clinical cues for the JA, overall, this thesis lacks PPI. Including perspectives from patients would have enhanced the understanding of what it's like to live with RA and engage in exercise-based rehabilitation. Similarly, including perspectives from healthcare researchers developing exercise-based interventions in RA would have enhanced the understanding around how dose of an intervention is selected prior to the intervention being evaluated by RCT. Their insights would have enriched research questions, study designs, and result interpretations. For example, PPI might have introduced qualitative methods like focus groups or semi-structured interviews across the three studies opposed to relying on current literature and using hypothetical scenarios. These methodologies may have provided more nuanced data about what factors influence dose choices.

6.5. Recommendations for future research.

The findings from this thesis would be developed further with additional research. Several directions for future research have emerged from the present findings, and these have been highlighted in the relevant chapters. This section outlines three key areas for future research that arose from the individual studies in this thesis.

6.5.1. Exploring the evidence underpinning dose for other musculoskeletal disorders other than RA.

Dose is a critical part of exercise-based rehabilitation interventions (Jette, 2017). In RA, study one indicates that dose of strengthening exercise appears to be a poor considered step in the research

process. This is a cause for concern as study two suggests dose of strengthening exercise is associated with clinical outcomes. A previous review suggests this may not be confined solely to strengthening exercise in RA (Gallois et al., 2017). Considering exercises are used in the management of many chronic healthcare conditions (Pedersen and Saltin, 2015), employing study one methodology to understand whether similar issues exist for strengthening exercise as well as other types of therapeutic exercise should be a research priority.

6.5.2. Evaluating dose-escalation methodology in as an alternative approach for optimising dose.

Study two shows dose is associated with clinical outcomes. However, study one provides evidence that dose of strengthening exercise may not be optimised prior to evaluation by RCT. Early phase clinical trials employing dose-escalation methodology may offer healthcare researchers wishing to optimise dose an alternative approach. Future research should explore whether using dose-escalation methodology yields better clinical outcomes opposed to the methods currently employed, where it has been identified in RA, the evidence currently used is low in quality and not be applicable to those living with disease. Better data driven casual models of dose specific to exercise type, goal and patient group are needed to drive better theory.

6.5.3. Improving understanding about how HCPs tailor dose in clinical practice.

While developing and optimising dose prior to evaluation by RCT is a research priority, how dosage is tailored at the point of contact is also critically important. Study two identified dosage was associated with participant characteristics measured prior (e.g., trial baseline) to point of contact (e.g., the face-to-face exercise sessions). Study three identified albeit in an artificial environment, HCPs adjust intensity of dose depending on certain clinical cues identified during the healthcare consultation (i.e. at the point of contact). Understanding what cues HCPs use to tailor exercise prescription for on may contribute to better health outcomes (Noone et al., 2024). Furthermore, research exploring the relationship between prescribing exercise-based interventions that are appropriately dosed according to current evidence and SDM may aid HCPs prescribing exercise in clinical settings.

6.6. Recommendations for healthcare professionals.

Healthcare professionals (HCPs) prescribing therapeutic exercise for rheumatoid arthritis (RA) may benefit from structuring their approach using the frameworks provided by the Royal Pharmaceutical Society (RPS) and the World Health Organization (WHO). Combining both frameworks offers a holistic and structured method that may be used to unify exercise prescription practices across professions involved in RA management, fostering a therapeutic alliance with the individual. Central to this alliance

is shared decision making, which emphasises the importance of considering the individual's perspectives in developing their exercise-based intervention. However, it remains essential that HCPs integrate current evidence into their decisions regarding exercise types and dosing. Interdisciplinary collaboration, particularly between professions such as occupational therapy and physiotherapy, can further enhance the effectiveness of this approach. Occupational therapists might benefit from building confidence in prescribing and progressing exercise prescriptions, whilst physiotherapists could gain from adopting a more holistic, individualised approach to exercise delivery that focuses more on meaningful occupation.

6.7. Overall conclusion.

The three studies in this thesis build on previous knowledge about how dose of strengthening exercise has been developed in RCTs and prescribed in clinical practice. Rigorous and forensic systematic review of contemporary exercise-based RCTs in RA identified that dose of strengthening exercise may not be optimised prior to evaluation. This is a significant cause for concern as dose is considered a critical aspect of therapeutic exercise prescription and demonstrated by study two to be associated with clinical outcomes. Furthermore, studies two and three indicate dose is influenced by multiple factors. This thesis provides practical recommendations as well as a number of further research questions worthy of investigation. While focused on strengthening exercise in RA, it is anticipated the results of this thesis can contribute to optimising exercise prescription across other types of therapeutic exercise and musculoskeletal disorders.

REFERENCES.

Aagaard, P. (2011) 'Neural Adaptions of Resistance Exercise', *in:* CARDINALE, M., NEWTON, R. & NOSAKA, K. (eds.) *Strength and Conditioning. Biological Principles and Practical Applications.* West Sussex: Wiley-Blackwell, pp. 105-124

Abbott, J. H. (2014) 'The distinction between randomized clinical trials (RCTs) and preliminary feasibility and pilot studies: what they are and are not'. *Journal of Orthopaedic & Sports Physical Therapy,* 44(8)**,** pp. 555-558. Available at: https://doi.org/10.2519/jospt.2014.0110

Adams, J., Bridle, C., Dosanjh, S., Heine, P., Lamb, S. E., Lord, J., Mcconkey, C., Nichols, V., Toye, F., Underwood, M. R., Williams, M. A., Williamson, E. M. & Sarah Trial, T. (2012) 'Strengthening and stretching for rheumatoid arthritis of the hand (SARAH): design of a randomised controlled trial of a hand and upper limb exercise intervention - ISRCTN89936343'. *BMC Musculoskeletal Disorders,* 13(1)**,** pp. 230. Available at: https://doi.org/10.1186/1471-2474-13-230

Adderley, U. J. & Thompson, C. (2015) 'Community nurses' judgement for the management of venous leg ulceration: A judgement analysis'. *International Journal of Nursing Studies,* 52(1)**,** pp. 345-354. Available at: https://doi.org/10.1016/j.ijnurstu.2014.09.004

Aga, A.-B., Lie, E., Uhlig, T., Olsen, I. C., Wierød, A., Kalstad, S., Rødevand, E., Mikkelsen, K., Kvien, T. K. & Haavardsholm, E. A. (2015) 'Time trends in disease activity, response and remission rates in rheumatoid arthritis during the past decade: results from the NOR-DMARD study 2000–2010'. *Annals of the Rheumatic Diseases,* 74(2)**,** pp. 381-388. Available at: https://doi.org/10.1136/annrheumdis-2013-204020

Aguilar, A., Stupans, I., Scutter, S. & King, S. (2014) 'Exploring how Australian occupational therapists and physiotherapists understand each other's professional values: implications for interprofessional education and practice'. *Journal of Interprofessional Care,* 28(1)**,** pp. 15-22. Available at: https://doi.org/10.3109/13561820.2013.820689

Aletaha, D., Eberl, G., Nell, V., Machold, K. & Smolen, J. (2002) 'Practical progress in realisation of early diagnosis and treatment of patients with suspected rheumatoid arthritis: results from two matched questionnaires within three years'. *Annals of the Rheumatic Diseases,* 61(7)**,** pp. 630-634. Available at: https://doi.org/10.1136/ard.61.7.630

Aletaha, D., Neogi, T., Silman, A. J., Funovits, J., Felson, D. T., Bingham, C. O., Birnbaum, N. S., Burmester, G. R., Bykerk, V. P., Cohen, M. D., Combe, B., Costenbader, K. H., Dougados, M., Emery, P., Ferraccioli, G., Hazes, J. M. W., Hobbs, K., Huizinga, T. W. J., Kavanaugh, A., Kay, J., Kvien, T. K., Laing, T., Mease, P., Ménard, H. A., Moreland, L. W., Naden, R. L., Pincus, T., Smolen, J. S., Stanislawska-Biernat, E., Symmons, D., Tak, P. P., Upchurch, K. S., Vencovský, J.,

Wolfe, F. & Hawker, G. (2010) '2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative'. *Arthritis & Rheumatism,* 62(9)**,** pp. 2569-2581. Available at: https://doi.org/10.1002/art.27584

Aletaha, D. & Smolen, J. S. (2018) 'Diagnosis and management of rheumatoid arthritis: a review'. *JAMA,* 320(13)**,** pp. 1360-1372. Available at: https://doi.org/10.1001/jama.2018.13103

Almeida, G. J. M. & Piva, S. R. (2011) 'Associations between changes in physical function and physical activity in response to an exercise program in patients with rheumatoid arthritis'. *Arthritis and Rheumatism. Conference: Annual Scientific Meeting of the American College of Rheumatology and Association of Rheumatology Health Professionals,* 63(10 SUPPL. 1)**,** pp. Available at: https://acrabstracts.org/wp-content/uploads/2018/06/2011_ACR_ARHP_Abstract_Supplement.pdf

Alves, C., Luime, J. J., Van, Z., Derkjen, Huisman, A.-M., Weel, A. E. a. M., Barendregt, P. J. & Hazes, J. M. W. (2011) 'Diagnostic performance of the ACR/EULAR 2010 criteria for rheumatoid arthritis and two diagnostic algorithms in an early arthritis clinic (REACH)'. *Annals of the Rheumatic Diseases,* 70(9)**,** pp. 1645-1647. Available at: https://doi.org/10.1136/ard.2010.142299

American College of Rheumatology Subcommittee on Rheumatoid Arthritis, G. (2002) 'Guidelines for the management of rheumatoid arthritis: 2002 Update'. *Arthritis & Rheumatism,* 46(2)**,** pp. 328-346. Available at: https://doi.org/10.1002/art.10148

American College of Sports Medicine. (1991) *Guidelines for Exercise Testing and Prescription. 4th ed.* Philadelphia: Lea and Febiger

American College of Sports Medicine. (2010) *ACSM's Guidelines for Exercise Testing and Prescription. 8th ed.* Philadelphia: Lippincott Williams & Wilkins

American College of Sports Medicine. (2014) *ACSM's Guidelines for Exercise Testing and Prescription. 9th ed.* Philadelphia: Lippincott Williams & Wilkins

American College of Sports Medicine. (2020) *ACSM's guidelines for exercise testing and prescription. 8th ed.* Philadelphia: Lippincott Williams & Wilkins

Anemaet, W. K. & Hammerich, A. S. (2014) 'A Framework for Exercise Prescription'. *Topics in Geriatric Rehabilitation,* 30(2)**,** pp. Available at: 10.1097/TGR.0000000000000011

Ankolekar, A., Dahl Steffensen, K., Olling, K., Dekker, A., Wee, L., Roumen, C., Hasannejadasl, H. & Fijten, R. (2021) 'Practitioners' views on shared decision-making implementation: A qualitative study'. *PLoS One,* 16(11)**,** pp. e0259844. Available at: https://doi.org/10.1371/journal.pone.0259844

Anvar, N., Matlabi, H., Safaiyan, A., Allahverdipour, H. & Kolahi, S. (2018) 'Effectiveness of self-management program on arthritis symptoms among older women: A randomized controlled

trial study'. *Health Care for Women International,* 39(12)**,** pp. 1326-1339. Available at: https://dx.doi.org/10.1080/07399332.2018.1438438

Aouni, J., Bacro, J. N., Toulemonde, G., Colin, P., Darchy, L. & Sebastien, B. (2020) 'Design optimization for dose-finding trials: a review'. *Journal of Biopharmaceutical Statistics,* 30(4)**,** pp. 662-673. Available at: https://doi.org/10.1080/10543406.2020.1730874

Arnett, F. C., Edworthy, S. M., Bloch, D. A., Mcshane, D. J., Fries, J. F., Cooper, N. S., Healey, L. A., Kaplan, S. R., Liang, M. H., Luthra, H. S., Medsger, T. A., Mitchell, D. M., Neustadt, D. H., Pinals, R. S., Schaller, J. G., Sharp, J. T., Wilder, R. L. & Hunder, G. G. (1988) 'The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis.'. *Arthritis & Rheumatism,* 31(3)**,** pp. 315-324. Available at: https://doi.org/10.1002/art.1780310302

Atkins, E., Kerr, J. & Goodlad, E. (2010) *A Practical Approach to Orthopaedic Medicine: A Practical Approach. 15th ed.* Edinburgh: Elsevier Health Sciences

Avery, K., Williamson, P., Gamble, C., Francischetto, E. O. C., Metcalfe, C., Davidson, P. & Blazeby, J. (2015) 'Optimising the design of internal pilot work to inform efficient randomised controlled trials: issues to consider when developing progression criteria'. *Trials,* 16(Suppl 2(P10))**,** pp. 1-1. Available at: https://doi.org/10.1186/1745-6215-16-S2-P10

Azeez, M., Clancy, C., O'dwyer, T., Lahiff, C., Wilson, F. & Cunnane, G. (2020) 'Benefits of exercise in patients with rheumatoid arthritis: a randomized controlled trial of a patient-specific exercise programme'. *Clinical rheumatology,* 39(6)**,** pp. 1783-1792. Available at: https://dx.doi.org/10.1007/s10067-020-04937-4

Baechle, T. R. & Earle, R. W. (2000) *Essentials of Strength and Conditioning. 2nd ed.* Champaign, Illinois: Human Kinetics

Baillet, A., Vaillant, M., Guinot, M., Juvin, R. & Gaudin, P. (2011) 'Efficacy of resistance exercises in rheumatoid arthritis: meta-analysis of randomized controlled trials'. *Rheumatology,* 51(3)**,** pp. 519-527. Available at: https://doi.org/10.1093/rheumatology/ker330

Bajuaifer, S., Grey, M. J., Hancock, N. J., Chandler, E. & Pomeroy, V. M. (2023) 'Maximum tolerable daily dose of mirror movement therapy ankle exercises after stroke: an early phase dose screening study'. *Physiotherapy,* pp. Available at: https://doi.org/10.1016/j.physio.2023.10.007

Barker, K. & Eickmeyer, S. (2020) 'Therapeutic exercise'. *Medical Clinics,* 104(2)**,** pp. 189-198. Available at: https://doi.org/10.1016/j.mcna.2019.10.003

Barrett, E. M., Scott, D. G. I., Wiles, N. J. & Symmons, D. P. M. (2000) 'The impact of rheumatoid arthritis on employment status in the early years of disease: a UK community-based study'.

Rheumatology, 39(12)**,** pp. 1403-1409. Available at: https://doi.org/10.1093/rheumatology/39.12.1403

Barton, C. J., Lack, S., Hemmings, S., Tufail, S. & Morrissey, D. (2015) 'The 'Best Practice Guide to Conservative Management of Patellofemoral Pain': incorporating level 1 evidence with expert clinical reasoning'. *British Journal of Sports Medicine,* 49(14)**,** pp. 923-934. Available at: https://doi.org/10.1136/bjsports-2014-093637

Bearne, L., Scott, D. & Hurley, M. (2002) 'Exercise can reverse quadriceps sensorimotor dysfunction that is associated with rheumatoid arthritis without exacerbating disease activity'. *Rheumatology,* 41(2)**,** pp. 157-166. Available at: https://doi.org/10.1093/rheumatology/41.2.157

Bennell, K. L., Dobson, F. & Hinman, R. S. (2014) 'Exercise in osteoarthritis: Moving from prescription to adherence'. *Best Practice & Research Clinical Rheumatology,* 28(1)**,** pp. 93-117. Available at: https://doi.org/10.1016/j.berh.2014.01.009

Bergstra, S., Murgia, A., Te Velde, A. & Caljouw, S. (2014) 'A systematic review into the effectiveness of hand exercise therapy in the treatment of rheumatoid arthritis'. *Clinical rheumatology,* 33(11)**,** pp. 1539-1548. Available at: https://doi.org/10.1007/s10067-014-2691-2

Bishop, F. L., Dima, A. L., Ngui, J., Little, P., Moss-Morris, R., Foster, N. E. & Lewith, G. T. (2015) '"Lovely Pie in the Sky Plans": A Qualitative Study of Clinicians' Perspectives on Guidelines for Managing Low Back Pain in Primary Care in England'. *Spine,* 40(23)**,** pp. 1842-1850. Available at: https://doi.org/10.1097/brs.0000000000001215

Black, R. J., Cross, M., Haile, L. M., Culbreth, G. T., Steinmetz, J. D., Hagins, H., Kopec, J. A., Brooks, P. M., Woolf, A. D., Ong, K. L., Kopansky-Giles, D. R., Dreinhoefer, K. E., Betteridge, N., Aali, A., Abbasifard, M., Abbasi-Kangevari, M., Abdurehman, A. M., Abedi, A., Abidi, H., Aboagye, R. G., Abolhassani, H., Abu-Gharbieh, E., Abu-Zaid, A., Adamu, K., Addo, I. Y., Adesina, M. A., Adnani, Q. E. S., Afzal, M. S., Ahmed, A., Aithala, J. P., Akhlaghdoust, M., Alemayehu, A., Alvand, S., Alvis-Zakzuk, N. J., Amu, H., Antony, B., Arabloo, J., Aravkin, A. Y., Arulappan, J., Ashraf, T., Athari, S. S., Azadnajafabad, S., Badawi, A., Baghcheghi, N., Baig, A. A., Balta, A. B., Banach, M., Banik, P. C., Barrow, A., Bashiri, A., Bearne, L. M., Bekele, A., Bensenor, I. M., Berhie, A. Y., Bhagavathula, A. S., Bhardwaj, P., Bhat, A. N., Bhojaraja, V. S., Bitaraf, S., Bodicha, B. B. A., Botelho, J. S., Briggs, A. M., Buchbinder, R., Castañeda-Orjuela, C. A., Charalampous, P., Chattu, V. K., Coberly, K., Cruz-Martins, N., Dadras, O., Dai, X., De Luca, K., Dessalegn, F. N., Dessie, G., Dhimal, M., Digesa, L. E., Diress, M., Doku, P. N., Edinur, H. A., Ekholuenetale, M., Elhadi, M., El-Sherbiny, Y. M., Etaee, F., Ezzeddini, R., Faghani, S., Filip, I., Fischer, F., Fukumoto, T., Ganesan, B., Gebremichael, M. A., Gerema, U., Getachew, M. E., Ghashghaee, A., Gill, T. K.,

Gupta, B., Gupta, S., Gupta, V. B., Gupta, V. K., Halwani, R., Hannan, M. A., Haque, S., et al. (2023) 'Global, regional, and national burden of rheumatoid arthritis, 1990–2020, and projections to 2050: a systematic analysis of the Global Burden of Disease Study 2021'. *The Lancet Rheumatology,* 5(10)**,** pp. e594-e610. Available at: https://doi.org/10.1016/S2665-9913(23)00211-4

Blüml, S., Sahin, E., Saferding, V., Goncalves-Alves, E., Hainzl, E., Niederreiter, B., Hladik, A., Lohmeyer, T., Brunner, J. S. & Bonelli, M. (2015) 'Phosphatase and tensin homolog (PTEN) in antigen-presenting cells controls Th17-mediated autoimmune arthritis'. *Arthritis Research & Therapy,* 17(1)**,** pp. 1-11. Available at: https://doi.org/10.1186/s13075-015-0742-y

Boniface, G., Gandhi, V., Norris, M., Williamson, E., Kirtley, S. & O'connell, N. (2020) 'A systematic review exploring the evidence reported to underpin exercise dose in clinical trials of rheumatoid arthritis'. *Rheumatology,* 59(11)**,** pp. 3147-3157. Available at: https://doi.org/10.1093/rheumatology/keaa150

Boniface, G., Gandhi, V., Norris, M., Williamson, E., Kirtley, S. & O'connell, N. (2021) 'Where's the evidence? A systematic review exploring the evidence underpinning exercise dose in clinical trials of rheumatoid arthritis'. *Physiotherapy,* 113(1)**,** pp. e16-e17. Available at: https://doi.org/10.1016/j.physio.2021.10.242

Boniface, G., Norris, M., Williamson, E., Gandhi, V., Kirtley, S. & O'connell, N. (2018) 'What evidence is used to underpin the design of strength-based exercise interventions evaluated in randomised controlled trials for rheumatoid arthritis? A systematic review protocol'. *BMJ Open,* 8(9)**,** pp. e024127. Available at: https://doi.org/10.1136%2Fbmjopen-2018-024127

Boniface, G., Sanchez-Santos, M., Norris, M., N., O. C., Williamson, E. & Lamb, S. E. (2022) 'Understanding prescribed dose in hand strengthening exercise for rheumatoid arthritis: A secondary analysis of the SARAH trial'. *Musculoskeletal Care,* 20(4)**,** pp. 899-907. Available at: https://doi.org/10.1002/msc.1646

Boniface, G., White, N., Tomlinson, C., Norris, M., O'connell, N., Williamson, E. & Harries, P. (2024) 'Prescribing hand strengthening exercise for patients with rheumatoid arthritis; clinical cues influencing occupational therapists' and physiotherapists' judgements'. *Musculoskeletal Care,* 22(1)**,** pp. e1849. Available at: https://doi.org/10.1002/msc.1849

Booth, J., Moseley, G. L., Schiltenwolf, M., Cashin, A., Davies, M. & Hübscher, M. (2017) 'Exercise for chronic musculoskeletal pain: a biopsychosocial approach'. *Musculoskeletal Care,* 15(4)**,** pp. 413-421. Available at: https://doi.org/10.1002/msc.1191

Borg, G. (1982) 'Psychophysical bases of perceived exertion'. *Medicine and Science in Sports and Exercise,* 14(5)**,** pp. 377-381. Available at: https://pubmed.ncbi.nlm.nih.gov/7154893/

Borg, G. (1998) *Borg's perceived exertion and pain scales.* Human kinetics

Boutron, I., Altman, D. G., Moher, D., Schulz, K. F. & Ravaud, P. (2017) 'CONSORT Statement for Randomized Trials of Nonpharmacologic Treatments: A 2017 Update and a CONSORT Extension for Nonpharmacologic Trial Abstracts'. *Annals of Internal Medicine,* 167(1)**,** pp. 40-47. Available at: https://doi.org/10.7326/M17-0046

Boutron, I., Moher, D., Altman, D. G., Schulz, K. F., Ravaud, P. & Group*, C. (2008) 'Extending the CONSORT statement to randomized trials of nonpharmacologic treatment: explanation and elaboration'. *Annals of Internal Medicine,* 148(4)**,** pp. 295-309. Available at: https://doi.org/10.7326/0003-4819-148-4-200802190-00008

Brant, H., Atherton, H., Ziebland, S., Mckinstry, B., Campbell, J. L. & Salisbury, C. (2016) 'Using alternatives to face-to-face consultations: a survey of prevalence and attitudes in general practice'. *British Journal of General Practice,* 66(648)**,** pp. 460-466. Available at: https://doi.org/10.3399/bjgp16X685597

Breedland, I., Van Scheppingen, C., Leijsma, M., Verheij-Jansen, N. P. & Van Weert, E. (2011) 'Effects of a group-based exercise and educational program on physical performance and disease self-management in rheumatoid arthritis: a randomized controlled study'. *Physical Therapy,* 91(6)**,** pp. 879-893. Available at: https://doi.org/10.2522/ptj.20090010

Bremander, A., Malm, K. & Andersson, M. L. (2020) 'Physical activity in established rheumatoid arthritis and variables associated with maintenance of physical activity over a seven-year period - a longitudinal observational study'. *BMC Rheumatology,* 4(53)**,** pp. 1-9. Available at: https://doi.org/10.1186/s41927-020-00151-6

British Association of Hand Therapists. (2020) *What is Hand Therapy?* [Online]. Available: https://www.hand-therapy.co.uk/patients/what_is_hand_therapy.aspx [Accessed 29th April 2020].

Brody, L. T. (2011) 'Effective therapeutic exercise prescription: the right exercise at the right dose'. *Journal of Hand Therapy,* 25(2)**,** pp. 220-231. Available at: https://doi.org/10.1016/j.jht.2011.09.009

Brorsson, S., Hilliges, M., Sollerman, C. & Nilsdotter, A. (2009) 'A six-week hand exercise programme improves strength and hand function in patients with rheumatoid arthritis'. *Journal of Rehabilitation Medicine,* 41(5)**,** pp. 338-342. Available at: https://doi.org/10.2340/16501977-0334

Brunswik, E. (1952) *The conceptual framework of psychology.* Chicago: University of Chicago Press

Buford, T. W., Roberts, M. D. & Church, T. S. (2013) 'Toward exercise as personalized medicine'. *Sports Medicine,* 43(3)**,** pp. 157-165. Available at: https://doi.org/10.1007/s40279-013-0018-0

Buljina, A. I., Taljanovic, M. S., Avdic, D. M. & Hunter, T. B. 2001. Physical and exercise therapy for treatment of the rheumatoid hand. *Arthritis Care & Research* [Online], 45. Available: http://cochranelibrary-wiley.com/o/cochrane/clcentral/articles/003/CN-00350003/frame.html.

Bultijnck, R., Deforche, B., Borrey, N., Van Bauwel, J., Lievens, M., Rammant, E., Fonteyne, V., Decaestecker, K., Steyaert, A., Lumen, N. & Ost, P. (2021) 'Exercise prescription dose for castrate-resistant prostate cancer patients: a phase I prescription dose escalation trial'. *World Journal of Urology,* 39(-)**,** pp. 357-364. Available at: https://doi.org/10.1007/s00345-020-03098-y

Burmester, G. R., Mcinnes, I. B., Kremer, J. M., Miranda, P., Vencovský, J., Godwood, A., Albulescu, M., Michaels, M. A., Guo, X. & Close, D. (2018) 'Mavrilimumab, a fully human granulocyte–macrophage colony-stimulating factor receptor α monoclonal antibody: long-term safety and efficacy in patients with rheumatoid arthritis'. *Arthritis & Rheumatology,* 70(5)**,** pp. 679-689. Available at: https://doi.org/10.1002/art.40420

Bushman, B. A. (2018) 'Developing the P (for Progression) in a FITT-VP Exercise Prescription'. *ACSM's Health & Fitness Journal,* 22(3)**,** pp. 6-9. Available at: https://journals.lww.com/acsm-healthfitness/toc/2018/05000

Byrne, P. S. & Long, B. (1976) *Doctors talking to patients: A study of the verbal behaviour of general practitioners consulting in their surgeries.* London: HMSO

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)**,** pp. 126-131. Available at: https://pubmed.ncbi.nlm.nih.gov/3920711

Cathain, A., Croot, L., Duncan, E., Rousseau, N., Sworn, K., Turner, K. M., Yardley, L. & Hoddinott, P. (2019) 'Guidance on how to develop complex interventions to improve health and healthcare'. *BMJ Open,* 9(8)**,** pp. e029954. Available at: https://doi.org/10.1136/bmjopen-2019-029954

Chartered Society of Physiotherapy. (2018) *Discovering physiotherapy research priorities that matter to patients, carers and clinicians.* London: Chartered Society of Physiotherapy

Cheung, T. T. & Mcinnes, I. B. (2017) 'Future therapeutic targets in rheumatoid arthritis?'. *Seminars in Immunopathology,* 39(June)**,** pp. 487-500. Available at: https://doi.org/10.1007/s00281-017-0623-3

Choy, E. (2012) 'Understanding the dynamics: pathways involved in the pathogenesis of rheumatoid arthritis'. *Rheumatology,* 51(suppl_5)**,** pp. v3-v11. Available at: http://dx.doi.org/10.1093/rheumatology/kes113

Chung, K. C., Pillsbury, M. S., Walters, M. R. & Hayward, R. A. (1998) 'Reliability and validity testing of the Michigan Hand Outcomes Questionnaire'. *Journal of Hand Surgery,* 23(4)**,** pp. 575-587. Available at: https://doi.org/10.1016/S0363-5023(98)80042-7

Cima, S. R., Barone, A., Porto, J. M. & Abreu, D. C. (2013) 'Strengthening exercises to improve hand strength and functionality in rheumatoid arthritis with hand deformities: a randomized, controlled trial'. *Rheumatology International,* 33(3)**,** pp. 725-732. Available at: https://doi.org/10.1007/s00296-012-2447-8

Collado-Mateo, D., Lavín-Pérez, A. M., Peñacoba, C., Del Coso, J., Leyton-Román, M., Luque-Casado, A., Gasque, P., Fernández-Del-Olmo, M. Á. & Amado-Alonso, D. (2021) 'Key Factors Associated with Adherence to Physical Exercise in Patients with Chronic Diseases and Older Adults: An Umbrella Review'. *International Journal of Environmental Research and Public Health,* 18(4)**,** pp. 1-24. Available at: https://doi.org/10.3390/ijerph18042023

Colucci, E., Clark, A., Lang, C. E. & Pomeroy, V. M. (2017) 'A rule-based, dose-finding design for use in stroke rehabilitation research: methodological development'. *Physiotherapy,* 103(4)**,** pp. 414-422. Available at: https://doi.org/10.1016/j.physio.2016.10.393

Connor, L., Dean, J., Mcnett, M., Tydings, D. M., Shrout, A., Gorsuch, P. F., Hole, A., Moore, L., Brown, R., Melnyk, B. M. & Gallagher-Ford, L. (2023) 'Evidence-based practice improves patient outcomes and healthcare system return on investment: Findings from a scoping review'. *Worldviews on Evidence-Based Nursing,* 20(1)**,** pp. 6-15. Available at: https://doi.org/10.1111/wvn.12621

Cooksey, R. W. (1996) *Judgement Analysis, Theory, Methods and Applications.* London: Academic Press.Inc

Cooney, Law, R., Matschke, V., Lemmey, A. B., Moore, J. P., Ahmad, Y., Jones, J. G., Maddison, P. & Thom, J. M. (2011) 'Benefits of exercise in rheumatoid arthritis'. *Journal of Aging Research,* 2011(Special issue)**,** pp. 1-14. Available at: https://doi.org/10.4061/2011/681640

Cooney, G. M., Dwan, K., Greig, C. A., Lawlor, D. A., Rimer, J., Waugh, F. R., Mcmurdo, M. & Mead, G. E. (2013) 'Exercise for depression'. *Cochrane Database of Systematic Reviews,* 2013(9)**,** pp. 1-119. Available at: https://doi.org/10.1002/14651858.CD004366.pub6

Cooney, J. K., Ahmad, Y. A., Moore, J. P., Sandoo, A. & Thom, J. M. (2019) 'The impact of cardiorespiratory fitness on classical cardiovascular disease risk factors in rheumatoid arthritis: a cross-sectional and longitudinal study'. *Rheumatology International,* 39(10)**,** pp. 1759-1766. Available at: https://doi.org/10.1007/s00296-019-04431-4

Cooper, N. J. (2000) 'Economic burden of rheumatoid arthritis: a systematic review'. *Rheumatology,* 39(1)**,** pp. 28-33. Available at: http://dx.doi.org/10.1093/rheumatology/39.1.28

Cornier, M.-A., Dabelea, D., Hernandez, T. L., Lindstrom, R. C., Steig, A. J., Stob, N. R., Van Pelt, R. E., Wang, H. & Eckel, R. H. (2008) 'The Metabolic Syndrome'. *Endocrine Reviews,* 29(7)**,** pp. 777-822. Available at: https://doi.org/10.1210/er.2008-0024

Couët, N., Desroches, S., Robitaille, H., Vaillancourt, H., Leblanc, A., Turcotte, S., Elwyn, G. & Légaré, F. (2015) 'Assessments of the extent to which health-care providers involve patients in decision making: a systematic review of studies using the OPTION instrument'. *Health Expectations,* 18(4)**,** pp. 542-561. Available at: https://doi.org/10.1111/hex.12054

Craig, P., Dieppe, P., Macintyre, S., Michie, S., Nazareth, I. & Petticrew, M. (2008) 'Developing and evaluating complex interventions: the new Medical Research Council guidance'. *BMJ,* 337(a1655)**,** pp. 1-6. Available at: https://doi.org/10.1136/bmj.a1655

Cumpston, M., Flemyng, E., Thomas, J., Higgins, J. P. T., Deeks, J. J. & Clarke, M. J. (2023) *Chapter I: Introduction.* [Online]. Cochrane. Available: https://www.training.cochrane.org/handbook [Accessed 1st Sept 2023].

De Jong, Z., Munneke, M., Zwinderman, A. H., Kroon, H. M., Jansen, A., Ronday, K. H., Van Schaardenburg, D., Dijkmans, B. a. C., Van Den Ende, C. H. M. & Breedveld, F. C. (2003) 'Is a long-term high-intensity exercise program effective and safe in patients with rheumatoid arthritis?: Results of a randomized controlled trial'. *Arthritis & Rheumatism,* 48(9)**,** pp. 2415-2424. Available at: https://doi.org/10.1002/art.11216

Delhag, B., Wollersjo, I. & Bjelle, A. (1992) 'Effect of active hand exercise and wax bath treatment in rheumatoid arthritis patients'. *Arthritis & Rheumatism,* 5(2)**,** pp. 87-92. Available at: https://doi.org/10.1002/art.1790050207

Denig, P., Wahlström, R., De Saintonge, M. C. & Haaijer-Ruskamp, F. (2002) 'The value of clinical judgement analysis for improving the quality of doctors' prescribing decisions'. *Medical Education,* 36(8)**,** pp. 770-780. Available at: https://doi.org/10.1046/j.1365-2923.2002.01202.x

Denness, C. (2013) 'What are consultation models for?'. *InnovAiT,* 6(9)**,** pp. 592-599. Available at: https://doi.org/10.1177/1755738013475436

Dept of Pt & Ot Aarhus University Hospital 2015. Leddegigt.

Deschenes, M. R. & Kraemer, W. J. (2002) 'Performance and physiologic adaptations to resistance training'. *American Journal of Physical Medicine & Rehabilitation,* 81(11)**,** pp. S3-S16. Available at: https://journals.lww.com/ajpmr/toc/2002/11001

Dias, J. J., Singh, H. P., Taub, N. & Thompson, J. (2012) 'Grip strength characteristics using force–time curves in rheumatoid hands'. *Journal of Hand Surgery (European Volume),* 38(2)**,** pp. 170-177. Available at: https://doi.org/10.1177/1753193412439169

Dite, W., Langford, Z. N., Cumming, T. B., Churilov, L., Blennerhassett, J. M. & Bernhardt, J. (2015) 'A Phase 1 exercise dose escalation study for stroke survivors with impaired walking'. *International journal of stroke : official journal of the International Stroke Society,* 10(7)**,** pp. 1051-1056. Available at: http://dx.doi.org/10.1111/ijs.12548

Dogu, B., Sirzai, H., Yilmaz, F., Polat, B. & Kuran, B. (2013) 'Effects of isotonic and isometric hand exercises on pain, hand functions, dexterity and quality of life in women with rheumatoid arthritis'. *Rheumatology international,* 33(10)**,** pp. 2625-2630. Available at: https://doi.org/10.1007/s00296-013-2787-z

Donaghy, E., Atherton, H., Hammersley, V., Mcneilly, H., Bikker, A., Robbins, L., Campbell, J. & Mckinstry, B. (2019) 'Acceptability, benefits, and challenges of video consulting: a qualitative study in primary care'. *British Journal of General Practice,* 69(686)**,** pp. e586-e594. Available at: https://doi.org/10.3399/bjgp19X704141

Donahue, K. E., Gartlehner, G., Jonas, D. E., Lux, L. J., Thieda, P., Jonas, B. L., Hansen, R. A., Morgan, L. C. & Lohr, K. N. (2008) 'Systematic review: comparative effectiveness and harms of disease-modifying medications for rheumatoid arthritis'. *Annals of Internal Medicine,* 148(2)**,** pp. 124-134. Available at: https://doi.org/10.7326/0003-4819-148-2-200801150-00192

Doody, C. & Mcateer, M. (2002) 'Clinical Reasoning of Expert and Novice Physiotherapists in an Outpatient Orthopaedic Setting'. *Physiotherapy,* 88(5)**,** pp. 258-268. Available at: https://doi.org/10.1016/S0031-9406(05)61417-4

Drummond, A. (2017) 'Feasibility and pilot studies: Why are they important?'. *British Journal of Occupational Therapy,* 80(6)**,** pp. 335-336. Available at: https://doi.org/10.1177/0308022617697743

Dulgeroglu, D., Bal, A., Karaahmet, O., Umay, E., Noyan, S. & Cakci, A. 2016. The effectiveness of galvanic electrotherapy and a conservative hand exercise program in a rheumatoid hand: a randomized controlled trial. *Turkish journal of physical medicine and rehabilitation* [Online], 62. Available: http://cochranelibrary-wiley.com/o/cochrane/clcentral/articles/293/CN-01166293/frame.html.

Dunford, F., Reeve, J. & Larmer, P. (2011) 'Determining differences between novice and expert physiotherapists in undertaking emergency on-call duties'. *New Zealand Journal of Physiotherapy,* 39(1)**,** pp. 17-26. Available at: https://openrepository.aut.ac.nz/server/api/core/bitstreams/960f564f-b2a8-4a20-9482-70006b4fb9be/content

Durcan, L., Wilson, F. & Cunnane, G. 2014. The effect of exercise on sleep and fatigue in rheumatoid arthritis: a randomized controlled study. *Journal of rheumatology* [Online], 41. Available:

http://cochranelibrary-wiley.com/o/cochrane/clcentral/articles/451/CN-01114451/frame.html.

Durstine, J. L., Moore, G. E., Painter, P. L. & Roberts, S. O. (2009) *ACSM's exercise management for persons with chronic diseases and disabilities. 3.* Leeds, United Kingdom: Human Kinetics

Dwyer, C. P., Macneela, P., Durand, H., Gibbons, A., Reynolds, B., Doherty, E., Conneely, S., Slattery, B. W., Murphy, A. W. & Mcguire, B. E. (2018) 'Judgement analysis of case severity and future risk of disability regarding chronic low back pain by general practitioners in Ireland'. *Plos one,* 13(3)**,** pp. 1-12. Available at: https://doi.org/10.1371/journal.pone.0194387

Ekelman, B. A., Hooker, L., Davis, A., Klan, J., Newburn, D., Detwiler, K. & Ricchino, N. (2014) 'Occupational Therapy Interventions for Adults with Rheumatoid Arthritis: An Appraisal of the Evidence'. *Occupational Therapy In Health Care,* 28(4)**,** pp. 347-361. Available at: https://doi.org/10.3109/07380577.2014.919687

El-Kotob, R. & Giangregorio, L. M. (2018) 'Pilot and feasibility studies in exercise, physical activity, or rehabilitation research'. *Pilot and feasibility studies,* 14(4)**,** pp. 1-7. Available at: https://doi.org/10.1186/s40814-018-0326-0

Elkan, A. C., Håkansson N Fau - Frostegård, J., Frostegård J Fau - Cederholm, T., Cederholm T Fau - Hafström, I. & Hafström, I. (2009) 'Rheumatoid cachexia is associated with dyslipidemia and low levels of atheroprotective natural antibodies against phosphorylcholine but not with dietary fat in patients with rheumatoid arthritis: a cross-sectional study'. *Arthritis Reseach and Therapy,* 11(2)**,** pp. 1-11. Available at: https://doi.org/10.1186%2Far2643

Ellegaard, K., Von Bulow, C., Ropke, A., Bartholdy, C., Hansen, I. S., Rifbjerg-Madsen, S., Henriksen, M. & Waehrens, E. E. (2019) 'Hand exercise for women with rheumatoid arthritis and decreased hand function: an exploratory randomized controlled trial'. *Arthritis research & therapy,* 21(1)**,** pp. 158. Available at: https://dx.doi.org/10.1186/s13075-019-1924-9

Elstein, A. S., Shulman, L. S. & Sprafka, S. A. (1978) *Medical problem solving an analysis of clinical reasoning.* Cambridge, MA and London, England: Harvard University Press

Elwyn, G., Durand, M. A., Song, J., Aarts, J., Barr, P. J., Berger, Z., Cochran, N., Frosch, D., Galasiński, D., Gulbrandsen, P., Han, P. K. J., Härter, M., Kinnersley, P., Lloyd, A., Mishra, M., Perestelo-Perez, L., Scholl, I., Tomori, K., Trevena, L., Witteman, H. O. & Van Der Weijden, T. (2017) 'A three-talk model for shared decision making: multistage consultation process'. *BMJ,* 359(j4891)**,** pp. 1-7. Available at: https://doi.org/10.1136/bmj.j4891

Elwyn, G., Frosch, D., Thomson, R., Joseph-Williams, N., Lloyd, A., Kinnersley, P., Cording, E., Tomson, D., Dodd, C. & Rollnick, S. (2012) 'Shared decision making: a model for clinical practice'. *Journal*

of General Internal Medicine, 27(10), pp. 1361-1367. Available at: https://doi.org/10.1007/s11606-012-2077-6

Eulenburg, C., Rahlf, A.-L., Kutasow, A. & Zech, A. (2015) 'Agreements and disagreements in exercise therapy prescriptions after hip replacement among rehabilitation professionals: a multicenter survey'. *BMC musculoskeletal disorders,* 16(1), pp. 1-9. Available at: https://doi.org/10.1186/s12891-015-0646-7

European Medicines Agency. (2017) *Guideline on strategies to identify and mitigate risks for first-in-human and early clinical trials with investigational medicinal products* [Online]. European Medicines Agency. Available: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-strategies-identify-and-mitigate-risks-first-human-and-early-clinical-trials-investigational-medicinal-products-revision-1_en.pdf [Accessed 1st May 2018].

Evans, D. (2003) 'Hierarchy of evidence: a framework for ranking evidence evaluating healthcare interventions'. *Journal of Clinical Nursing,* 12(1), pp. 77-84. Available at: https://doi.org/10.1046/j.1365-2702.2003.00662.x

Eversden, L., Maggs, F., Nightingale, P. & Jobanputra, P. (2007) 'A pragmatic randomised controlled trial of hydrotherapy and land exercises on overall well being and quality of life in rheumatoid arthritis'. *BMC Musculoskeletal Disorders,* 8(23), pp. 1-7. Available at: http://dx.doi.org/10.1186/1471-2474-8-23

Fatahi, N., Hellström, M., Skott, C. & Mattsson, B. (2008) 'General practitioners' views on consultations with interpreters: a triad situation with complex issues'. *Scandinavian Journal of Primary Health Care,* 26(1), pp. 40-45. Available at: https://doi.org/10.1080/02813430701877633

Fischer, F., Lange, K., Klose, K., Greiner, W. & Kraemer, A. (2016) 'Barriers and strategies in guideline implementation—a scoping review'. *Healthcare,* 4(3), pp. 1-16. Available at: https://doi.org/10.3390%2Fhealthcare4030036

Flint-Wagner, H. G., Lisse, J., Lohman, T. G., Going, S. B., Guido, T., Cussler, E., Gates, D. & Yocum, D. E. (2009) 'Assessment of a sixteen-week training program on strength, pain, and function in rheumatoid arthritis patients'. *Journal of Clinical Rheumatology,* 15(4), pp. 165-171. Available at: https://doi.org/10.1097/rhu.0b013e318190f95f

Fraser, A., Vallow, J., Preston, A. & Cooper, R. G. (1999) 'Predicting 'normal' grip strength for rheumatoid arthritis patients'. *Rheumatology,* 38(6), pp. 521-528. Available at: https://doi.org/10.1093/rheumatology/38.6.521

Gabriel, D. A., Kamen, G. & Frost, G. (2006) 'Neural Adaptations to Resistive Exercise'. *Sports Medicine,* 36(2), pp. 133-149. Available at: https://doi.org/10.2165/00007256-200636020-00004

Gagliardi, A. R. & Brouwers, M. C. (2015) 'Do guidelines offer implementation advice to target users? A systematic review of guideline applicability'. *BMJ Open,* 5(2)**,** pp. e007047. Available at: https://doi.org/10.1136/bmjopen-2014-007047

Gallois, M., Davergne, T., Ledinot, P., Ravaud, P. & Regnaux, J.-P. (2017) 'Dosage of preventive or therapeutic exercise interventions: review of published randomized controlled trials and survey of authors'. *Archives of Physical Medicine and Rehabilitation,* 98(12)**,** pp. 2558-2565. Available at: https://doi.org/10.1016/j.apmr.2017.03.030

Galloway, M., Marsden, D. L., Callister, R., Erickson, K. I., Nilsson, M. & English, C. (2023) 'How little is enough? The feasibility of conducting a dose-escalation study for exercise training in people with stroke'. *Journal of Stroke and Cerebrovascular Diseases,* 32(8)**,** pp. 1-11. Available at: https://doi.org/10.1016/j.jstrokecerebrovasdis.2023.107190

Garber, C. E., Blissmer, B., Deschenes, M. R., Franklin, B. A., Lamonte, M. J., Lee, I., Nieman, D. C. & Swain, D. P. (2011) 'American College of Sports Medicine position stand - 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)**,** pp. 1334-1359. Available at: https://doi.org/10.1249/mss.0b013e318213fefb

Garcia-Morales, J. M., Lozada-Mellado, M., Hinojosa-Azaola, A., Llorente, L., Ogata-Medel, M., Pineda-Juarez, J. A., Alcocer-Varela, J., Cervantes-Gaytan, R. & Castillo-Martinez, L. (2020) 'Effect of a Dynamic Exercise Program in Combination With Mediterranean Diet on Quality of Life in Women With Rheumatoid Arthritis'. *Journal of clinical rheumatology : practical reports on rheumatic & musculoskeletal diseases,* 26(7S Suppl 2)**,** pp. S116-S122. Available at: https://dx.doi.org/10.1097/RHU.0000000000001064

Gbd 2021. (2021) 'Global, regional, and national burden of rheumatoid arthritis, 1990-2020, and projections to 2050: a systematic analysis of the Global Burden of Disease Study 2021'. *The Lancet Rheumatology,* 5(10)**,** pp. e594-e610. Available at: https://doi.org/10.1016%2FS2665-9913(23)00211-4

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)**,** pp. Available at: https://doi.org/10.1002/14651858.CD011279.pub3

Gerlag, D. M., Raza, K., Van Baarsen, L. G., Brouwer, E., Buckley, C. D., Burmester, G. R., Gabay, C., Catrina, A. I., Cope, A. P. & Cornelis, F. (2012) 'EULAR recommendations for terminology and research in individuals at risk of rheumatoid arthritis: report from the Study Group for Risk

Factors for Rheumatoid Arthritis'. *Annals of the Rheumatic Diseases,* 71(5), pp. 638-641. Available at: https://doi.org/10.1136/annrheumdis-2011-200990

Gerosa, M., De Angelis, V., Riboldi, P. & Meroni, P. (2008) 'Rheumatoid arthritis: a female challenge'. *Women's Health,* 4(2), pp. 195-201. Available at: https://doi.org/10.2217/17455057.4.2.195

Glasziou, P., Meats E Fau - Heneghan, C., Heneghan C Fau - Shepperd, S. & Shepperd, S. (2008) 'What is missing from descriptions of treatment in trials and reviews?'. *BMJ,* 336(7659), pp. 1472-1474. Available at: https://doi.org/10.1136/bmj.39590.732037.47

Gleadhill, C., Bolsewicz, K., Davidson, S. R., Kamper, S. J., Tutty, A., Robson, E., Da Silva, P. V., Donald, B., Dooley, K. & Manvell, J. (2022) 'Physiotherapists' opinions, barriers, and enablers to providing evidence-based care: a mixed-methods study'. *BMC Health Services Research,* 22(1), pp. 1-16. Available at: https://doi.org/10.1186/s12913-022-08741-5

Gómez-Salgado, J., Jacobsohn, L., Frade, F., Romero-Martin, M. & Ruiz-Frutos, C. (2018) 'Applying the WHO international classification of functioning, disability and health in nursing assessment of population health'. *International Journal of Environmental Research and Public Health,* 15(10), pp. 2245. Available at: https://doi.org/10.3390/ijerph15102245

Gordon, D. A., Stein, J. L. & Broder, I. (1973) 'The extra-articular features of rheumatoid arthritis: a systematic analysis of 127 cases'. *The American Journal of Medicine,* 54(4), pp. 445-452. Available at: https://doi.org/10.1016/0002-9343(73)90040-5

Gorry, G. A. (1970) 'Modelling the diagnostic process'. *Academic Medicine,* 45(5), pp. 293-302. Available at: https://journals.lww.com/academicmedicine/toc/1970/05000

Grassi, W., De Angelis, R., Lamanna, G. & Cervini, C. (1998) 'The clinical features of rheumatoid arthritis'. *European Journal of Radiology,* 27(pp. S18-S24. Available at: https://doi.org/10.1016/S0720-048X(98)00038-2

Greenhalgh, S. & Selfe, J. (2010) *Red flags II A guide to solving serious pathology of the spine.* China: Churchill Livingstone

Groen, G. J. & Patel, V. L. (1985) 'Medical problem-solving: some questionable assumptions'. *Med Educ,* 19(2), pp. 95-100. Available at: https://doi.org/10.1111/j.1365-2923.1985.tb01148.x

Gronwald, T., Törpel, A., Herold, F. & Budde, H. (2020) 'Perspective of Dose and Response for Individualized Physical Exercise and Training Prescription'. *Journal of Functional Morphology and Kinesiology,* 5(3), pp. 1-7. Available at: https://doi.org/10.3390/jfmk5030048

Hakkinen, A., Sokka, T., Kotaniemi, A. & Hannonen, P. (2001) 'A randomized two-year study of the effects of dynamic strength training on muscle strength, disease activity, functional capacity, and bone mineral density in early rheumatoid arthritis'. *Arthritis & Rheumatism,* 44(3), pp.

515-22. Available at: https://doi.org/10.1002/1529-0131(200103)44:3%3C515::AID-ANR98%3E3.0.CO;2-5

Häkkinen, A., Sokka, T., Kotaniemi, A. & Hannonen, P. (2001) 'A randomized two-year study of the effects of dynamic strength training on muscle strength, disease activity, functional capacity, and bone mineral density in early rheumatoid arthritis'. *Arthritis & Rheumatism,* 44(3)**,** pp. 515-522. Available at: https://doi.org/10.1002/1529-0131(200103)44:3%3C515::AID-ANR98%3E3.0.CO;2-5

Hall, A. M., Copsey, B., Williams, M., Srikesavan, C. & Lamb, S. E. (2017) 'Mediating Effect of Changes in Hand Impairments on Hand Function in Patients With Rheumatoid Arthritis: Exploring the Mechanisms of an Effective Exercise Program'. *Arthritis Care & Research,* 69(7)**,** pp. 982-988. Available at: https://doi.org/10.1002/acr.23093

Hall, J., Skevington, S. M., Maddison, P. J. & Chapman, K. (1996) 'A randomized and controlled trial of hydrotherapy in rheumatoid arthritis'. *Arthritis & Rheumatism: Official Journal of the American College of Rheumatology,* 9(3)**,** pp. 206-215. Available at: https://doi.org/10.1002/1529-0131(199606)9:3%3C206::AID-ANR1790090309%3E3.0.CO;2-J

Hall, P. (2005) 'Interprofessional teamwork: Professional cultures as barriers'. *Journal of Interprofessional Care,* 19(sup1)**,** pp. 188-196. Available at: http://dx.doi.org/10.1080/13561820500081745

Hammond, A. (2004) 'What is the role of the occupational therapist?'. 18(pp. 491-505. Available at:

Hammond, A. & Freeman, K. (2004) 'The long-term outcomes from a randomized controlled trial of an educational-behavioural joint protection programme for people with rheumatoid arthritis'. *Clinical Rehabilitation,* 18(5)**,** pp. 520-528. Available at: https://doi.org/10.1191/0269215504cr766oa

Hammond, A. & Prior, Y. (2016) 'The effectiveness of home hand exercise programmes in rheumatoid arthritis: a systematic review'. *British medical bulletin,* 119(1)**,** pp. 49-62. Available at: https://doi.org/10.1093/bmb/ldw024

Hammond, A., Young, A. & Kidao, R. (2004) 'A randomised controlled trial of occupational therapy for people with early rheumatoid arthritis'. *Annals of the Rheumatic Diseases,* 63(1)**,** pp. 23-30. Available at: https://doi.org/10.1136%2Fard.2002.001511

Hammond, K. R. (1996) *Human judgment and social policy: Irreducible uncertainty, inevitable error, unavoidable injustice.* Oxford University Press on Demand

Han, A., V, R., Judd, M., Taixiang, W., Wells, G. & Tugwell, P. (2004) 'Tai chi for treating rheumatoid arthritis'. *Cochrane Database of Systematic Reviews,* 3(January)**,** pp. 1-22. Available at: https://doi.org/10.1002/14651858.cd004849

Hancock, H. C., Mason, J. M. & Murphy, J. J. (2012) 'Using the method of judgement analysis to address variations in diagnostic decision making'. *BMC Rresearch Notes,* 5(139)**,** pp. 139-139. Available at: https://doi.org/10.1186/1756-0500-5-139

Hansen, A. R., Graham, D. M., Pond, G. R. & Siu, L. L. (2014) 'Phase 1 trial design: is 3+ 3 the best?'. *Cancer Control,* 21(3)**,** pp. 200-208. Available at: http://dx.doi.org/10.1177/107327481402100304

Hansen, D., Rovelo Ruiz, G., Doherty, P., Iliou, M.-C., Vromen, T., Hinton, S., Frederix, I., Wilhelm, M., Schmid, J.-P., Abreu, A., Ambrosetti, M., Garcia-Porrero, E., Coninx, K., Dendale, P. & On Behalf of The, E. E. W. G. (2018) 'Do clinicians prescribe exercise similarly in patients with different cardiovascular diseases? Findings from the EAPC EXPERT working group survey'. *European Journal of Preventive Cardiology,* 25(7)**,** pp. 682-691. Available at: https://doi.org/10.1177/2047487318760888

Hansen, T., Hansen, G., Langgaard, A. & Rasmussen, J. (1993) 'Longterm physical training in rheumatoid arthritis. A randomized trial with different training programs and blinded observers'. *Scandinavian Journal of Rheumatology,* 22(3)**,** pp. 107-112. Available at: https://doi.org/10.3109/03009749309099253

Hansford, H. J., Wewege, M. A., Cashin, A. G., Hagstrom, A. D., Clifford, B. K., Mcauley, J. H. & Jones, M. D. (2022) 'If exercise is medicine, why don't we know the dose? An overview of systematic reviews assessing reporting quality of exercise interventions in health and disease'. *British Journal of Sports Medicine,* 56(12)**,** pp. 692-700. Available at: http://dx.doi.org/10.1136/bjsports-2021-104977

Hariohm, K., Jeyanthi, S., Kumar, J. S. & Prakash, V. (2017) 'Description of interventions is under-reported in physical therapy clinical trials'. *Brazilian Journal of Physical Therapy,* 21(4)**,** pp. 281-286. Available at: https://doi.org/10.1016/j.bjpt.2017.05.006

Harris, R. & Millard, J. (1955) 'Paraffin-wax baths in the treatment of rheumatoid arthritis'. *Annals of the Rheumatic Diseases,* 14(3)**,** pp. 278-282. Available at: https://doi.org/10.1136%2Fard.14.3.278

Harvey, L. (2018) 'Feasibility and pilot studies pave the way for definitive trials'. *Spinal Cord,* 56(8)**,** pp. 723-724. Available at: https://doi.org/10.1038/s41393-018-0184-x

Haskell, W. L., Lee, I.-M., Pate, R. R., Powell, K. E., Blair, S. N., Franklin, B. A., Macera, C. A., Heath, G. W., Thompson, P. D. & Bauman, A. (2007) 'Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association'. *Circulation,* 116(9)**,** pp. 1081-1093. Available at: https://doi.org/10.1161/circulationaha.107.185649

Health and Care Professions Council. (2023a) *The standards of proficiency for occupational therapists* [Online]. Available: https://www.hcpc-uk.org/standards/standards-of-proficiency/occupational-therapists/ [Accessed 20th August 2023].

Health and Care Professions Council. (2023b) *The standards of proficiency for physiotherapists* [Online]. Available: https://www.hcpc-uk.org/standards/standards-of-proficiency/physiotherapists/ [Accessed 20th August 2023].

Health and Care Professions Council. (2024) *Who we are and what we do* [Online]. Available: https://www.hcpc-uk.org/about-us/corporate-governance/freedom-of-information/who-we-are-and-what-we-do/#:~:text=The%20HCPC%20is%20the%20statutory,objective%20of%20protecting%20the%20public. [Accessed 1st Feb 2024].

Health Research Authority. (2017) *Phase 1 Clinical Trials* [Online]. Available: https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/phase-1-clinical-trials/ [Accessed 8th Nov 2017].

Heidari, B. (2011) 'Rheumatoid Arthritis: Early diagnosis and treatment outcomes'. *Caspian Journal of Internal Medicine,* 2(1)**,** pp. 161-170. Available at: https://pubmed.ncbi.nlm.nih.gov/24024009

Heine, P., Williams, M., Williamson, E., Bridle, C., Adams, J., O'brien, A., Evans, D. & Lamb, S. (2012) 'Development and delivery of an exercise intervention for rheumatoid arthritis: strengthening and stretching for rheumatoid arthritis of the hand (SARAH) trial'. *Physiotherapy,* 98(2)**,** pp. 121-130. Available at: https://doi.org/10.1016/j.physio.2011.03.001

Herold, F., Müller, P., Gronwald, T. & Müller, N. G. (2019) 'Dose–Response Matters! – A Perspective on the Exercise Prescription in Exercise–Cognition Research'. *Frontiers in Psychology,* 10(2338)**,** pp. Available at: https://doi.org/10.3389/fpsyg.2019.02338

Herold, F., Törpel, A., Hamacher, D., Budde, H., Zou, L., Strobach, T., Müller, N. G. & Gronwald, T. (2021) 'Causes and consequences of interindividual response variability: A call to apply a more rigorous research design in acute exercise-cognition studies'. *Frontiers in Physiology,* 12(Article 682891)**,** pp. 1-15. Available at: https://doi.org/10.3389/fphys.2021.682891

Hewlett, S., Sanderson, T., May, J., Alten, R., Bingham Iii, C. O., Cross, M., March, L., Pohl, C., Woodworth, T. & Bartlett, S. J. (2012) ''I'm hurting, I want to kill myself': rheumatoid arthritis flare is more than a high joint count—an international patient perspective on flare where medical help is sought'. *Rheumatology,* 51(1)**,** pp. 69-76. Available at: https://doi.org/10.1093/rheumatology/ker172

Hicks, J. E. (1994) 'Exercise in rheumatoid arthritis'. *Physical Medicine and Rehabilitation Clinics,* 5(4)**,** pp. 701-728. Available at: https://doi.org/10.1016/S1047-9651(18)30491-1

Higgins, J. P. T., Altman, D. G., Gøtzsche, P. C., Jüni, P., Moher, D., Oxman, A. D., Savović, J., Schulz, K. F., Weeks, L. & Sterne, J. a. C. (2011) 'The Cochrane Collaboration's tool for assessing risk of bias in randomised trials'. *BMJ,* 343(Oct)**,** pp. d5928. Available at: https://doi.org/10.1136/bmj.d5928

Higgins, S. C., Adams, J. & Hughes, R. (2018) 'Measuring hand grip strength in rheumatoid arthritis'. *Rheumatology International,* 38(5)**,** pp. 707-714. Available at: https://doi.org/10.1007/s00296-018-4024-2

Higgs, J., Jensen, G. M., Loftus, S. & Christensen, N. (2019) *Clinical reasoning in the health professions. 4th edtion.* Edinburgh: Elsevier Health Sciences

Hobbs, F. D. R., Bankhead, C., Mukhtar, T., Stevens, S., Perera-Salazar, R., Holt, T. & Salisbury, C. (2016) 'Clinical workload in UK primary care: a retrospective analysis of 100 million consultations in England, 2007–14'. *The Lancet,* 387(10035)**,** pp. 2323-2330. Available at: https://doi.org/10.1016/S0140-6736(16)00620-6

Hoenig, H., Groff, G., Pratt, K., Goldberg, E. & Franck, W. (1993) 'A randomized controlled trial of home exercise on the rheumatoid hand'. *The Journal of Rheumatology,* 20(5)**,** pp. 785-789. Available at: PMID: 8336303

Hoffmann, T. C., Erueti, C. & Glasziou, P. P. (2013) 'Poor description of non-pharmacological interventions: analysis of consecutive sample of randomised trials'. *BMJ,* 347(pp. f3755. Available at: http://dx.doi.org/10.1136/bmj.f3755

Hoffmann, T. C., Glasziou, P. P., Boutron, I., Milne, R., Perera, R., Moher, D., Altman, D. G., Barbour, V., Macdonald, H., Johnston, M., Lamb, S. E., Dixon-Woods, M., Mcculloch, P., Wyatt, J. C., Chan, A. & Michie, S. (2014) 'Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide'. *BMJ,* 348(g1687)**,** pp. 1-12. Available at: http://dx.doi.org/10.1136/bmj.g1687

Holden, S. & Barton, C. J. (2019) ''What should I prescribe?': time to improve reporting of resistance training programmes to ensure accurate translation and implementation'. *British Journal of Sports Medicine,* 53(5)**,** pp. 264-265. Available at: http://dx.doi.org/10.1136/bjsports-2017-098664

Holden, S., Rathleff, M. S., Jensen, M. B. & Barton, C. J. (2018) 'How can we implement exercise therapy for patellofemoral pain if we don't know what was prescribed? A systematic review'. *British Journal of Sports Medicine,* 52(386)**,** pp. 1-8. Available at: https://doi.org/10.1136/bjsports-2017-097547

Hoogeboom, T. J., Kousemaker, M. C., Van Meeteren, N. L., Howe, T., Bo, K., Tugwell, P., Ferreira, M., De Bie, R. A., Van Den Ende, C. H. & Stevens-Lapsley, J. E. (2021) 'i-CONTENT tool for assessing

therapeutic quality of exercise programs employed in randomised clinical trials'. *British journal of sports medicine,* 55(20)**,** pp. 1153-1160. Available at: https://doi.org/10.1136/bjsports-2019-101630

Howick, J., Chalmers, I., Glsziou, P., Greenhalgh, T., Heneghan, C., Liberati, A., Moschetti, I., Phillips, B., Thornton, H. (2011a) *The 2011 Oxford CEBM Levels of Evidence (Introductory Document)* [Online]. Oxford Centre for Evidence-Based Medicine. Available: https://www.cebm.net/index.aspx?o=5653 [Accessed 21st February 2018].

Howick, J., Chalmers, I., Glsziou, P., Greenhalgh, T., Heneghan, C., Liberati, A., Moschetti, I., Phillips, B., Thornton, H. (2011b) *Explanation of the 2011 Oxford Centre for Evidence-Based Medicine (OCEBM) Levels of Evidence (Background Document)* [Online]. Oxford Centre for Evidence-Based Medicine. Available: https://www.cebm.net/index.aspx?o=5653 [Accessed 1st May 2018].

Hughes, J. G. (2009) 'Exploring the impact of rheumatoid arthritis on patients' lives'. *International Journal of Therapy and Rehabilitation,* 16(11)**,** pp. 594-601. Available at: https://doi.org/10.12968/ijtr.2009.16.11.44940

Humphrey, V. N. & Colby, L. A. (2018) 'Therapeutic Exercise: Foundational Concepts', *in:* KISNER, C., COLBY, L. A. & BORSTAD, J. (eds.) *Therapeutic Exercise: Foundations and Techniques.* 7th ed. Philadelphia: E.A Davis Company, pp. 1-42

Humphreys, J. H., Verstappen, S. M., Hyrich, K. L., Chipping, J. R., Marshall, T. & Symmons, D. P. (2013) 'The incidence of rheumatoid arthritis in the UK: comparisons using the 2010 ACR/EULAR classification criteria and the 1987 ACR classification criteria. Results from the Norfolk Arthritis Register'. *Annals of Rheumatic Diseases,* 72(8)**,** pp. 1315-20. Available at: https://doi.org/10.1136/annrheumdis-2012-201960

Hurkmans, E. J., Jones, A., Li, L. C. & Vliet Vlieland, T. P. M. (2011) 'Quality appraisal of clinical practice guidelines on the use of physiotherapy in rheumatoid arthritis: a systematic review'. *Rheumatology,* 50(10)**,** pp. 1879-1888. Available at: https://doi.org/10.1093/rheumatology/ker195

Hurley, M. V., Walsh, N. E., Mitchell, H. L., Pimm, T. J., Patel, A., Williamson, E., Jones, R. H., Dieppe, P. A. & Reeves, B. C. (2007) 'Clinical effectiveness of a rehabilitation program integrating exercise, self-management, and active coping strategies for chronic knee pain: A cluster randomized trial'. *Arthritis Care & Research,* 57(7)**,** pp. 1211-1219. Available at: https://doi.org/10.1002/art.22995

Iacono, T. & Johnson, H. (2004) 'Patients with disabilities and complex communication needs: The GP consultation'. *Australian Family Physician,* 33(8)**,** pp. 585-589. Available at: https://search.informit.org/doi/10.3316/informit.372293433542991

Innes, J. A., Dover, A. R. & Fairhurst, K. (2018) *Macleod's Clinical Examination.* London: Elsevier

Institute for Health Metrics and Evaluation. (2019a) *Cardiovascular diseases—Level 2 cause* [Online]. [Accessed 26th Jan 2023].

Institute for Health Metrics and Evaluation. (2019b) *Rheumatoid arthritis - Level 3 cause* [Online]. Available: https://www.healthdata.org/results/gbd_summaries/2019/rheumatoid-arthritis-level-3-cause [Accessed 26th Jan 2023].

Iqbal, M. Z., Rochette, A., Mayo, N. E., Valois, M.-F., Bussières, A. E., Ahmed, S., Debigaré, R., Letts, L. J., Macdermid, J. C. & Ogourtsova, T. (2023) 'Exploring if and how evidence-based practice of occupational and physical therapists evolves over time: A longitudinal mixed methods national study'. *Plos One,* 18(3)**,** pp. e0283860. Available at: https://doi.org/10.1371/journal.pone.0283860

Iversen, M. D. (2002) 'Physical therapy for the management of RA: rehabilitation measures are most effective when started early'. *The Journal of Musculoskeletal Medicine,* 24(6)**,** pp. 352-358. Available at: https://go.gale.com/ps/i.do?id=GALE%7CA165910312&sid=googleScholar&v=2.1&it=r&linkaccess=abs&issn=08992517&p=HRCA&sw=w&userGroupName=anon%7Eab004900&aty=open-web-entry

Jahanbin, I., Moghadam, M. H., Nazarinia, M. A., Ghodsbin, F., Bagheri, Z. & Ashraf, A. R. (2014) 'The Effect of Conditioning Exercise on the Health Status and Pain in Patients with Rheumatoid Arthritis: A Randomized Controlled Clinical Trial'. *International Journal of Community Based Nursing & Midwifery,* 2(3)**,** pp. 169-176. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/pmc4201199/

Japp, A. G., Robertson, C., Wright, R. J., Reed, M. J. & Robson, A. (2018) *Macleod's Clinical Diagnosis. 2nd ed.* London: Elsevier

Jenkins, J., Shields, M., Patterson, C. & Kee, F. (2007) 'Decision making in asthma exacerbation: a clinical judgement analysis'. *Archives of Disease in Childhood,* 92(8)**,** pp. 672-677. Available at: https://doi.org/10.1136/adc.2007.117424

Jenkinson, C. & Layte, R. (1997) 'Development and testing of the UK SF-12'. *Journal of health services research & policy,* 2(1)**,** pp. 14-18. Available at: https://doi.org/10.1177/135581969700200105

Jensen, G. M., Resnik, L. J. & Haddad, A. M. (2019) 'Expertise and Clinical Reasoning', *in:* HIGGS, J., JENSEN, G. M., LOFTUS, S. & CHRISTENSEN, N. (eds.) *Clinical reasoning in the health professions.* 4th ed. Edinburgh: Elsevier Health Sciences, pp. 67-78

Jette, A. M. (2017) 'The Importance of Dose of a Rehabilitation Intervention'. *Physical Therapy,* 97(11)**,** pp. 1043-1043. Available at: https://doi.org/10.1093/ptj/pzx085

Kapandji, A. I. (1992) 'Clinical evaluation of the thumb's opposition'. *Journal of Hand Therapy,* 5(2)**,** pp. 102-106. Available at: https://doi.org/10.1016/S0894-1130(12)80265-1

Katon, W. & Schulberg, H. (1992) 'Epidemiology of depression in primary care'. *General hospital psychiatry,* 14(4)**,** pp. 237-247. Available at: https://doi.org/10.1016/0163-8343(92)90094-Q

Kay, J. & Upchurch, K. S. (2012) 'ACR/EULAR 2010 rheumatoid arthritis classification criteria'. *Rheumatology,* 51(suppl_6)**,** pp. vi5-vi9. Available at: https://doi.org/10.1093/rheumatology/kes279

Keller, V. F. & Carroll, J. G. (1994) 'A new model for physician-patient communication'. *Patient Education and Counseling,* 23(2)**,** pp. 131-140. Available at: https://doi.org/10.1016/0738-3991(94)90051-5

Kent, P., O'sullivan, P. B., Keating, J. & Slade, S. C. (2018) 'Evidence-based exercise prescription is facilitated by the Consensus on Exercise Reporting Template (CERT)'. *British Journal of Sports Medicine,* 52(3)**,** pp. 147-148. Available at: https://doi.org/10.1136/bjsports-2016-097405

Khan, M. K., Khan, I. A. & Liaquat, A. (2022) 'Therapeutic Potential of Curcumin with and without Strengthening Exercises in Improving Rheumatoid Arthritis'. *Journal of the College of Physicians and Surgeons--Pakistan : JCPSP,* 32(12)**,** pp. 1640-1643. Available at: https://dx.doi.org/10.29271/jcpsp.2022.12.1640

Kirwan, J., De Saintonge, D. C., Joyce, C., Holmes, J. & Currey, H. (1986) 'Inability of rheumatologists to describe their true policies for assessing rheumatoid arthritis'. *Annals of the Rheumatic Diseases,* 45(2)**,** pp. 156-161. Available at: https://doi.org/10.1136%2Fard.45.2.156

Kirwan, J. R., De Saintonge, D. M. C. & Joyce, C. (1990) 'Clinical judgment analysis'. *QJM: An International Journal of Medicine,* 76(3)**,** pp. 935-949. Available at: https://doi.org/10.1093/oxfordjournals.qjmed.a068496

Kojima, T., Ishikawa, H., Tanaka, S., Haga, N., Nishida, K., Yukioka, M., Hashimoto, J., Miyahara, H., Niki, Y., Kimura, T., Oda, H., Asai, S., Funahashi, K., Kojima, M. & Ishiguro, N. (2018) 'Characteristics of functional impairment in patients with long-standing rheumatoid arthritis based on range of motion of joints: Baseline data from a multicenter prospective observational cohort study to evaluate the effectiveness of joint surgery in the treat-to-target era'. *Modern*

Rheumatology, 28(3), pp. 474-481. Available at: https://doi.org/10.1080/14397595.2017.1349593

Korn, E. L., Moscow, J. A. & Freidlin, B. (2023) 'Dose optimization during drug development: whether and when to optimize'. *Journal of the National Cancer Institute,* 115(5), pp. 492-497. Available at: https://doi.org/10.1093/jnci/djac232

Kraemer, W. J., Adams, K., Cafarelli, E., Dudley, G. A., Dooly, C., Feigenbaum, M. S., Fleck, S. J., Franklin, B., Fry, A. C., Hoffman, J. R., Newton, R. U., Potteiger, J., Stone, M. H., Ratamess, N. A. & Triplett-Mcbride, T. (2002) 'American College of Sports Medicine Position Stand - Progression models in resistance training for healthy adults'. *Medicine & Science in Sports & Exercise,* 34(2), pp. Available at: https://doi.org/10.1097/00005768-200202000-00027

Kraemer, W. J., Ratamess, N. A., Flanagan, S. D., Shurley, J. P., Todd, J. S. & Todd, T. C. (2017) 'Understanding the science of resistance training: an evolutionary perspective'. *Sports Medicine,* 47(12), pp. 2415-2435. Available at: https://doi.org/10.1007/s40279-017-0779-y

Kramer, S. F., Cumming, T., Johnson, L., Churilov, L. & Bernhardt, J. (2020) 'Determining Maximal Tolerable Aerobic Training Intensity in the Acute Phase after Stroke: a Novel Dose Ranging Trial Protocol'. *Journal of Stroke and Cerebrovascular Diseases,* 29(12), pp. 105359. Available at: https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.105359

Krieger, J. L., Schnitzer, M. & Watzinger, M. (2024) 'Standing on the shoulders of science'. *Strategic Management Journal,* n/a(n/a), pp. 1-26. Available at: https://doi.org/10.1002/smj.3598

Laitinen, A.-M., Boström, C., Hyytiä, S. & Stolt, M. (2022) 'Experiences of foot health in patients with rheumatoid arthritis: a qualitative study'. *Disability and Rehabilitation,* 44(1), pp. 88-95. Available at: https://doi.org/10.1080/09638288.2020.1758966

Lamb, S. E., Williamson, E. M., Heine, P. J., Adams, J., Dosanjh, S., Dritsaki, M., Glover, M. J., Lord, J., Mcconkey, C., Nichols, V., Rahman, A., Underwood, M., Williams, M. A., On Behalf of The, S. & Stretching for Rheumatoid Arthritis of the Hand Trial Trial, T. (2015) 'Exercises to improve function of the rheumatoid hand (SARAH): a randomised controlled trial'. *The Lancet* 385(9966), pp. 421-429. Available at: https://doi.org/10.1016/S0140-6736(14)60998-3

Lange, E., Kucharski, D., Svedlund, S., Svensson, K., Bertholds, G., Gjertsson, I. & Mannerkorpi, K. (2018) 'Effects of aerobic and resistance exercise in older adults with rheumatoid arthritis: A randomized controlled trial'. *Arthritis care & Research,* 71(1), pp. 61-70. Available at: https://doi.org/10.1002/acr.23589

Le Tourneau, C., Lee, J. J. & Siu, L. L. (2009) 'Dose Escalation Methods in Phase I Cancer Clinical Trials'. *JNCI: Journal of the National Cancer Institute,* 101(10), pp. 708-720. Available at: http://dx.doi.org/10.1093/jnci/djp079

Lederman, E. (2010) 'The myth of core stability'. *Journal of Bodywork and Movement Therapies,* 14(1)**,** pp. 84-98. Available at: https://doi.org/10.1016/j.jbmt.2009.08.001

Ledingham, J., Snowden, N. & Ide, Z. (2017) 'Diagnosis and early management of inflammatory arthritis'. *BMJ,* 358(j3248)**,** pp. 1-8. Available at: https://doi.org/10.1136/bmj.j3248

Lehane, E., Leahy-Warren, P., O'riordan, C., Savage, E., Drennan, J., O'tuathaigh, C., O'connor, M., Corrigan, M., Burke, F. & Hayes, M. (2019) 'Evidence-based practice education for healthcare professions: an expert view'. *BMJ Evidence-Based Medicine,* 24(November)**,** pp. 103-108. Available at: https://doi.org/10.1136/bmjebm-2018-111019

Leigh, E. (2010) *Services for people with rheumatoid arthritis: tenth report of session 2009-10, report, together with formal minutes, oral and written evidence (Vol. 46).* London: The Stationery Office

Lemmey, A. B., Marcora, S. M., Chester, K., Wilson, S., Casanova, F. & Maddison, P. J. (2009) 'Effects of high-intensity resistance training in patients with rheumatoid arthritis: A randomized controlled trial'. *Arthritis Care & Research,* 61(12)**,** pp. 1726-1734. Available at: https://doi.org/10.1002/art.24891

Liao, C.-D., Chen, H.-C., Huang, S.-W. & Liou, T.-H. (2021) 'Exercise therapy for sarcopenia in rheumatoid arthritis: A meta-analysis and meta-regression of randomized controlled trials'. *Clinical Rehabilitation,* 36(2)**,** pp. 145-157. Available at: https://doi.org/10.1177/02692155211035539

Lindqvist, E., Jonsson, K., Saxne, T. & Eberhardt, K. (2003) 'Course of radiographic damage over 10 years in a cohort with early rheumatoid arthritis'. *Annals of the Rheumatic Diseases,* 62(7)**,** pp. 611-616. Available at: https://doi.org/10.1136%2Fard.62.7.611

Lindqvist, E., Saxne, T., Geborek, P. & Eberhardt, K. (2002) 'Ten year outcome in a cohort of patients with early rheumatoid arthritis: health status, disease process, and damage'. *Annals of the Rheumatic Diseases,* 61(12)**,** pp. 1055-1059. Available at: https://doi.org/10.1136%2Fard.61.12.1055

Lindström, A.-C. & Bernhardsson, S. (2018) 'Evidence-Based Practice in Primary Care Occupational Therapy: A Cross-Sectional Survey in Sweden'. *Occupational Therapy International,* 2018(Oct)**,** pp. 1-9. Available at: https://doi.org/10.1155/2018/5376764

Listing, J., Kekow, J., Manger, B., Burmester, G.-R., Pattloch, D., Zink, A. & Strangfeld, A. (2015) 'Mortality in rheumatoid arthritis: the impact of disease activity, treatment with glucocorticoids, TNFα inhibitors and rituximab'. *Annals of the Rheumatic Diseases,* 74(2)**,** pp. 415-421. Available at: https://doi.org/10.1136/annrheumdis-2013-204021

Loew, L., Brosseau, L., Kenny, G. P., Durand-Bush, N., Poitras, S., De Angelis, G. & Wells, G. A. (2017) 'An evidence-based walking program among older people with knee osteoarthritis: the PEP (participant exercise preference) pilot randomized controlled trial'. *Clinical Rheumatology,* 36(7), pp. 1607-1616. Available at: https://doi.org/10.1007/s10067-017-3606-9

Lourenzi, F. M., Jones, A., Pereira, D. F., Dos Santos, J. H. C. A., Furtado, R. N. V. & Natour, J. (2017) 'Effectiveness of an overall progressive resistance strength program for improving the functional capacity of patients with rheumatoid arthritis: a randomized controlled trial'. *Clinical Rehabilitation,* 31(11), pp. 1482-1491. Available at: https://doi.org/10.1177/0269215517698732

Lütze, U. & Archenholtz, B. (2007) 'The impact of arthritis on daily life with the patient perspective in focus'. *Scandinavian Journal of Caring Sciences,* 21(1), pp. 64-70. Available at: https://doi.org/10.1111/j.1471-6712.2007.00443.x

Lwin, M. N., Serhal, L., Holroyd, C. & Edwards, C. J. (2020) 'Rheumatoid arthritis: the impact of mental health on disease: a narrative review'. *Rheumatology and Therapy,* 7(June), pp. 457-471. Available at: https://doi.org/10.1007/s40744-020-00217-4

Mackie, P., Crowfoot, G., Gyawali, P., Janssen, H., Holliday, E., Dunstan, D. & English, C. (2021a) 'Acute effects of frequent light-intensity standing-based exercises that interrupt 8 hours of prolonged sitting on postprandial glucose in stroke survivors: A dose-escalation trial'. *Journal of Physical Activity and Health,* 18(6), pp. 644-652. Available at: https://doi.org/10.1123/jpah.2020-0516

Mackie, P., Crowfoot, G., Janssen, H., Holliday, E., Dunstan, D. & English, C. (2021b) 'The Effects of Interrupting Prolonged Sitting With Frequent Bouts of Light-Intensity Standing Exercises on Blood Pressure in Stroke Survivors: A Dose Escalation Trial'. *Journal of Physical Activity and Health,* 18(6), pp. 988-997. Available at: https://doi.org/10.1123/jpah.2020-0763

Madenci, E. & Gursoy, S. (2003) 'Hand deformity in rheumatoid arthritis and its impact on the quality of life'. *The Pain Clinic,* 15(3), pp. 255-259. Available at: https://doi.org/10.1163/156856903767650772

Mancuso, C. A., Rincon, M., Sayles, W. & Paget, S. A. (2007) 'Comparison of energy expenditure from lifestyle physical activities between patients with rheumatoid arthritis and healthy controls'. *Arthritis Care & Research,* 57(4), pp. 672-678. Available at: https://doi.org/10.1002/art.22689

Manning, V. L., Hurley, M. V., Scott, D. L., Coker, B., Choy, E. & Bearne, L. M. (2014) 'Education, self-management, and upper extremity exercise training in people with rheumatoid arthritis: A randomized controlled trial'. *Arthritis care & research,* 66(2), pp. 217-227. Available at: https://doi.org/10.1002/acr.22102

Marcora, S. M., Lemmey, A. B. & Maddison, P. J. (2005) 'Can progressive resistance training reverse cachexia in patients with rheumatoid arthritis? Results of a pilot study'. *The Journal of Rheumatology,* 32(6), pp. 1031-1039. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15940763

Markenson, J. A. (1991) 'Worldwide trends in the socioeconomic impact and long-term prognosis of rheumatoid arthritis'. *Seminars in Arthritis and Rheumatism,* 21(2 (Suppl 1)), pp. 4-12. Available at: https://doi.org/10.1016/0049-0172(91)90046-3

Matthews, J. N., Altman, D. G., Campbell, M. J. & Royston, P. (1990) 'Analysis of serial measurements in medical research'. *British Medical Journal,* 300(679), pp. 230-235. Available at: https://doi.org/10.1136/bmj.300.6719.230

Mcalindon, T. E., Bannuru, R. R., Sullivan, M., Arden, N., Berenbaum, F., Bierma-Zeinstra, S., Hawker, G., Henrotin, Y., Hunter, D. & Kawaguchi, H. (2014) 'OARSI guidelines for the non-surgical management of knee osteoarthritis'. *Osteoarthritis and Cartilage,* 22(3), pp. 363-388. Available at: https://doi.org/10.1016/j.joca.2014.01.003

Mcguigan, M. R., Egan, A. D. & Foster, C. (2004) 'Salivary cortisol responses and perceived exertion during high intensity and low intensity bouts of resistance exercise'. *Journal of Sports Science & Medicine,* 3(1), pp. 8-15. Available at: https://pubmed.ncbi.nlm.nih.gov/24497815

Mcintosh, E. (1996) 'The cost of rheumatoid arthritis'. *Rheumatology,* 35(8), pp. 781-790. Available at: https://doi.org/10.1093/rheumatology/35.8.781

Mcmillan, S. S., King, M. & Tully, M. P. (2016) 'How to use the nominal group and Delphi techniques'. *International Journal of Clinical Pharmacy,* 38(3), pp. 655-662. Available at: https://doi.org/10.1007/s11096-016-0257-x

Medical Research Council. (2000) A framework for development and evaluation of RCT's for complex interventions to improve health. London: MRC

Medical Research Council. (2006) Developing and evaluating complex interventions: new guidance. London: MRC

Mohanty, B., Padhan, P. & Singh, P. (2018) 'Comparing the Effect of Proprioceptive Retraining Technique against Home Exercise Programme on Hand Functions in Patients with Rheumatoid Arthritis'. *Indian Journal of Physiotherapy & Occupational Therapy,* 12(3), pp. 48-53. Available at: https://doi.org/10.5958/0973-5674.2018.00055.2

Moher, D., Shamseer, L., Clarke, M., Ghersi, D., Liberati, A., Petticrew, M., Shekelle, P. & Stewart, L. A. (2015) 'Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement'. *Systematic Reviews,* 4(1), pp. 1-9. Available at: https://doi.org/10.1186/2046-4053-4-1

Moore, G. E. (2004) 'The role of exercise prescription in chronic disease'. *British Journal of Sports Medicine,* 38(1)**,** pp. 6. Available at: http://dx.doi.org/10.1136/bjsm.2003.010314

Moran, M., Bickford, J., Barradell, S. & Scholten, I. (2020) 'Embedding the international classification of functioning, disability and health in health professions curricula to enable interprofessional education and collaborative practice'. *Journal of Medical Education and Curricular Development,* 7(pp. 1-8. Available at: https://doi.org/10.1177/2382120520933855

Moritani, T. & Devries, H. A. (1979) 'Neural factors versus hypertrophy in the time course of muscle strength gain'. *American Journal of Physical Medicine & Rehabilitation,* 58(3)**,** pp. 115-130. Available at:

National Health Service. (2019) *Symptoms: Rheumatoid Arthritis* [Online]. Available: https://www.nhs.uk/conditions/rheumatoid-arthritis/symptoms/ [Accessed 20th March 2022].

National Health Service. (2021) *Agenda For Change – pay rates* [Online]. Available: www.nhscareers.nhs.uk/working-in-the-nhs/pay-and-benefits/agenda-for-change-pay-rates/ [Accessed 1st May 2023].

National Institute for Health and Care Excellence. (2012) *The guidelines manual - NICE process and methods (PMG6)* [Online]. Available: https://www.nice.org.uk/process/pmg6/chapter/reviewing-the-evidence [Accessed 1st February 2024].

National Institute for Health and Care Excellence. (2015) Addendum to Clinical Guidelines 79, Rheumatoid arthritis: the management of rheumatoid arthritis in adults. London:

National Institute for Health and Care Excellence 2017a. Sarilumab for moderate to severe rheumatoid arthritis - Technology appraisal guidance (TA485). London: NICE.

National Institute for Health and Care Excellence 2017b. Tofacitinib for moderate to severe rheumatoid arthritis - Technology appraisal guidance (TA480). London: NICE.

National Institute for Health and Care Excellence 2018. Rheumatoid arthritis in adults: management. NICE guideline [NG100]. London: NICE.

National Institute for Health and Care Excellence 2020. Upadacitinib for treating severe rheumatoid arthritis - Technology appraisal guidance (TA665). London: NICE.

National Institute for Health and Care Excellence 2021a. Adalimumab, etanercept, infliximab and abatacept for treating moderate rheumatoid arthritis after conventional DMARDs have failed - Technology appraisal guidance (TA715). London: NICE.

National Institute for Health and Care Excellence. (2021b) *Chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain* [Online].

Available: https://www.nice.org.uk/guidance/ng193/chapter/Recommendations [Accessed 1st February 2023].

National Institute for Health and Care Excellence. (2021c) *Shared decision making (NG197)* [Online]. Available: https://www.nice.org.uk/guidance/ng197 [Accessed 2nd November 2024].

National Institute for Health and Care Excellence. (2023) *What we do* [Online]. Available: https://www.nice.org.uk/about/what-we-do [Accessed 2nd December 2023].

Neuberger, G. B., Aaronson, L. S., Gajewski, B., Embretson, S. E., Cagle, P. E., Loudon, J. K. & Miller, P. A. (2007) 'Predictors of exercise and effects of exercise on symptoms, function, aerobic fitness, and disease outcomes of rheumatoid arthritis'. *Arthritis Care & Research,* 57(6)**,** pp. 943-952. Available at: https://doi.org/10.1002/art.22903

Neuberger, G. B., Press, A. N., Lindsley, H. B., Hinton, R., Cagle, P. E., Carlson, K., Scott, S., Dahl, J. & Kramer, B. (1997) 'Effects of exercise on fatigue, aerobic fitness, and disease activity measures in persons with rheumatoid arthritis'. *Research in Nursing & Health,* 20(3)**,** pp. 195-204. Available at: https://doi.org/10.1002/(SICI)1098-240X(199706)20:3%3C195::AID-NUR3%3E3.0.CO;2-D

Newton, R. U., Cormie, P. & Cardinale, M. (2011) 'Principles of athlete testing', *in:* CARDINALE, M., NEWTON, R. & NOSAKA, K. (eds.) *Strength and Conditioning - Biological Principles and Practical Applications.* West Sussex: Wiley-Blackwell, pp. 255-270

Nichols, V. P., Williamson, E., Toye, F. & Lamb, S. E. (2017) 'A longitudinal, qualitative study exploring sustained adherence to a hand exercise programme for rheumatoid arthritis evaluated in the SARAH trial'. *Disability and rehabilitation,* 39(18)**,** pp. 1856-1863. Available at: https://doi.org/10.1080/09638288.2016.1212111

Nicolson, P. J. A., Hinman, R. S., Wrigley, T. V., Stratford, P. W. & Bennell, K. L. (2018) 'Self-reported Home Exercise Adherence: A Validity and Reliability Study Using Concealed Accelerometers'. *Journal of Orthopaedic & Sports Physical Therapy,* 48(12)**,** pp. 943-950. Available at: https://www.jospt.org/doi/10.2519/jospt.2018.8275

Nilsen, T. S., Scott, J. M., Michalski, M., Capaci, C., Thomas, S., Sasso, J., Eves, N. D. & Jones, L. W. (2018) 'Novel Methods for Reporting of Exercise Dose and Adherence: An Exploratory Analysis'. *Medicine and Science in Sports and Exercise,* 50(6)**,** pp. 1134-1141. Available at: https://doi.org/10.1249%2FMSS.0000000000001545

Nilsson, J., Andersson, M. L. E., Hafström, I., Svensson, B., Forslind, K., Ajeganova, S., Leu Agelii, M. & Gjertsson, I. (2021) 'Influence of Age and Sex on Disease Course and Treatment in Rheumatoid Arthritis'. *Open Access Rheumatology: Research and Reviews,* 13(null)**,** pp. 123-138. Available at: https://doi.org/10.2147/OARRR.S306378

Noone, J., Mucinski, J. M., Delany, J. P., Sparks, L. M. & Goodpaster, B. H. (2024) 'Understanding the variation in exercise responses to guide personalized physical activity prescriptions'. *Cell Metabolism,* pp. Available at: https://doi.org/10.1016/j.cmet.2023.12.025

North, B., Kocher, H. M. & Sasieni, P. (2019) 'A new pragmatic design for dose escalation in phase 1 clinical trials using an adaptive continual reassessment method'. *BMC Cancer,* 19(1)**,** pp. 1-10. Available at: https://doi.org/10.1186/s12885-019-5801-3

O'brien, A., Jones, P., Mullis, R., Mulherin, D. & Dziedzic, K. (2006) 'Conservative hand therapy treatments in rheumatoid arthritis--a randomized controlled trial'. *Rheumatology* 45(5)**,** pp. 577-583. Available at: https://doi.org/10.1093/rheumatology/kei215

Ocebm Levels of Evidence Working Group. (2016) *The Oxford Levels of Evidence 2* [Online]. Oxford Centre for Evidence-Based Medicine. Available: https://www.cebm.net/index.aspx?o=5653 [Accessed 21st February 2018].

Office for National Statistics. (2024) *Population estimates for the UK, England, Wales, Scotland, and Northern Ireland: mid-2022* [Online]. Available: https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/bulletins/annualmidyearpopulationestimates/mid2022 [Accessed 30th March 2024].

Osthoff, A.-K. R., Juhl, C. B., Knittle, K., Dagfinrud, H., Hurkmans, E., Braun, J., Schoones, J., Vlieland, T. P. V. & Niedermann, K. (2018a) 'Effects of exercise and physical activity promotion: meta-analysis informing the 2018 EULAR recommendations for physical activity in people with rheumatoid arthritis, spondyloarthritis and hip/knee osteoarthritis'. *RMD open,* 4(2)**,** pp. e000713. Available at:

Osthoff, A.-K. R., Niedermann, K., Braun, J., Adams, J., Brodin, N., Dagfinrud, H., Duruoz, T., Esbensen, B. A., Günther, K.-P., Hurkmans, E., Juhl, C. B., Kennedy, N., Kiltz, U., Knittle, K., Nurmohamed, M., Pais, S., Severijns, G., Swinnen, T. W., Pitsillidou, I. A., Warburton, L., Yankov, Z. & Vliet Vlieland, T. P. M. (2018b) '2018 EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis'. *Annals of the Rheumatic Diseases,* 77(9)**,** pp. 1251-1260. Available at: https://doi.org/10.1136/annrheumdis-2018-213585

Oxford English Dictionaries. (2019) *Definition of dose in English* [Online]. Available: https://www.lexico.com/en/definition/dose [Accessed 14th August 2019].

Papathanasiou, T., Strathe, A., Overgaard, R. V., Lund, T. M. & Hooker, A. C. (2019) 'Optimizing dose-finding studies for drug combinations based on exposure-response models'. *The AAPS Journal,* 21(Sept)**,** pp. 1-11. Available at: https://doi.org/10.1208/s12248-019-0365-3

Pavlova, A. V., Shim, J. S. C., Moss, R., Maclean, C., Brandie, D., Mitchell, L., Greig, L., Parkinson, E., Alexander, L., Brown, V. T., Morrissey, D., Cooper, K. & Swinton, P. A. (2023) 'Effect of resistance exercise dose components for tendinopathy management: a systematic review with meta-analysis'. *British Journal of Sports Medicine,* 57(20)**,** pp. 1327-1334. Available at: https://doi.org/10.1136/bjsports-2022-105754

Pawlikowska, T., Leach, J., Lavallee, P., Charlton, R. & Piercy, J. (2007) 'Consultation models', *in:* CHARLTON, R. (ed) *Learning to consult.* Oxford: Radcliffe Publishing Ltd, pp. 178-215

Pedersen, B. K. & Saltin, B. (2015) 'Exercise as medicine–evidence for prescribing exercise as therapy in 26 different chronic diseases'. *Scandinavian journal of medicine & science in sports,* 25(S3)**,** pp. 1-72. Available at: https://doi.org/10.1111/sms.12581

Peiris, C., Shields, N., Kingsley, M., Yeung, J., Hau, R. & Taylor, N. (2017) 'Maximum Tolerated Dose of Walking for Community-Dwelling People Recovering From Hip Fracture: A Dose-Response Trial'. *Archives of Physical Medicine and Rehabilitation,* 98(pp. 2533-2539. Available at: http://dx.doi.org/10.1016/j.apmr.2017.03.027

Pelland, L., Brosseau, L., Casimiro, L., Welch, V., Tugwell, P. & Wells, G. A. (2002) 'Electrical stimulation for the treatment of rheumatoid arthritis'. *Cochrane Database of Systematic Reviews,* 7(Sept)**,** pp. 1-17. Available at: https://doi.org/10.1002/14651858.CD003687

Pendleton, D. (1984) *The consultation: an approach to learning and teaching.* Oxford: Oxford University Press

Peterson, M. C., Holbrook, J. H., Von Hales, D. E., Smith, N. L. & Staker, L. V. (1992) 'Contributions of the history, physical examination, and laboratory investigation in making medical diagnoses'. *Western Journal of Medicine,* 156(2)**,** pp. 163. Available at: https://pubmed.ncbi.nlm.nih.gov/1536065

Petty, N. J. & Moore, A. P. (2011) *Principles of Neuromusculoskeletal Treatment and Management: A Handbook for Therapists.* Edinburgh: Elsevier Health Sciences

Piantadosi, S. (2017) *Clinical trials: a methodologic perspective.* John Wiley & Sons

Pinheiro, J. C. & Duffull, S. B. (2009) 'Exposure response – getting the dose right'. *Pharmaceutical Statistics,* 8(3)**,** pp. 173-175. Available at: https://doi.org/10.1002/pst.401

Piva, S. R., Khoja, S. S., Toledo, F. G. S., Wasko, M. C., Fitzgerald, G. K., Goodpaster, B. H., Smith, C. N. & Delitto, A. (2018) 'Neuromuscular Electrical Stimulation Compared to Volitional Exercise in Improving Muscle Function in Rheumatoid Arthritis: A Randomized Pilot Study'. *Arthritis care & research,* 71(3)**,** pp. 352-361. Available at: https://doi.org/10.1002/acr.23602

Potter, M., Gordon, S. & Hamer, P. (2004) 'The nominal group technique: a useful consensus methodology in physiotherapy research'. *New Zealand Journal of Physiotherapy,* 32(3)**,** pp. 126-130. Available at: https://www.researchgate.net/publication/254724490

Pruessner, J. C., Kirschbaum, C., Meinlschmid, G. & Hellhammer, D. H. (2003) 'Two formulas for computation of the area under the curve represent measures of total hormone concentration versus time-dependent change'. *Psychoneuroendocrinology,* 28(7)**,** pp. 916-931. Available at: https://doi.org/10.1016/S0306-4530(02)00108-7

Putrik, P., Ramiro, S., Kvien, T. K., Sokka, T., Pavlova, M., Uhlig, T., Boonen, A. & Europe, W. G. E. I. a. T. T. O. R. a. I. (2014) 'Inequities in access to biologic and synthetic DMARDs across 46 European countries'. *Annals of the Rheumatic Diseases,* 73(1)**,** pp. 198-206. Available at: https://doi.org/10.1136/annrheumdis-2012-202603

Rahnama, N. & Mazloum, V. (2012) 'Effects of strengthening and aerobic exercises on pain severity and function in patients with knee rheumatoid arthritis'. *International Journal of Preventive Medicine,* 3(7)**,** pp. 493-498. Available at: https://pubmed.ncbi.nlm.nih.gov/22891151

Rall, L. C., Meydani, S. N., Kehayias, J. J., Dawson-Hughes, B. & Roubenoff, R. (1996) 'The effect of progressive resistance training in rheumatoid arthritis. Increased strength without changes in energy balance or body composition'. *Arthritis & Rheumatism,* 39(3)**,** pp. 415-426. Available at: https://doi.org/10.1002/art.1780390309

Ramírez-Vélez, R., Lobelo, F. & Izquierdo, M. (2017) 'Exercise for disease prevention and management: a precision medicine approach'. *Journal of the American Medical Directors Association,* 18(7)**,** pp. 633-634. Available at: xhttps://doi.org/10.1016/j.jamda.2017.04.012

Rapolienė, J. & Kriščiūnas, A. (2006) 'The effectiveness of occupational therapy in restoring the functional state of hands in rheumatoid arthritis patients'. *Medicina,* 42(10)**,** pp. 823-828. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17090982

Rassafiani, M., Ziviani, J., Rodger, S. & Dalgleish, L. (2009) 'Identification of occupational therapy clinical expertise: Decision-making characteristics'. *Australian Occupational Therapy Journal,* 56(3)**,** pp. 156-166. Available at: https://doi.org/10.1111/j.1440-1630.2007.00718.x

Ratamess, N. A., Alvar, B. A., Evetoch, T., Housh, T. J., Kiibler, B., Kraemer, W. J. & Triplett, N. T. (2009) 'Progression models in resistance training for healthy adults'. *Medicine & Science in Sports & Exercise,* 41(3)**,** pp. 687-708. Available at: https://doi.org/10.1249/mss.0b013e3181915670

Robertson, R. J., Goss, F. L., Rutkowski, J., Lenz, B., Dixon, C., Timmer, J., Frazee, K., Dube, J. & Andreacci, J. (2003) 'Concurrent validation of the OMNI perceived exertion scale for resistance exercise'. *Medicine & Science in Sports & Exercise,* 35(2)**,** pp. 333-341. Available at: https://doi.org/10.1249/01.mss.0000048831.15016.2a

Rodrigues, R., Ferraz, R. B., Kurimori, C. O., Guedes, L. K., Lima, F. R., De Sa-Pinto, A. L., Gualano, B. & Roschel, H. (2020) 'Low-Load Resistance Training With Blood-Flow Restriction in Relation to Muscle Function, Mass, and Functionality in Women With Rheumatoid Arthritis'. *Arthritis care & research,* 72(6)**,** pp. 787-797. Available at: https://dx.doi.org/10.1002/acr.23911

Rodriguez Sanchez-Laulhe, P., Luque-Romero, L. G., Barrero-Garcia, F. J., Biscarri-Carbonero, A., Blanquero, J., Suero-Pineda, A. & Heredia-Rizo, A. M. (2022) 'An Exercise and Educational and Self-management Program Delivered With a Smartphone App (CareHand) in Adults With Rheumatoid Arthritis of the Hands: Randomized Controlled Trial'. *JMIR mHealth and uHealth,* 10(4)**,** pp. e35462. Available at: https://dx.doi.org/10.2196/35462

Rønningen, A. & Kjeken, I. (2008) 'Effect of an intensive hand exercise programme in patients with rheumatoid arthritis'. *Scandinavian journal of occupational therapy,* 15(3)**,** pp. 173-183. Available at: https://doi.org/10.1080/11038120802031129

Ross, R., Goodpaster, B. H., Koch, L. G., Sarzynski, M. A., Kohrt, W. M., Johannsen, N. M., Skinner, J. S., Castro, A., Irving, B. A., Noland, R. C., Sparks, L. M., Spielmann, G., Day, A. G., Pitsch, W., Hopkins, W. G. & Bouchard, C. (2019) 'Precision exercise medicine: understanding exercise response variability'. *British Journal of Sports Medicine,* 53(18)**,** pp. 1141-1153. Available at: https://doi.org/10.1136/bjsports-2018-100328

Roubenoff, R. (2009) 'Rheumatoid cachexia: a complication of rheumatoid arthritis moves into the 21st century'. *Arthritis Research & Therapy,* 11(2)**,** pp. 108-108. Available at: https://doi.org/10.1186/ar2658

Roubenoff, R. & Rall, L. C. (1993) 'Humoral mediation of changing body composition during aging and chronic inflammation'. *Nutrition Reviews,* 51(1)**,** pp. 1-11. Available at: https://doi.org/10.1111/j.1753-4887.1993.tb03045.x

Roubenoff, R., Roubenoff, R., Ward, L., Holland, S. & Hellmann, D. (1992) 'Rheumatoid cachexia: depletion of lean body mass in rheumatoid arthritis. Possible association with tumor necrosis factor'. *The Journal of Rheumatology,* 19(10)**,** pp. 1505-1510. Available at: https://pubmed.ncbi.nlm.nih.gov/1464859/

Roubenoff, R., Roubenoff, R. A., Cannon, J. G., Kehayias, J. J., Zhuang, H., Dawson-Hughes, B., Dinarello, C. A. & Rosenberg, I. H. (1994) 'Rheumatoid cachexia: cytokine-driven hypermetabolism accompanying reduced body cell mass in chronic inflammation'. *The Journal of Clinical Investigation,* 93(6)**,** pp. 2379-2386. Available at: https://doi.org/10.1172/JCI117244

Rowbotham, S., Conte, K. & Hawe, P. (2019) 'Variation in the operationalisation of dose in implementation of health promotion interventions: insights and recommendations from a

scoping review'. *Implementation Science,* 14(1), pp. 56. Available at: https://doi.org/10.1186/s13012-019-0899-x

Royal College of Occupational Therapists. (2024) *What is occupational therapy?* [Online]. Available: https://www.rcot.co.uk/about-occupational-therapy/what-is-occupational-therapy [Accessed 2nd March 2024].

Royal College of Podiatry. (2024) *Rheumatoid Arthritis* [Online]. Available: https://rcpod.org.uk/common-foot-problems/rheumatoid-arthritis [Accessed 1st February 2024].

Royal Pharmaceutical Society 2016. A Competency Framework for all Prescribers. Royal Pharmaceutical Society.

Royal Pharmaceutical Society 2021. A Competency Framework for all Prescribers. Royal Pharmaceutical Society.

Sackett, D. L., Rosenberg, W. M. C., Gray, J. a. M., Haynes, R. B. & Richardson, W. S. (1996) 'Evidence based medicine: what it is and what it isn't'. *BMJ,* 312(7023), pp. 71-72. Available at: https://doi.org/10.1136/bmj.312.7023.71

Santo, R. C., Fernandes, K. Z., Lora, P. S., Filippin, L. I. & Xavier, R. M. (2018) 'Prevalence of rheumatoid cachexia in rheumatoid arthritis: a systematic review and meta-analysis'. *Journal of Cachexia, Sarcopenia and Muscle,* 9(5), pp. 816-825. Available at: https://doi.org/10.1002/jcsm.12320

Sayah, A. & English, J. C. (2005) 'Rheumatoid arthritis: A review of the cutaneous manifestations'. *Journal of the American Academy of Dermatology,* 53(2), pp. 191-209. Available at: https://doi.org/10.1016/j.jaad.2004.07.023

Scott, B. R., Duthie, G. M., Thornton, H. R. & Dascombe, B. J. (2016) 'Training Monitoring for Resistance Exercise: Theory and Applications'. *Sports Medicine,* 46(5), pp. 687-698. Available at: https://doi.org/10.1007/s40279-015-0454-0

Scott, D. L. & Houssien, D. A. (1996) 'Joint Assessment in Rheumatoid Arthritis'. *Rheumatology,* 35(suppl_2), pp. 14-18. Available at: https://doi.org/10.1093/rheumatology/35.suppl_2.14

Scott, D. L., Wolfe, F. & Huizinga, T. W. J. (2010) 'Rheumatoid arthritis'. *The Lancet,* 376(9746), pp. 1094-1108. Available at: https://doi.org/10.1016/S0140-6736(10)60826-4

Scurlock-Evans, L., Upton, P. & Upton, D. (2014) 'Evidence-Based Practice in physiotherapy: a systematic review of barriers, enablers and interventions'. *Physiotherapy,* 100(3), pp. 208-219. Available at: https://doi.org/10.1016/j.physio.2014.03.001

Seneca, T., Hauge, E. M. & Maribo, T. (2015) 'Comparable effect of partly supervised and self-administered exercise programme in early rheumatoid arthritis—a randomised, controlled trial'. *Danish Medical Journal,* 62(8), pp. A5127. Available at: PMID: 26239594

Shams, S., Martinez, J. M., Dawson, J. R., Flores, J., Gabriel, M., Garcia, G., Guevara, A., Murray, K., Pacifici, N. & Vargas, M. V. (2021) 'The therapeutic landscape of rheumatoid arthritis: current state and future directions'. *Frontiers in Pharmacology,* 12(Article 680043)**,** pp. 1-27. Available at: https://doi.org/10.3389/fphar.2021.680043

Shanteau, J. (2023) *CWS Calculator V1 R4* [Online]. Available: https://www.academia.edu/31669790/CWS_Calculator_V1_R4 [Accessed 1st May 2023].

Shinde, S. B. & Varadharajulu, G. (2017) 'Effect of Therapeutic Exercise Programme in Adults with Early Rheumatoid Arthritis'. *Indian Journal of Physiotherapy & Occupational Therapy,* 11(3)**,** pp. 76-80. Available at: http://dx.doi.org/10.5958/0973-5674.2017.00077.6

Silverman, J., Kurtz, S. & Draper, J. (2016) *Skills for communicating with patients. 3rd ed.* CRC Press

Singh, J. A., Christensen, R., Wells, G. A., Suarez-Almazor, M. E., Buchbinder, R., Lopez-Olivo, M. A., Ghogomu, E. T. & Tugwell, P. (2009) 'Biologics for rheumatoid arthritis: an overview of Cochrane reviews'. *Cochrane Database of Systematic Reviews,* 4(Art. No.: CD007848.)**,** pp. 1-72. Available at: https://doi.org/10.1002/14651858.CD007848.pub2

Skivington, K., Matthews, L., Simpson, S. A., Craig, P., Baird, J., Blazeby, J. M., Boyd, K. A., Craig, N., French, D. P., Mcintosh, E., Petticrew, M., Rycroft-Malone, J., White, M. & Moore, L. (2021) 'A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance'. *BMJ,* 374(n2061)**,** pp. 1-11. Available at: https://doi.org/10.1136/bmj.n2061

Slade, S. C., Dionne, C. E., Underwood, M. & Buchbinder, R. (2016a) 'Consensus on Exercise Reporting Template (CERT): explanation and elaboration statement'. *British Journal of Sports Medicine,* 50(23)**,** pp. 1428-1437. Available at: https://doi.org/10.1136/bjsports-2016-096651

Slade, S. C., Dionne, C. E., Underwood, M., Buchbinder, R., Beck, B., Bennell, K., Brosseau, L., Costa, L., Cramp, F. & Cup, E. (2016b) 'Consensus on exercise reporting template (CERT): modified Delphi study'. *Physical Therapy,* 96(10)**,** pp. 1514-1524. Available at: https://doi.org/10.2522/ptj.20150668

Slade, S. C. & Keating, J. L. (2012) 'Exercise prescription: a case for standardised reporting'. *British Journal of Sports Medicine,* 46(16)**,** pp. 1110-1113. Available at: https://doi.org/10.1136/bjsports-2011-090290

Smolen, J. S., Aletaha, D. & Mcinnes, I. B. (2016) 'Rheumatoid arthritis'. *Lancet,* 388(10055)**,** pp. 2023-2038. Available at: https://doi.org/10.1016/s0140-6736(16)30173-8

Sokka, T., Kautiainen, H., Möttönen, T. & Hannonen, P. (1999) 'Work disability in rheumatoid arthritis 10 years after the diagnosis'. *The Journal of Rheumatology,* 26(8)**,** pp. 1681-1685. Available at: PMID: 10451062

Somers, T. J., Blumenthal, J. A., Dorfman, C. S., Huffman, K. M., Edmond, S. N., Miller, S. N., Wren, A. A., Caldwell, D. & Keefe, F. J. (2022) 'Effects of a Weight and Pain Management Program in Patients With Rheumatoid Arthritis With Obesity: A Randomized Controlled Pilot Investigation'. *Journal of clinical rheumatology : practical reports on rheumatic & musculoskeletal diseases,* 28(1), pp. 7-13. Available at: https://dx.doi.org/10.1097/RHU.0000000000001793

Spitaels, D., Vankrunkelsven, P., Desfosses, J., Luyten, F., Verschueren, S., Van Assche, D., Aertgeerts, B. & Hermens, R. (2017) 'Barriers for guideline adherence in knee osteoarthritis care: A qualitative study from the patients' perspective'. *Journal of Evaluation in Clinical Practice,* 23(1), pp. 165-172. Available at: https://doi.org/10.1111/jep.12660

Srikesavan, C., Williamson, E., Sugavanam, P., Adams, J., Eldridge, L. & Lamb, S. E. (2018) 'Impact evaluation of an online training on the Strengthening And Stretching for Rheumatoid Arthritis of the Hand (SARAH) programme recommended in the NICE guidelines for rheumatoid arthritis'. *Rheumatology,* 57(suppl_3), pp. April 2018, key075.214. Available at: https://doi.org/10.1093/rheumatology/key075.214

Sterne, J. a. C., Hernán, M. A., Reeves, B. C., Savović, J., Berkman, N. D., Viswanathan, M., Henry, D., Altman, D. G., Ansari, M. T., Boutron, I., Carpenter, J. R., Chan, A., Churchill, R., Deeks, J. J., Hróbjartsson, A., Kirkham, J., Jüni, P., Loke, Y. K., Pigott, T. D., Ramsay, C. R., Regidor, D., Rothstein, H. R., Sandhu, L., Santaguida, P. L., Schünemann, H. J., Shea, B., Shrier, I., Tugwell, P., Turner, L., Valentine, J. C., Waddington, H., Waters, E., Wells, G. A., Whiting, P. F. & Higgins, J. P. T. (2016) 'ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions'. *BMJ,* 355(i4919), pp. Available at: https://doi.org/10.1136/bmj.i4919

Stewart, M., Brown, J. B., Weston, W. W., Freeman, T., Ryan, B. L., Mcwilliam, C. L. & Mcwhinney, I. R. (2024) *Patient-centered medicine: transforming the clinical method. 4th ed.* CRC Press

Stott, N. & Davis, R. (1979) 'The exceptional potential in each primary care consultation'. *The Journal of the Royal College of General Practitioners,* 29(201), pp. 201-205. Available at: http://www.ncbi.nlm.nih.gov/pubmed/448665

Strasser, B., Leeb, G., Strehblow, C., Schobersberger, W., Haber, P. & Cauza, E. (2011) 'The effects of strength and endurance training in patients with rheumatoid arthritis'. *Clinical rheumatology,* 30(5), pp. 623-632. Available at: https://doi.org/10.1007/s10067-010-1584-2

Stucki, G., Cieza, A., Ewert, T., Kostanjsek, N., Chatterji, S. & Üstün, T. B. (2002) 'Application of the International Classification of Functioning, Disability and Health (ICF) in clinical practice'. *Disability and Rehabilitation,* 24(5), pp. 281-282. Available at: https://doi.org/10.1080/09638280110105222

Suarez-Almazor, M. E., Belseck, E., Shea, B., Wells, G. & Tugwell, P. (2000) 'Methotrexate for rheumatoid arthritis'. *Cochrane Database of Systematic Reviews,* 2(CD000957)**,** pp. -. Available at: https://doi.org/10.1002/14651858.cd000957

Summers, G. D., Deighton, C. M., Rennie, M. J. & Booth, A. H. (2008) 'Rheumatoid cachexia: a clinical perspective'. *Rheumatology,* 47(8)**,** pp. 1124-1131. Available at: https://doi.org/10.1093/rheumatology/ken146

Swan, J., Robertson, M. & Evans, S. (2009) Managing Clinical Research in the UK - Evidence on the challenges of conducting clinical research projects in the UK. Coventry: WARWICK BUSINESS SCHOOL

Swisher, A. K. (2010) 'Yes, "Exercise is Medicine"….but It Is So Much More!'. *Cardiopulmonary Physical Therapy Journal,* 21(4)**,** pp. 4. Available at: https://pubmed.ncbi.nlm.nih.gov/21206672

Symmons, D., Turner G Fau - Webb, R., Webb R Fau - Asten, P., Asten P Fau - Barrett, E., Barrett E Fau - Lunt, M., Lunt M Fau - Scott, D., Scott D Fau - Silman, A. & Silman, A. (2002) 'The prevalence of rheumatoid arthritis in the United Kingdom: new estimates for a new century'. *Rheumatology,* 41(7)**,** pp. 793-800. Available at: http://dx.doi.org/10.1093/rheumatology/41.7.793

Symmons, D. P. M., Barrett, E. M., Bankhead, C. R., Scott, D. G. L. & Silman, A. J. (1994) 'The incidence of rheumatoid arthritis in the United Kingdom: results from the Norfolk arthritis register'. *Rheumatology,* 33(8)**,** pp. 735-739. Available at: https://doi.org/10.1093/rheumatology/33.8.735

Taylor, N. F., Dodd, K. J., Shields, N. & Bruder, A. (2007) 'Therapeutic exercise in physiotherapy practice is beneficial: a summary of systematic reviews 2002–2005'. *Australian Journal of Physiotherapy,* 53(1)**,** pp. 7-16. Available at: https://doi.org/10.1016/S0004-9514(07)70057-0

Taylor, N. F., Shields, N., Thompson, A. L., O'halloran, P. D., Harding, K. E., Dennett, A. M., Hau, R. & Peiris, C. L. (2023) 'A walking programme for adults living in the community after hip fracture: A feasibility randomized controlled trial'. *Clinical Rehabilitation,* 37(1)**,** pp. 47-59. Available at: https://doi.org/10.1177/02692155221128721

Teuwen, M. M. H., Van Weely, S. F. E., Vliet Vlieland, T. P. M., Van Wissen, M. a. T., Peter, W. F., Den Broeder, A. A., Van Schaardenburg, D., Van Den Hout, W. B., Van Den Ende, C. H. M. & Gademan, M. G. J. (2024) 'Effectiveness of longstanding exercise therapy compared with usual care for people with rheumatoid arthritis and severe functional limitations: a randomised controlled trial'. *Annals of the rheumatic diseases,* 83(4)**,** pp. 437-445. Available at: https://dx.doi.org/10.1136/ard-2023-224912

The Chartered Society of Physiotherapy. (2018) *What is physiotherapy?* [Online]. Chartered Society of Physiotherapy. Available: https://www.csp.org.uk/careers-jobs/what-physiotherapy [Accessed 14/11/2018 2018].

Thomas, A. & Law, M. (2013) 'Research Utilization and Evidence-Based Practice in Occupational Therapy: A Scoping Study'. *The American Journal of Occupational Therapy,* 67(4)**,** pp. e55-e65. Available at: https://doi.org/10.5014/ajot.2013.006395

Thomas, K. S., Muir, K. R., Doherty, M., Jones, A. C., O'reilly, S. C. & Bassey, E. J. (2002) 'Home based exercise programme for knee pain and knee osteoarthritis: randomised controlled trial'. *British Medical Journal,* 325(7367)**,** pp. 752. Available at: https://doi.org/10.1136/bmj.325.7367.752

Thomas, R. P., Willems, B., Shanteau, J., Raacke, J. & Friel, B. Measureing the Performance of Experts: An Application to Air Traffic Control. Proceedings of the Human Factors and Ergonomics Society Annual Meeting, 2001. SAGE Publications Sage CA: Los Angeles, CA, 286-290.

Tonga, E., Düger, T. & Karatas, M. (2016) 'Effectiveness of client-centered occupational therapy in patients with rheumatoid arthritis: Exploratory randomized controlled trial'. *Archives of rheumatology,* 31(1)**,** pp. 6. Available at: https://doi.org/10.5606/ArchRheumatol.2016.5478

Tricoli, V. (2011) *Skeletal Muscle Physiology. 1st.* Blackwell Publishing

Trowbridge, R., Rencic, J. & Durning, S. (2015) 'Introduction/Preface', *in:* TROWBRIDGE, R., RENCIC, J. & DURNING, S. (eds.) *Teaching clinical reasoning.* Philadelphia: American College of Physicians, pp. xvii-xxii

Unsworth, C. A. (2001) 'The Clinical Reasoning of Novice and Expert Occupational Therapists'. *Scandinavian Journal of Occupational Therapy,* 8(4)**,** pp. 163-173. Available at: https://doi.org/10.1080/110381201317166522

Van Den Berg, M., Ronday, H., Peeters, A., Le Cessie, S., Van Der Giesen, F., Breedveld, F. & Vliet Vlieland, T. (2006) 'Using internet technology to deliver a home-based physical activity intervention for patients with rheumatoid arthritis: A randomized controlled trial'. *Arthritis Care & Research: Official Journal of the American College of Rheumatology,* 55(6)**,** pp. 935-945. Available at: https://doi.org/10.1002/art.22339

Van Den Ende, C., Hazes, J., Le Cessie, S., Mulder, W., Belfor, D., Breedveld, F. & Dijkmans, B. (1996) 'Comparison of high and low intensity training in well controlled rheumatoid arthritis. Results of a randomised clinical trial'. *Annals of the Rheumatic Diseases,* 55(11)**,** pp. 798-805. Available at: https://doi.org/10.1136/ard.55.11.798

Van Den Ende, C. H. M., Breedveld, F. C., Le Cessie, S., Dijkmans, B. a. C., De Mug, A. W. & Hazes, J. M. W. (2000) 'Effect of intensive exercise on patients with active rheumatoid arthritis: a

randomised clinical trial'. *Annals of the Rheumatic Diseases,* 59(8)**,** pp. 615-621. Available at: https://doi.org/10.1136/ard.59.8.615

Van Rensburg, J. C., Fletcher, L., Viljoen, M., Coertzen, C., Grant, R., Ramagole, M., Collins, R. & Ker, J. (2010) 'Efficacy of an exercise program on the functional capacity and disease activity in females with rheumatoid arthritis'. *Journal of Science and Medicine in Sport,* 1(pp. e60. Available at: http://dx.doi.org/10.1016/j.jsams.2010.10.589

Van Rensburg, J. C., Ker, J. A., Grant, C. C. & Fletcher, L. (2012) 'Effect of exercise on cardiac autonomic function in females with rheumatoid arthritis'. *Clinical rheumatology,* 31(8)**,** pp. 1155-1162. Available at: https://doi.org/10.1007/s10067-012-1985-5

Van Riel, P. (2014) 'The development of the disease activity score (DAS) and the disease activity score using 28 joint counts (DAS28)'. *Clin Exp Rheumatol,* 32(5 Suppl 85)**,** pp. 65-74. Available at:

Veitiene, D. & Tamulaitiene, M. (2004) 'The efficiency of home and outpatient exercise program in patients with rheumatoid arthritis'. *Medicina (Kaunas, Lithuania),* 40(5)**,** pp. 434-438. Available at: PMID: 15170412

Versus Arthritis. (2023) *Rheumatoid Arthritis (RA)* [Online]. Available: https://versusarthritis.org/about-arthritis/conditions/rheumatoid-arthritis/ [Accessed 26th February 2024].

Vliet Vlieland, T. P., Van Der Wijk, T. P., Jolie, I. M., Zwinderman, A. H. & Hazes, J. M. (1996) 'Determinants of hand function in patients with rheumatoid arthritis'. *The Journal of Rheumatology,* 23(5)**,** pp. 835-840. Available at: PMID: 8724294

Voils, C. I., Chang, Y., Crandell, J., Leeman, J., Sandelowski, M. & Maciejewski, M. L. (2012) 'Informing the dosing of interventions in randomized trials'. *Contemporary clinical trials,* 33(6)**,** pp. 1225-1230. Available at: https://doi.org/10.1016/j.cct.2012.07.011

Waghorn, J., Bates, I., Davies, J. G., Jubraj, B., Rakow, T. & Stevenson, J. M. (2021) 'Clinical Judgement Analysis: An innovative approach to explore the individual decision-making processes of pharmacists'. *Research in Social and Administrative Pharmacy,* 17(12)**,** pp. 2097-2107. Available at: https://doi.org/10.1016/j.sapharm.2021.05.006

Wallis, J., Webster, K., Levinger, P., Singh, P., Fong, C. & Taylor, N. (2015) 'The maximum tolerated dose of walking for people with severe osteoarthritis of the knee: a phase I trial'. *Osteoarthritis and Cartilage,* 23(8)**,** pp. 1285-1293. Available at: https://doi.org/10.1016/j.joca.2015.04.001

Wallis, J., Webster, K. E., Levinger, P., Singh, P., Fong, C. & Taylor, N. F. (2017) 'A walking program for people with severe knee osteoarthritis did not reduce pain but may have benefits for cardiovascular health: a phase II randomised controlled trial'. *Osteoarthritis and Cartilage,* 25(12)**,** pp. 1969-1979. Available at: http://dx.doi.org/10.1016/j.joca.2016.12.017

Walston, Z., Whelehan, D. F. & O'shea, N. (2022) 'Clinical decision making in physical therapy – Exploring the 'heuristic' in clinical practice'. *Musculoskeletal Science and Practice,* 62(102674), pp. 1-4. Available at: https://doi.org/10.1016/j.msksp.2022.102674

Wasfy, M. M. & Baggish, A. L. (2016) 'Exercise Dose in Clinical Practice'. *Circulation,* 133(23), pp. 2297-2313. Available at: https://doi.org/10.1161/CIRCULATIONAHA.116.018093

Weiss, D. J. & Shanteau, J. (2003) 'Empirical Assessment of Expertise'. *Human Factors,* 45(1), pp. 104-116. Available at: https://doi.org/10.1518/hfes.45.1.104.27233

Weiss, D. J. & Shanteau, J. (2014) 'Who's the best? A relativistic view of expertise'. *Applied Cognitive Psychology,* 28(4), pp. 447-457. Available at: https://doi.org/10.1002/acp.3015

Weiss, D. J., Shanteau, J. & Harries, P. (2006) 'People who judge people'. *Journal of Behavioral Decision Making,* 19(5), pp. 441-454. Available at: https://doi.org/10.1002/bdm.529

Wen, Z. & Chai, Y. (2021) 'Effectiveness of resistance exercises in the treatment of rheumatoid arthritis: A meta-analysis'. *Medicine* 100(13), pp. 1-8. Available at: https://doi.org/10.1097/md.0000000000025019

Wessel, J. (2004) 'The effectiveness of hand exercises for persons with rheumatoid arthritis: a systematic review'. *Journal of Hand Therapy,* 17(2), pp. 174-180. Available at: https://doi.org/10.1197/j.jht.2004.02.006

Wherton, J. & Greenhalgh, T. (2020) *Evaluation of the attend anywhere/near me video consulting service in Scotland, 2019-20.* Edinburgh: Scottish Government

Whitehead, A. L., Sully, B. G. & Campbell, M. J. (2014) 'Pilot and feasibility studies: is there a difference from each other and from a randomised controlled trial?'. *Contemporary Clinical Trials,* 38(1), pp. 130-133. Available at: https://doi.org/10.1016/j.cct.2014.04.001

Wigton, R. S. (1996) 'Social judgement theory and medical judgement'. *Thinking & Reasoning,* 2(2-3), pp. 175-190. Available at: https://doi.org/10.1080/135467896394492

Wigton, R. S., Darr, C. A., Corbett, K. K., Nickol, D. R. & Gonzales, R. (2008) 'How do community practitioners decide whether to prescribe antibiotics for acute respiratory tract infections?'. *Journal of general internal medicine,* 23(10), pp. 1615-1620. Available at: https://doi.org/10.1007%2Fs11606-008-0707-9

Williams, C. A., Haslam, R. A. & Weiss, D. J. (2008) 'The Cochran–Weiss–Shanteau performance index as an indicator of upper limb risk assessment expertise'. *Ergonomics,* 51(8), pp. 1219-1237. Available at: https://doi.org/10.1080/00140130802087094

Williams, M. A., Haskell, W. L., Ades, P. A., Amsterdam, E. A., Bittner, V., Franklin, B. A., Gulanick, M., Laing, S. T. & Stewart, K. J. (2007) 'Resistance exercise in individuals with and without cardiovascular disease: 2007 update: a scientific statement from the American Heart

Association Council on Clinical Cardiology and Council on Nutrition, Physical Activity, and Metabolism'. *Circulation,* 116(5)**,** pp. 572-584. Available at: https://doi.org/10.1161/CIRCULATIONAHA.107.185214

Williams, M. A., Heine, P. J., Bruce, J., Brosseau, L. & Lamb, S. (2012) 'Exercise therapy for the rheumatoid hand'. *Cochrane Database of Systematic Reviews,* 4)**,** pp. Available at:

Williams, M. A., Srikesavan, C., Heine, P. J., Bruce, J., Brosseau, L., Hoxey-Thomas, N. & Lamb, S. E. (2018) 'Exercise for rheumatoid arthritis of the hand'. *Cochrane Database of Systematic Reviews,* 7)**,** pp. Available at: https://doi.org/10.1002/14651858.CD003832.pub3

Williams, M. A., Williamson, E. M., Heine, P. J., Nichols, V., Glover, M. J., Dritsaki, M., Adams, J., Dosanjh, S., Underwood, M., Rahman, A., Mcconkey, C., Lord, J. & Lamb, S. E. (2015) 'Strengthening And stretching for Rheumatoid Arthritis of the Hand (SARAH). A randomised controlled trial and economic evaluation'. *Health Technology Assessment,* 19(19)**,** pp. 1-219. Available at: https://doi.org/10.3310/hta19190

Williamson, E., Srikesavan, C., Thompson, J., Tonga, E., Eldridge, L., Adams, J. & Lamb, S. E. (2020) 'Translating the Strengthening and Stretching for Rheumatoid Arthritis of the Hand Programme from clinical trial to clinical practice: An effectiveness–implementation study'. *Hand Therapy,* 25(3)**,** pp. 87-97. Available at: https://doi.org/10.1177/1758998320948538

Wood, L., Foster, N. E., Dean, S. G., Booth, V., Hayden, J. A. & Booth, A. (2024) 'Contexts, behavioural mechanisms and outcomes to optimise therapeutic exercise prescription for persistent low back pain: a realist review'. *British Journal of Sports Medicine,* 58(4)**,** pp. 222-230. Available at: https://doi.org/10.1136/bjsports-2023-107598

World Health Organization. (2010) Global recommendations on physical activity for health. Switzerland:

World Health Organization. (2019a) *Global Strategy on Diet, Physical Activity and Health* [Online]. World Health Organisation. Available: https://www.who.int/dietphysicalactivity/pa/en/ [Accessed 27/03/2019 2019].

World Health Organization. (2019b) *International Classification of Diseases, Eleventh Revision (ICD-11)* [Online]. Available: https://icd.who.int/browse11. [Accessed 26th Jan 2024].

World Health Organization. (2024) *International Classification of Functioning, Disability and Health (ICF)* [Online]. Available: https://www.who.int/standards/classifications/international-classification-of-functioning-disability-and-health [Accessed 14th October 2024].

Yamato, T. P., Maher, C. G., Saragiotto, B. T., Hoffmann, T. C. & Moseley, A. M. (2016) 'How completely are physiotherapy interventions described in reports of randomised trials?'. *Physiotherapy,* 102(2)**,** pp. 121-126. Available at: https://doi.org/10.1016/j.physio.2016.03.001

Yun, H.-W., Kim, C.-J., Ahn, J.-A. & Schlenk, E. A. (2023) 'Effects of a self-determination theory-based physical activity programme for postmenopausal women with rheumatoid arthritis: A randomized controlled trial'. *International journal of nursing practice,* 29(6)**,** pp. e13199. Available at: https://dx.doi.org/10.1111/ijn.13199

Zadro, J., O'keeffe, M. & Maher, C. (2019) 'Do physical therapists follow evidence-based guidelines when managing musculoskeletal conditions? Systematic review'. *BMJ Open,* 9(10)**,** pp. e032329. Available at: https://doi.org/10.1136/bmjopen-2019-032329

Zhang, W., Moskowitz, R., Nuki, G., Abramson, S., Altman, R., Arden, N., Bierma-Zeinstra, S., Brandt, K., Croft, P. & Doherty, M. (2008) 'OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines'. *Osteoarthritis and Cartilage,* 16(2)**,** pp. 137-162. Available at: https://doi.org/10.1016/j.joca.2007.12.013

APPENDIX 1. STUDY ONE. PUBLISHED PROTOCOL.

Open access Protocol

BMJ Open

What evidence is used to underpin the design of strength-based exercise interventions evaluated in randomised controlled trials for rheumatoid arthritis? A systematic review protocol

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ABSTRACT

Introduction Healthcare researchers designing strength-based exercise interventions must choose an appropriate dose to test before evaluating its effect using a definitive/phase-III randomised controlled trial (RCT). Compared with early phase testing employed by pharmaceutical trials, it is questionable whether exercise-based trials employ the same rigour for establishing tolerated dosage. Consequently, it is unclear if participants are initially prescribed optimal doses of exercise, which may potentially impact on study outcomes. Using trials of strength-based exercise interventions in adults with rheumatoid arthritis (RA) as an exemplar, the aims of this review are to (1) identify the proportion of RCTs that use phase I/II trials with dose escalation methodology for setting prescription parameters, (2) determine type and level of evidence used to justify prescription parameters of strength-based exercise interventions evaluated by RCTs, (3) explore consistency and applicability of the evidence underpinning prescription parameters in RCTs and (4) explore if a relationship exists between risk of bias for RCTs evaluating strength-based interventions and the level of evidence used to underpin prescription parameters.

Methods and analysis Focusing on RCT's evaluating strength-based exercise interventions in adults with RA published after 2000, the following databases will be searched: Allied and Complementary Medicine Database, Cochrane Central Register of Controlled Trials, Cumulative Index to Nursing and Allied Health Literature, Excerpta Medica Database, Medline and Physiotherapy Evidence Database. For each RCT, we will identify the evidence used to underpin prescription parameters. Both trial and underpinning evidence will have key information about the intervention extracted using the template for intervention description and replication checklist. Risk of bias will be assessed according to Cochrane. Levels of evidence will be assessed against the Oxford Centre for Evidence-Based Medicine and relationships between RCT and underpinning evidence explored and described narratively. Two independent assessors will be involved throughout data selection and extraction with recourse to a third reviewer should agreement not be reached.

Ethics and dissemination No ethical issues are identified. Dissemination will be via publication.

Strengths and limitations of this study

- ► This review presents a novel approach to investigating the dose prescriptions used for exercise interventions evaluated in randomised controlled trials (RCTs) using trials in rheumatoid arthritis as an example.
- ► It will identify how many RCTs evaluating strength-based exercise interventions in rheumatoid arthritis report using early phase trials to set prescription parameters.
- ► This review will examine consistency and applicability of the evidence used by healthcare researchers to underpin the prescription parameters.
- ► A limitation of the review is that we must rely on the description of interventions provided by the authors, so findings will be reliant on the quality of this reporting.

PROSPERO registration number CRD42018090963.

INTRODUCTION

Developing the interventions evaluated as part of a clinical trial is a critical stage of the research process. An integral part of this process focuses on determining safe and effective prescription of dose, yet the approaches used by healthcare researchers differ depending on the type of intervention being tested. Those evaluating investigational medicinal products commonly use early phase clinical trials (eg, phase I/II), employing different dose escalation designs[1 2] as an essential step to safeguard participants and optimise potential for efficacy.[3 4] Conversely, researchers evaluating complex rehabilitation interventions involving exercise seldom take this approach. Instead, many follow the Medical Research Council (MRC) framework for developing and evaluating randomised

APPENDIX 2. STUDY ONE. FULL PUBLICATION.

RHEUMATOLOGY

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Review

A systematic review exploring the evidence reported to underpin exercise dose in clinical trials of rheumatoid arthritis

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Abstract

We aimed to evaluate the evidence reported to underpin exercise dose in randomised controlled trials (RCTs) using strengthening exercise in RA. We searched six different databases between 1 January 2000 and 3 April 2019. We included RCTs, where a main component of the intervention and/or control used strengthening exercise. Evidence sources cited to underpin dose were judged for their quality, consistency and applicability. Thirty-two RCTs were reviewed. Four (12.5%) piloted the intervention without using dose-escalation designs to determine optimal dose-response. Twenty (62.5%) reported no evidence underpinning dose. Where reported, quality, consistency and applicability of the underpinning evidence was a cause for methodological concern. The majority of RCTs did not report the evidence underpinning dose. When reported, the evidence was often not applicable to the clinical population. Frequently, the dose used differed to the dose reported/recommended by the underpinning evidence. Our findings illustrate exercise dose may not be optimised for use with clinical populations prior to evaluation by RCT.

Key words: rheumatoid arthritis, exercise, dose response, RCT, systematic review, intervention

Rheumatology key messages

- The majority of exercise trials in RA don't report evidence underpinning dose of strengthening exercise.
- Exercise trials in RA seldom pilot their interventions to determine dose-response.
- Evidence used by exercise trials in RA to underpin dose is often low in quality.

Introduction

In the United Kingdom (UK), exercise is recommended by clinical guidelines alongside pharmaceutical interventions for the management of RA [1]. One type of exercise that has grown in popularity, with more clinical trials evaluating its safety and effectiveness being published, is strengthening exercise [2]. Once considered to be detrimental for people living with RA because it was thought to cause damage to the joints [3], strengthening exercise is commonly used to counter the cachectic effects (muscle wasting) of the disease [4]. However, uncertainty exists regarding what exercise dose is most effective for improving the RA symptoms, function and other patient-centred outcomes [5]. Dose refers to the amount of treatment prescribed [6], and exercise dose is made up of the following parameters: exercise type, sets, repetitions, load and/or intensity, recovery time/method of progression, session duration, frequency of exercise sessions and duration of the evaluated programme [7, 8]. A recent research priority setting partnership identified that establishing the most effective dose

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APPENDIX 3. STUDY ONE. LITERATURE SEARCH STRATGIES.

MEDLINE Search Strategy.

Database and platform: MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present (via OVID)

Search date: 18 May 2018 with update search (covering May 2018 to April 2019) conducted on 3 April 2019.

Search filter: Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity-maximizing version (2008 revision); Ovid format.

1. Arthritis, Rheumatoid/
2. (RA or rheumatoid).ti,ab.
3. (rheumatoid adj1 arthritis).ti,ab,kw.
4. or/1-3
5. Exercise/
6. Exercise Therapy/
7. Plyometric Exercise/
8. Exercise Movement Techniques/
9. Physical Therapy Modalities/
10. Physical Fitness/
11. Physical Endurance/
12. (exercis$ adj3 (home or programme$ or program$ or therap$ or technique$ or train$ or treatment$ or intervention$ or supervised)).ti,ab,kw.
13. ((therapeutic or land or intensi$ or dynamic or isometric or isotonic or isokinetic) adj3 (exercis$ or train$)).ti,ab,kw.
14. (physical adj1 (activ$ or education$ or fitness or train$ or therap$ or treatment$ or intervention$)).ti,ab,kw.
15. (physio or physiotherap$).ti,ab,kw.
16. (cycle or cycling or bicycle or walk$).ti,ab,kw.
17. (physical adj1 condition$ adj1 (exercis$ or train$ or programme$ or program$)).ti,ab,kw.
18. ((muscle or grip$) adj2 (programme$ or program$ or therap$ or technique$ or train$ or treatment$ or intervention$ or exercis$)).ti,ab,kw.
19. ((hand$ or wrist$ or shoulder$ or knee$ or ankle$ or joint$ or elbow$ or hip or cervical or lumbar or trunk) adj1 (strength$ or exercis$ or therap$)).ti,ab,kw.

20. Resistance Training/

21. ((resistance or strength$ or weight or endurance) adj1 (programme$ or program$ or therap$ or technique$ or train$ or treatment$ or intervention$ or exercis$)).ti,ab,kw.

22. or/5-21

23. 4 and 22

24. randomized controlled trial.pt.

25. controlled clinical trial.pt.

26. randomized.ab.

27. placebo.ab.

28. drug therapy.fs.

29. randomly.ab.

30. trial.ab.

31. groups.ab.

32. or/24-31

33. 23 and 32

34. exp animals/ not humans.sh.

35. 33 not 34

36. limit 35 to yr="2000-2018"

EMBASE Search Strategy.

Database and platform: Embase 1974 to 2018 Week 20 (via OVID)

Search date:18 May 2018 with update search (covering May 2018 to April 2019) conducted on 3 April 2019.

Search filter: McMaster EMBASE RCT search filter (Best balance of sensitivity and specificity)

1. Rheumatoid Arthritis/
2. (RA or rheumatoid).ti,ab.
3. (rheumatoid adj1 arthritis).ti,ab,kw.
4. or/1-3
5. Exercise/
6. Dynamic Exercise/
7. Endurance Training/
8. Exercise Intensity/
9. Isokinetic Exercise/
10. Isometric Exercise/
11. Isotonic Exercise/
12. Muscle Exercise/
13. Kinesiotherapy/
14. Plyometrics/
15. Fitness/
16. Physical Activity/
17. Grip Strength/
18. Muscle Strength/
19. Physical Capacity/
20. Muscle Training/
21. Hand Grip/
22. Pinch Strength/
23. Hand Strength/
24. Isometrics/
25. (exercis$ adj3 (home or programme$ or program$ or therap$ or technique$ or train$ or treatment$ or intervention$ or supervised)).ti,ab,kw.
26. ((therapeutic or land or intensi$ or dynamic or isometric or isotonic or isokinetic) adj3 (exercis$ or train$)).ti,ab,kw.

27. (physical adj1 (activ$ or education$ or fitness or train$ or therap$ or treatment$ or intervention$)).ti,ab,kw.

28. (physio or physiotherap$).ti,ab,kw.

29. (cycle or cycling or bicycle or walk$).ti,ab,kw.

30. (physical adj1 condition$ adj1 (exercis$ or train$ or programme$ or program$)).ti,ab,kw.

31. ((muscle or grip$) adj2 (programme$ or program$ or therap$ or technique$ or train$ or treatment$ or intervention$ or exercis$)).ti,ab,kw.

32. ((hand$ or wrist$ or shoulder$ or knee$ or ankle$ or joint$ or elbow$ or hip or cervical or lumbar or trunk) adj1 (strength$ or exercis$ or therap$)).ti,ab,kw.

33. Resistance Training/

34. ((resistance or strength$ or weight or endurance) adj1 (programme$ or program$ or therap$ or technique$ or train$ or treatment$ or intervention$ or exercis$)).ti,ab,kw.

35. or/5-34

36. 4 and 35

37. random:.tw.

38. placebo:.mp.

39. double-blind:.tw.

40. or/37-39

41. 36 and 40

42. limit 41 to yr="2000-2018"

CINAHL Search Strategy.

Database and platform: CINAHL (via EbscoHost)

Search date: 18 May 2018 with update search (covering May 2018 to April 2019) conducted on 3 April 2019.

Search filter used: SIGN Search Filter for identifying randomised trials in CINAHL for EBSCO (created by Mark Clowes).

1. (MH "Arthritis, Rheumatoid")
2. (TI "RA" or "rheumatoid") OR (AB "RA" or "rheumatoid")
3. (TI (rheumatoid N1 arthritis)) OR (AB (rheumatoid N1 arthritis))
4. S1 OR S2 OR S3
5. (MH "Exercise")
6. (MH "Therapeutic Exercise")
7. (MH "Plyometrics")
8. (MH "Physical Therapy")
9. (MH "Physical Fitness")
10. (MH "Physical Endurance")
11. (TI (exercis* N3 (home or programme* or program* or therap* or technique* or train* or treatment* or intervention* or supervised)) OR (AB (exercis* N3 (home or programme* or program* or therap* or technique* or train* or treatment* or intervention* or supervised))
12. (TI (therapeutic or land or intensi* or dynamic or isometric or isotonic or isokinetic) N3 (exercis* or train*)) OR (AB (therapeutic or land or intensi* or dynamic or isometric or isotonic or isokinetic) N3 (exercis* or train*))
13. (TI (physical N1 (activ* or education* or fitness or train* or therap* or treatment* or intervention*)) OR (AB (physical N1 (activ* or education* or fitness or train* or therap* or treatment* or intervention*))
14. (TI "physio" or "physiotherap*") OR (AB "physio" or "physiotherap*")
15. (TI "cycle" or "cycling" or "bicycle" or "walk*") OR (AB "cycle" or "cycling" or "bicycle" or "walk*")
16. (TI (physical N1 condition* N1 (exercis* or train* or programme* or program*)) OR (AB (physical N1 condition* N1 (exercis* or train* or programme* or program*))
17. (TI (muscle or grip*) N2 (programme* or program* or therap* or technique* or train* or treatment* or intervention* or exercis*)) OR (AB (muscle or grip*) N2 (programme* or program* or therap* or technique* or train* or treatment* or intervention* or exercis*))

18. (TI (hand* or wrist* or shoulder* or knee* or ankle* or joint* or elbow* or hip or cervical or lumbar or trunk) N1 (strength* or exercis* or therap*)) OR (AB (hand* or wrist* or shoulder* or knee* or ankle* or joint* or elbow* or hip or cervical or lumbar or trunk) N1 (strength* or exercis* or therap*))
19. (MH "Resistance Training")
20. (MH "Muscle Strengthening")
21. (MH "Grip Strength")
22. (MH "Muscle Strength")
23. (MH "Athletic Training Programs")
24. (TI (resistance or strength* or weight or endurance) N1 (programme* or program* or therap* or technique* or train* or treatment* or intervention* or exercis*)) OR (AB (resistance or strength* or weight or endurance) N1 (programme* or program* or therap* or technique* or train* or treatment* or intervention* or exercis*))
25. S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24
26. S4 AND S25
27. (MH "Clinical Trials+")
28. PT Clinical trial
29. TX clinic* n1 trial*
30. TX ((singl* n1 blind*) or (singl* n1 mask*)) or TX ((doubl* n1 blind*) or (doubl* n1 mask*)) or TX ((tripl* n1 blind*) or (tripl* n1 mask*)) or TX ((trebl* n1 blind*) or (trebl* n1 mask*))
31. TX randomi* control* trial*
32. (MH "Random Assignment")
33. TX random* allocat*
34. TX placebo*
35. (MH "Placebos")
36. (MH "Quantitative Studies")
37. TX allocat* random*
38. S27 or S28 or S29 or S30 or S31 or S32 or S33 OR S34 OR S35 OR S36 OR S37
39. S26 and S38
40. PY 2000-2018
41. S39 and S40

AMED Search Strategy.

Database and platform: AMED (Allied and Complementary Medicine) 1985 to May 2018 (via OVID)

Search date: 18 May 2018 with update search (covering 2018 to 2019) conducted on 3 April 2019.

1. Arthritis Rheumatoid/
2. (RA or rheumatoid).ti,ab.
3. (rheumatoid adj1 arthritis).ti,ab.
4. 1 or 2 or 3
5. Exercise/
6. Exercise Therapy/
7. Exercise Movement Techniques/
8. Physical Therapy Modalities/
9. Physical Fitness/
10. Physical Endurance/
11. Exercise Tolerance/
12. Rehabilitation/
13. (exercis$ adj3 (home or programme$ or program$ or therap$ or technique$ or train$ or treatment$ or intervention$ or supervised)).ti,ab.
14. ((therapeutic or land or intensi$ or dynamic or isometric or isotonic or isokinetic) adj3 (exercis$ or train$)).ti,ab.
15. (physical adj1 (activ$ or education$ or fitness or train$ or therap$ or treatment$ or intervention$)).ti,ab.
16. (physio or physiotherap$).ti,ab.
17. (cycle or cycling or bicycle or walk$).ti,ab.
18. (physical adj1 condition$ adj1 (exercis$ or train$ or programme$ or program$)).ti,ab.
19. ((muscle or grip$) adj2 (programme$ or program$ or therap$ or technique$ or train$ or treatment$ or intervention$ or exercis$)).ti,ab.
20. ((hand$ or wrist$ or shoulder$ or knee$ or ankle$ or joint$ or elbow$ or hip or cervical or lumbar or trunk) adj1 (strength$ or exercis$ or therap$)).ti,ab.
21. Hand Strength/
22. Resistance Training/
23. ((resistance or strength$ or weight or endurance) adj1 (programme$ or program$ or therap$ or technique$ or train$ or treatment$ or intervention$ or exercis$)).ti,ab.

24. 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23

25. 4 and 24

26. limit 25 to yr="2000-2018"

CENTRAL Search Strategy.

Database and platform: CENTRAL (via http://cochranelibrary-wiley.com/cochranelibrary/)

Search date: 18 May 2018 with update search (covering 2018 to 2019) conducted on 3 April 2019.

1. (mh "Arthritis, Rheumatoid") in Trials
2. (RA or rheumatoid):ti,ab,kw in Trials
3. (rheumatoid next/1 arthritis):ti,ab,kw in Trials
4. #1 or #2 or #3
5. (mh "Exercise") in Trials
6. (mh "Exercise Therapy") in Trials
7. (mh "Plyometric Exercise") in Trials
8. (mh "Exercise Movement Techniques") in Trials
9. (mh "Physical Therapy Modalities") in Trials
10. (mh "Physical Fitness") in Trials
11. (mh "Physical Endurance") in Trials
12. (exercis* next/3 (home or programme* or program* or therap* or technique* or train* or treatment* or intervention* or supervised)):ti,ab,kw in Trials
13. ((therapeutic or land or intensi* or dynamic or isometric or isotonic or isokinetic) next/3 (exercis* or train*)):ti,ab,kw in Trials
14. (physical next/1 (activ* or education* or fitness or train* or therap* or treatment* or intervention*)):ti,ab,kw in Trials
15. (physio or physiotherap*):ti,ab,kw in Trials
16. (cycle or cycling or bicycle or walk*):ti,ab,kw in Trials
17. (physical next/1 condition* next/1 (exercis* or train* or programme* or program*)):ti,ab,kw in Trials
18. ((muscle or grip*) next/2 (programme* or program* or therap* or technique* or train* or treatment* or intervention* or exercis*)):ti,ab,kw in Trials
19. [mh "Hand Strength"] in Trials
20. ((hand* or wrist* or shoulder* or knee* or ankle* or joint* or elbow* or hip or cervical or lumbar or trunk) next/1 (strength* or exercis* or therap*)):ti,ab,kw in Trials
21. (mh "Resistance Training") in Trials
22. ((resistance or strength* or weight or endurance) next/1 (programme* or program* or therap* or technique* or train* or treatment* or intervention* or exercis*)):ti,ab,kw in Trials

23. #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22

24. #4 and #23

25. #24 Publication Year from 2000 to 2018

PEDro Search Strategy.

Database and platform: PEDro (http://search.pedro.org.au/advanced-search)

Search date: 18 May 2018 with update search (covering 2018 to 2019) conducted on 3 April 2019.

SEARCH STRATEGY 1

1. Abstract & Title: Rheumatoid Arthritis

AND

2. Therapy: fitness training

AND

3. Method: clinical trial

AND

4. Published Since: 2000

OR

SEARCH STRATEGY 2

1. Abstract & Title: Rheumatoid Arthritis

AND

2. Therapy: strength training

AND

3. Method: clinical trial

AND

4. Published Since: 2000

OR

SEARCH STRATEGY 3

1. Abstract & Title: Rheumatoid Arthritis Exercis*

AND

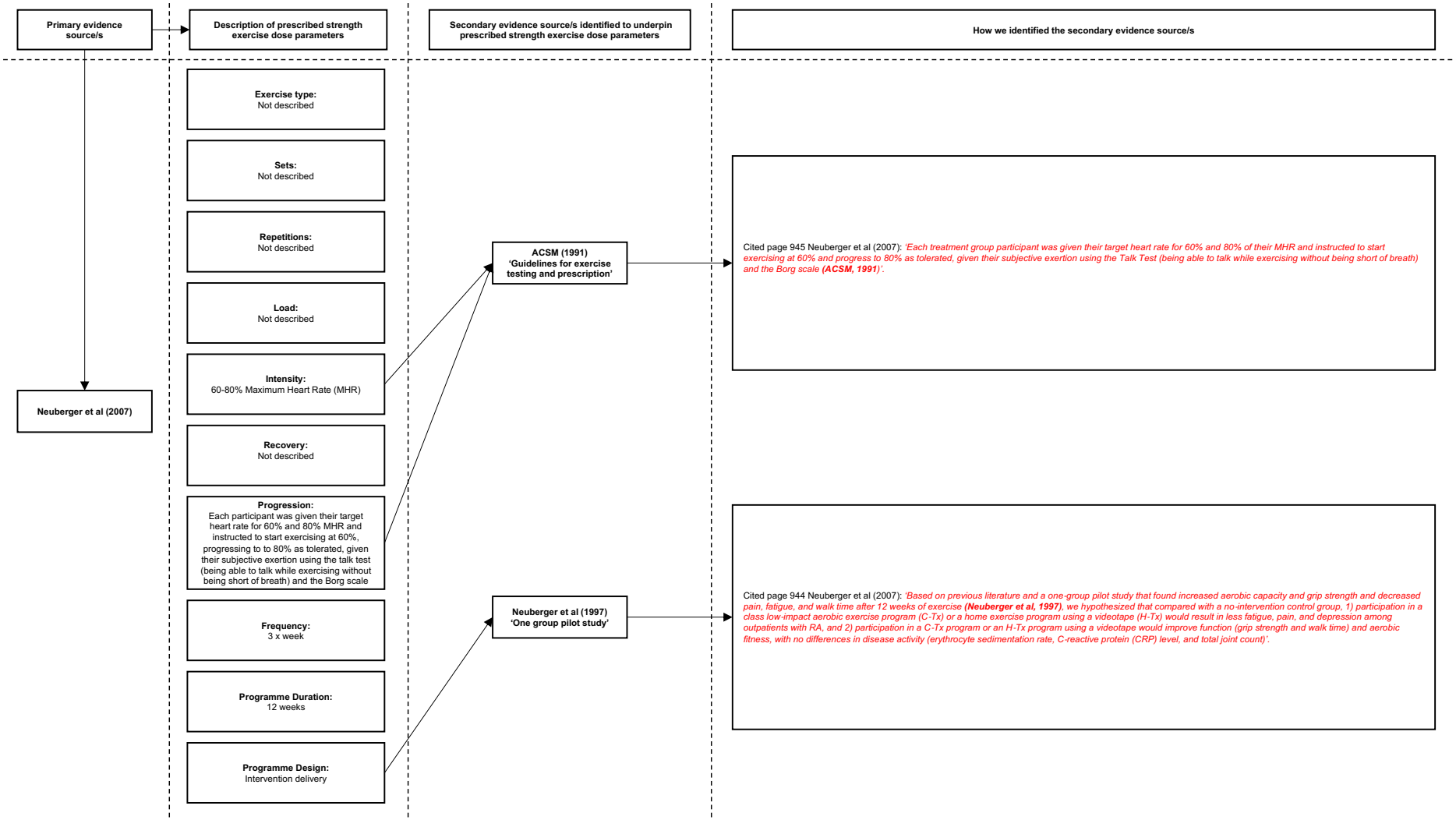
2. Method: Clinical trial

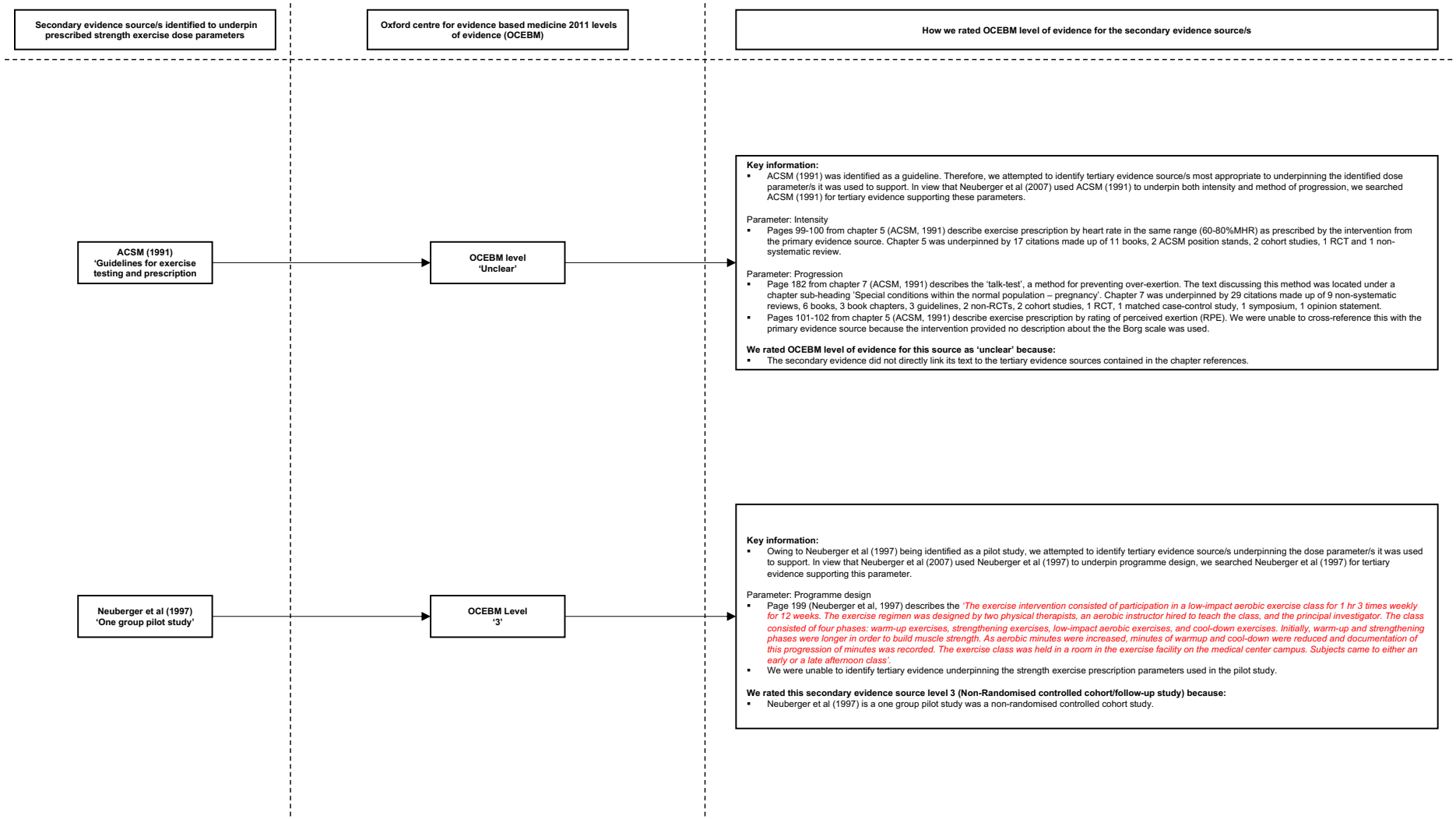
AND

3. Published since: 2000

APPENDIX 4. STUDY ONE. UNDERPINNING EVIDENCE.

Neuberger et al (2007)

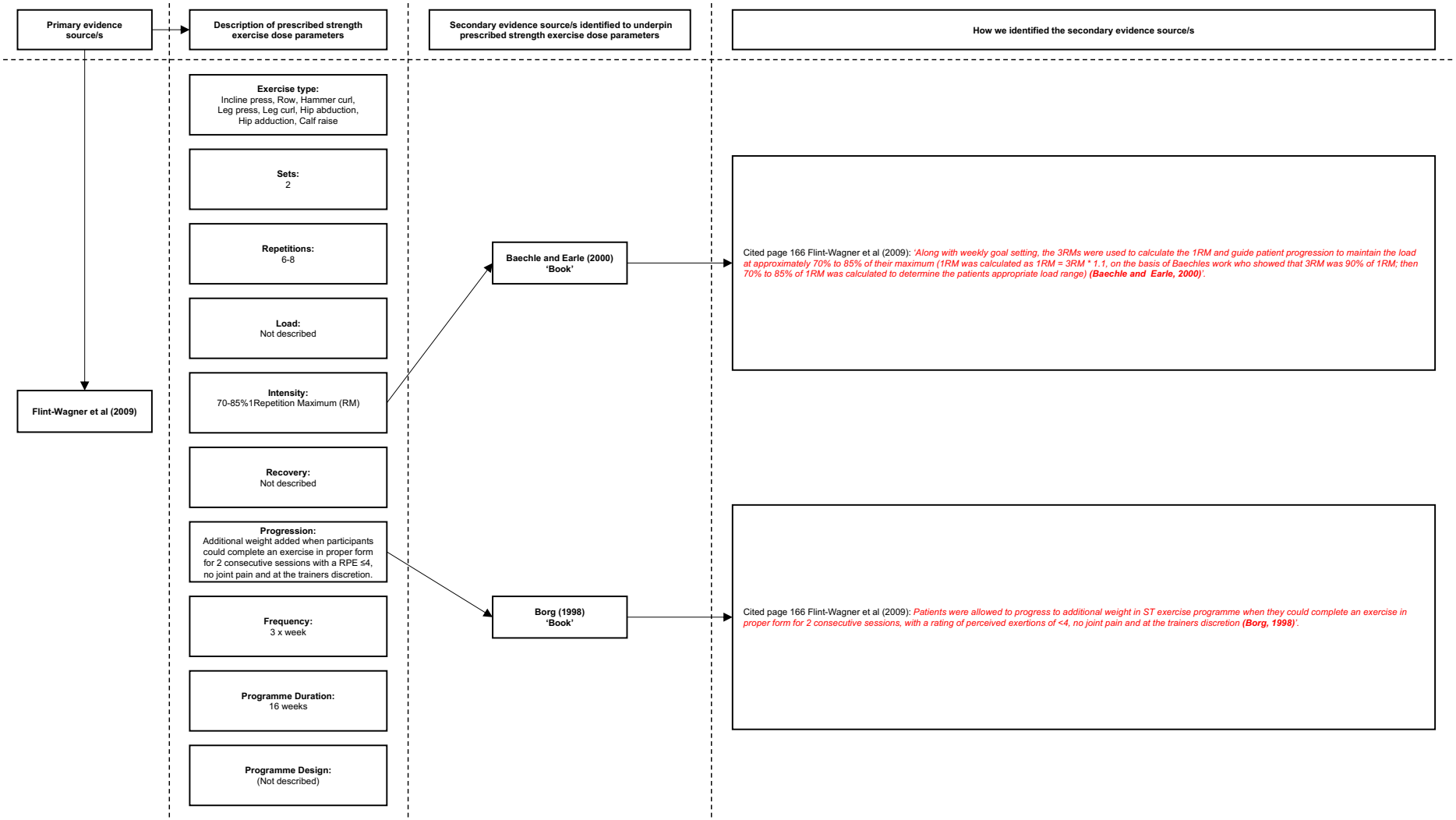

Primary evidence source/s
Description of prescribed strength exercise dose parameters
Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
How we identified the secondary evidence source/s
Neuberger et al (2007)
Exercise type: Not described
Sets: Not described
Repetitions: Not described
Load: Not described
Intensity: 60-80% Maximum Heart Rate (MHR)
Recovery: Not described
Progression: Each participant was given their target heart rate for 60% and 80% MHR and instructed to start exercising at 60%, progressing to to 80% as tolerated, given their subjective exertion using the talk test (being able to talk while exercising without being short of breath) and the Borg scale
Frequency: 3 x week
Programme Duration: 12 weeks
Programme Design: Intervention delivery
ACSM (1991) 'Guidelines for exercise testing and prescription'
Neuberger et al (1997) 'One group pilot study'
Cited page 945 Neuberger et al (2007): 'Each treatment group participant was given their target heart rate for 60% and 80% of their MHR and instructed to start exercising at 60% and progress to 80% as tolerated, given their subjective exertion using the Talk Test (being able to talk while exercising without being short of breath) and the Borg scale (ACSM, 1991)'.
Cited page 944 Neuberger et al (2007): 'Based on previous literature and a one-group pilot study that found increased aerobic capacity and grip strength and decreased pain, fatigue, and walk time after 12 weeks of exercise (Neuberger et al, 1997), we hypothesized that compared with a no-intervention control group, 1) participation in a class low-impact aerobic exercise program (C-Tx) or a home exercise program using a videotape (H-Tx) would result in less fatigue, pain, and depression among outpatients with RA, and 2) participation in a C-Tx program or an H-Tx program using a videotape would improve function (grip strength and walk time) and aerobic fitness, with no differences in disease activity (erythrocyte sedimentation rate, C-reactive protein (CRP) level, and total joint count)'.

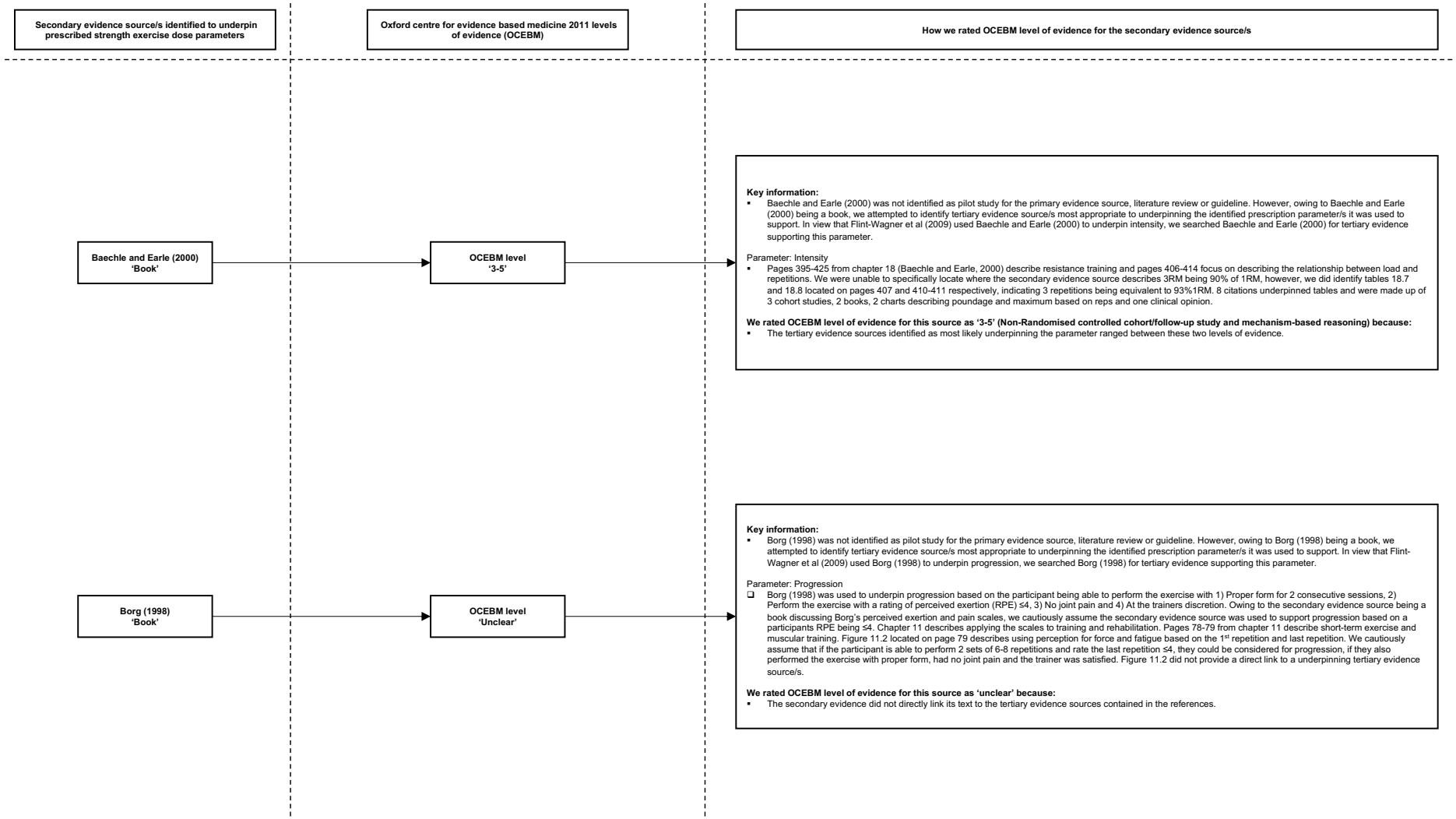

Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
Oxford centre for evidence based medicine 2011 levels of evidence (OCEBM)
How we rated OCEBM level of evidence for the secondary evidence source/s
ACSM (1991) 'Guidelines for exercise testing and prescription
OCEBM level 'Unclear'
Key information:
ACSM (1991) was identified as a guideline. Therefore, we attempted to identify tertiary evidence source/s most appropriate to underpinning the identified dose parameter/s it was used to support. In view that Neuberger et al (2007) used ACSM (1991) to underpin both intensity and method of progression, we searched ACSM (1991) for tertiary evidence supporting these parameters.
Parameter: Intensity
Pages 99-100 from chapter 5 (ACSM, 1991) describe exercise prescription by heart rate in the same range (60-80%MHR) as prescribed by the intervention from the primary evidence source. Chapter 5 was underpinned by 17 citations made up of 11 books, 2 ACSM position stands, 2 cohort studies, 1 RCT and 1 non-systematic review.
Parameter: Progression
Page 182 from chapter 7 (ACSM, 1991) describes the 'talk-test', a method for preventing over-exertion. The text discussing this method was located under a chapter sub-heading 'Special conditions within the normal population – pregnancy'. Chapter 7 was underpinned by 29 citations made up of 9 non-systematic reviews, 6 books, 3 book chapters, 3 guidelines, 2 non-RCTs, 2 cohort studies, 1 RCT, 1 matched case-control study, 1 symposium, 1 opinion statement.
Pages 101-102 from chapter 5 (ACSM, 1991) describe exercise prescription by rating of perceived exertion (RPE). We were unable to cross-reference this with the primary evidence source because the intervention provided no description about the the Borg scale was used.
We rated OCEBM level of evidence for this source as 'unclear' because:
The secondary evidence did not directly link its text to the tertiary evidence sources contained in the chapter references.
Neuberger et al (1997) 'One group pilot study'
OCEBM Level '3'
Key information:
Owing to Neuberger et al (1997) being identified as a pilot study, we attempted to identify tertiary evidence source/s underpinning the dose parameter/s it was used to support. In view that Neuberger et al (2007) used Neuberger et al (1997) to underpin programme design, we searched Neuberger et al (1997) for tertiary evidence supporting this parameter.
Parameter: Programme design
Page 199 (Neuberger et al, 1997) describes the 'The exercise intervention consisted of participation in a low-impact aerobic exercise class for 1 hr 3 times weekly for 12 weeks. The exercise regimen was designed by two physical therapists, an aerobic instructor hired to teach the class, and the principal investigator. The class consisted of four phases: warm-up exercises, strengthening exercises, low-impact aerobic exercises, and cool-down exercises. Initially, warm-up and strengthening phases were longer in order to build muscle strength. As aerobic minutes were increased, minutes of warmup and cool-down were reduced and documentation of this progression of minutes was recorded. The exercise class was held in a room in the exercise facility on the medical center campus. Subjects came to either an early or a late afternoon class'.
We were unable to identify tertiary evidence underpinning the strength exercise prescription parameters used in the pilot study.
We rated this secondary evidence source level 3 (Non-Randomised controlled cohort/follow-up study) because:
Neuberger et al (1997) is a one group pilot study was a non-randomised controlled cohort study.

Dose parameter / Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Neuberger et al (2007)	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	60-80% MHR	Insufficiently described	Each participant was given their target HR for 60% & 80% MHR and instructed to start exercising at 60% and progress to 80% as tolerated given their subjective exertion using the Talk test (being able to talk while exercising without being short of breath) and the Borg scale.	3 x week	12 weeks	Exercise type: n/a Sets: n/a Repetitions: n/a Load: n/a Intensity: Consistent Recovery: n/a Progression: Unclear Frequency: n/a Duration: n/a
ACSM (1991)	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	60-80% MHR	Citation not used to support parameter	60-80% MHR: Unclear Talk test: Consistent Borg scale: Unclear	Citation not used to support parameter	Citation not used to support parameter	

RCT Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Neuberger et al (2007)	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	60-80%1RM	Insufficiently described	Each participant was given their target HR for 60% & 80% MHR and instructed to start exercising at 60% and progress to 80% as tolerated given their subjective exertion using the Talk Test (being able to talk while exercising without being short of breath) and the Borg scale.	3 x week	12 weeks	Exercise type: Unclear Sets: Unclear Repetitions: Unclear Load: Unclear Intensity: Unclear Recovery: Unclear Progression: Inconsistent Frequency: Consistent Duration: Consistent
Neuberger et al (1997)	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	Initially warm-up and strengthening phases were longer in order to build muscle strength. As aerobic minutes were increased, minutes of warm-up and cool-down were reduced.	3 x week	12 weeks	

Flint-Wagner et al (2009)

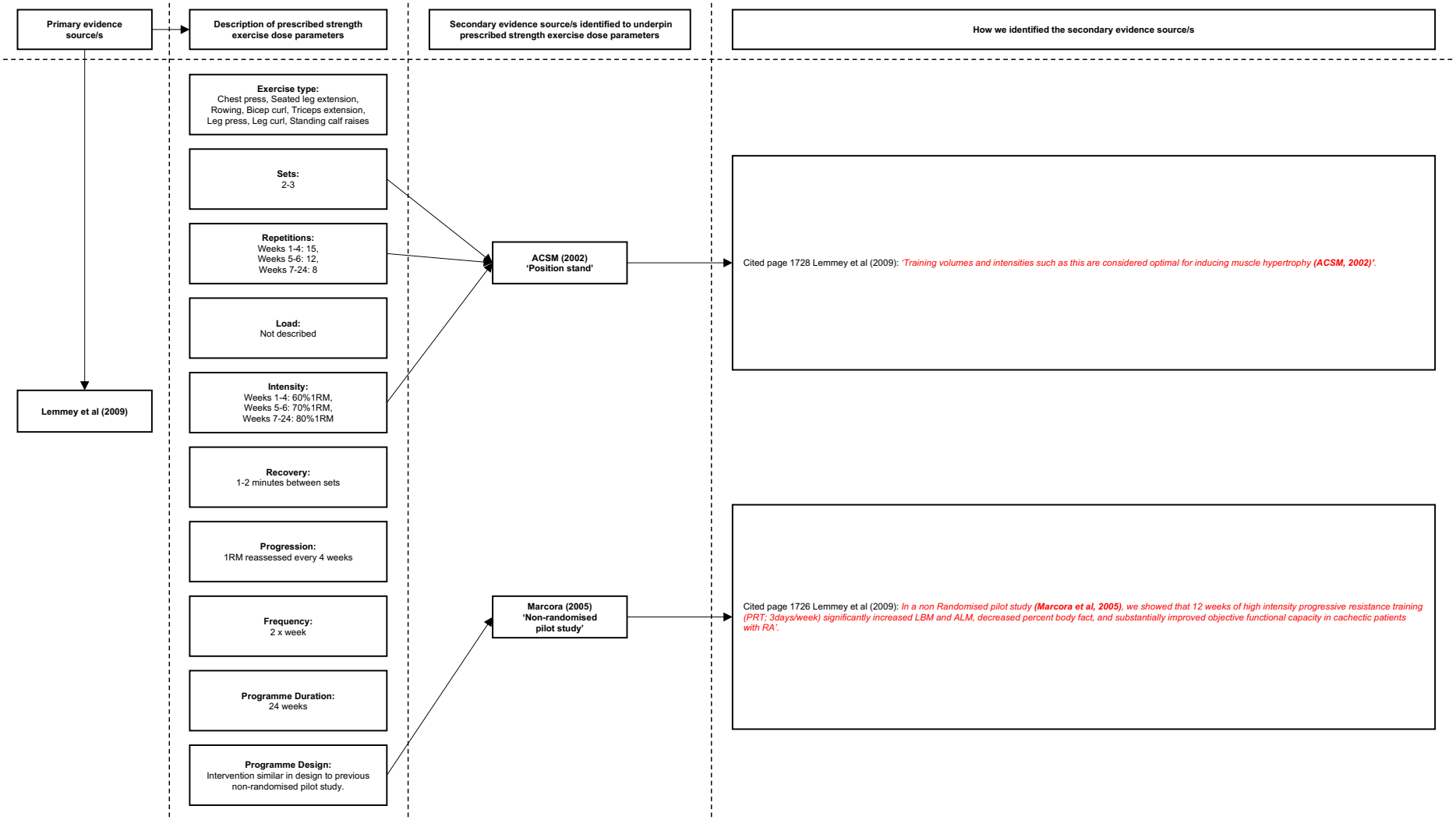

Primary evidence source/s
Description of prescribed strength exercise dose parameters
Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
How we identified the secondary evidence source/s
Flint-Wagner et al (2009)
Exercise type: Incline press, Row, Hammer curl, Leg press, Leg curl, Hip abduction, Hip adduction, Calf raise
Sets: 2
Repetitions: 6-8
Load: Not described
Intensity: 70-85%1Repetition Maximum (RM)
Recovery: Not described
Progression: Additional weight added when participants could complete an exercise in proper form for 2 consecutive sessions with a RPE ≤4, no joint pain and at the trainers discretion.
Frequency: 3 x week
Programme Duration: 16 weeks
Programme Design: (Not described)
Baechle and Earle (2000) 'Book'
Borg (1998) 'Book'
Cited page 166 Flint-Wagner et al (2009): 'Along with weekly goal setting, the 3RMs were used to calculate the 1RM and guide patient progression to maintain the load at approximately 70% to 85% of their maximum (1RM was calculated as 1RM = 3RM * 1.1, on the basis of Baechles work who showed that 3RM was 90% of 1RM; then 70% to 85% of 1RM was calculated to determine the patients appropriate load range) (Baechle and Earle, 2000)'.
Cited page 166 Flint-Wagner et al (2009): Patients were allowed to progress to additional weight in ST exercise programme when they could complete an exercise in proper form for 2 consecutive sessions, with a rating of perceived exertions of <4, no joint pain and at the trainers discretion (Borg, 1998)'.

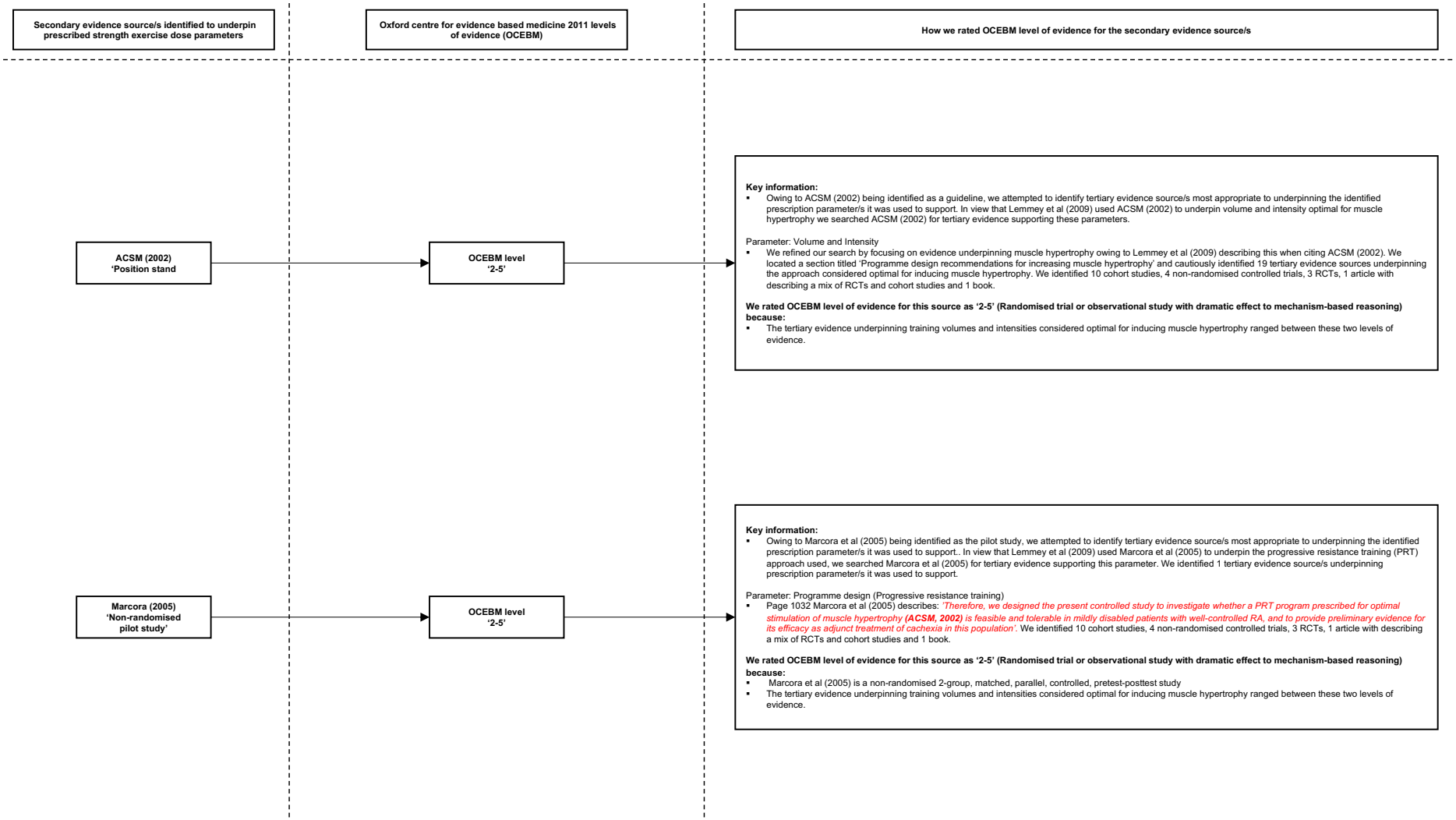

Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
Oxford centre for evidence based medicine 2011 levels of evidence (OCEBM)
How we rated OCEBM level of evidence for the secondary evidence source/s
Baechle and Earle (2000) 'Book'
OCEBM level '3-5'
Key information:
Baechle and Earle (2000) was not identified as pilot study for the primary evidence source, literature review or guideline. However, owing to Baechle and Earle (2000) being a book, we attempted to identify tertiary evidence source/s most appropriate to underpinning the identified prescription parameter/s it was used to support. In view that Flint-Wagner et al (2009) used Baechle and Earle (2000) to underpin intensity, we searched Baechle and Earle (2000) for tertiary evidence supporting this parameter.
Parameter: Intensity
Pages 395-425 from chapter 18 (Baechle and Earle, 2000) describe resistance training and pages 406-414 focus on describing the relationship between load and repetitions. We were unable to specifically locate where the secondary evidence source describes 3RM being 90% of 1RM, however, we did identify tables 18.7 and 18.8 located on pages 407 and 410-411 respectively, indicating 3 repetitions being equivalent to 93%1RM. 8 citations underpinned tables and were made up of 3 cohort studies, 2 books, 2 charts describing poundage and maximum based on reps and one clinical opinion.
We rated OCEBM level of evidence for this source as '3-5' (Non-Randomised controlled cohort/follow-up study and mechanism-based reasoning) because:
The tertiary evidence sources identified as most likely underpinning the parameter ranged between these two levels of evidence.
Borg (1998) 'Book'
OCEBM level 'Unclear'
Key information:
Borg (1998) was not identified as pilot study for the primary evidence source, literature review or guideline. However, owing to Borg (1998) being a book, we attempted to identify tertiary evidence source/s most appropriate to underpinning the identified prescription parameter/s it was used to support. In view that Flint-Wagner et al (2009) used Borg (1998) to underpin progression, we searched Borg (1998) for tertiary evidence supporting this parameter.
Parameter: Progression
Borg (1998) was used to underpin progression based on the participant being able to perform the exercise with 1) Proper form for 2 consecutive sessions, 2) Perform the exercise with a rating of perceived exertion (RPE) ≤4, 3) No joint pain and 4) At the trainers discretion. Owing to the secondary evidence source being a book discussing Borg's perceived exertion and pain scales, we cautiously assume the secondary evidence source was used to support progression based on a participants RPE being ≤4. Chapter 11 describes applying the scales to training and rehabilitation. Pages 78-79 from chapter 11 describe short-term exercise and muscular training. Figure 11.2 located on page 79 describes using perception for force and fatigue based on the 1st repetition and last repetition. We cautiously assume that if the participant is able to perform 2 sets of 6-8 repetitions and rate the last repetition ≤4, they could be considered for progression, if they also performed the exercise with proper form, had no joint pain and the trainer was satisfied. Figure 11.2 did not provide a direct link to a underpinning tertiary evidence source/s.
We rated OCEBM level of evidence for this source as 'unclear' because:
The secondary evidence did not directly link its text to the tertiary evidence sources contained in the references.

Dose parameter Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Flint-Wagner et al (2009)	1. Incline press 2. Row 3. Hammer curl 4. Leg press 5. Leg curl 6. Hip abduction 7. Hip adduction 8. Calf raise	2 sets	6-8 repetitions	Insufficiently described	70-85% 1Repetition Maximum (RM)	Insufficiently described	Additional weight added when participants could complete an exercise in proper form for 2 consecutive sessions with a RPE ≤4, no joint pain and at the trainers discretion. Along with weekly goal setting, the 3RMs were used to calculate the 1RM and guide patient progression to maintain load at approximately 70% to 85% of their maximum (1RM was calculated as 1RM – 3RM * 1.1 on the basis of Baechle's work showed that 3RM was 90% of 1RM; then 70% to 85% of 1RM was calculated to determine the patients appropriate load range.	3 x week	16 weeks	Exercise type: n/a Sets: n/a Repetitions: n/a Load: n/a Intensity: Unclear Recovery: n/a Progression: n/a Frequency: n/a Duration: n/a
Baechle and Earle (2000)	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Unclear	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	

RCT Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Flint-Wagner et al (2009)	1. Incline press 2. Row 3. Hammer curl 4. Leg press 5. Leg curl 6. Hip abduction 7. Hip adduction 8. Calf raise	2 sets	6-8 repetitions	Insufficiently described	70-85% 1Repetition Maximum (RM)	Insufficiently described	Additional weight added when participants could complete an exercise in proper form for 2 consecutive sessions with a RPE ≤4, no joint pain and at the trainers discretion. Along with weekly goal setting, the 3RMs were used to calculate the 1RM and guide patient progression to maintain load at approximately 70% to 85% of their maximum (1RM was calculated as 1RM – 3RM * 1.1 on the basis of Baechle's work showed that 3RM was 90% of 1RM; then 70% to 85% of 1RM was calculated to determine the patients appropriate load range.	3 x week	16 weeks	Exercise type: n/a Sets: n/a Repetitions: n/a Load: n/a Intensity: Unclear Recovery: n/a Progression: Unclear Frequency: n/a Duration: n/a
Borg (1998)	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Unclear	Citation not used to support parameter	Citation not used to support parameter	

Lemmey et al (2009)

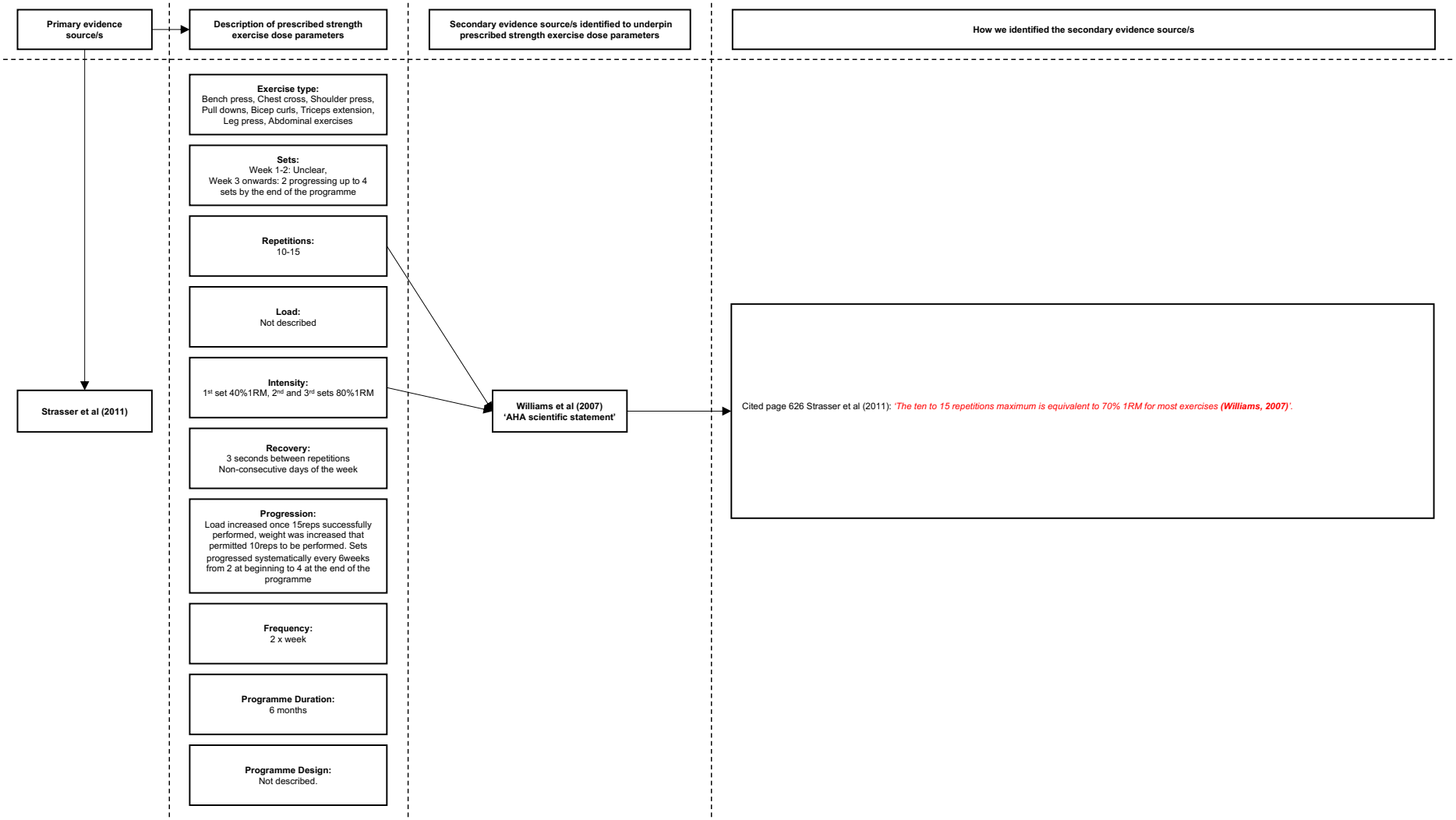

Primary evidence source/s
Description of prescribed strength exercise dose parameters
Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
How we identified the secondary evidence source/s
Lemmey et al (2009)
Exercise type: Chest press, Seated leg extension, Rowing, Bicep curl, Triceps extension, Leg press, Leg curl, Standing calf raises
Sets: 2-3
Repetitions: Weeks 1-4: 15, Weeks 5-6: 12, Weeks 7-24: 8
Load: Not described
Intensity: Weeks 1-4: 60%1RM, Weeks 5-6: 70%1RM, Weeks 7-24: 80%1RM
Recovery: 1-2 minutes between sets
Progression: 1RM reassessed every 4 weeks
Frequency: 2 x week
Programme Duration: 24 weeks
Programme Design: Intervention similar in design to previous non-randomised pilot study.
ACSM (2002) 'Position stand'
Marcora (2005) 'Non-randomised pilot study'
Cited page 1728 Lemmey et al (2009): 'Training volumes and intensities such as this are considered optimal for inducing muscle hypertrophy (ACSM, 2002)'.
Cited page 1726 Lemmey et al (2009): In a non Randomised pilot study (Marcora et al, 2005), we showed that 12 weeks of high intensity progressive resistance training (PRT; 3days/week) significantly increased LBM and ALM, decreased percent body fact, and substantially improved objective functional capacity in cachectic patients with RA'.

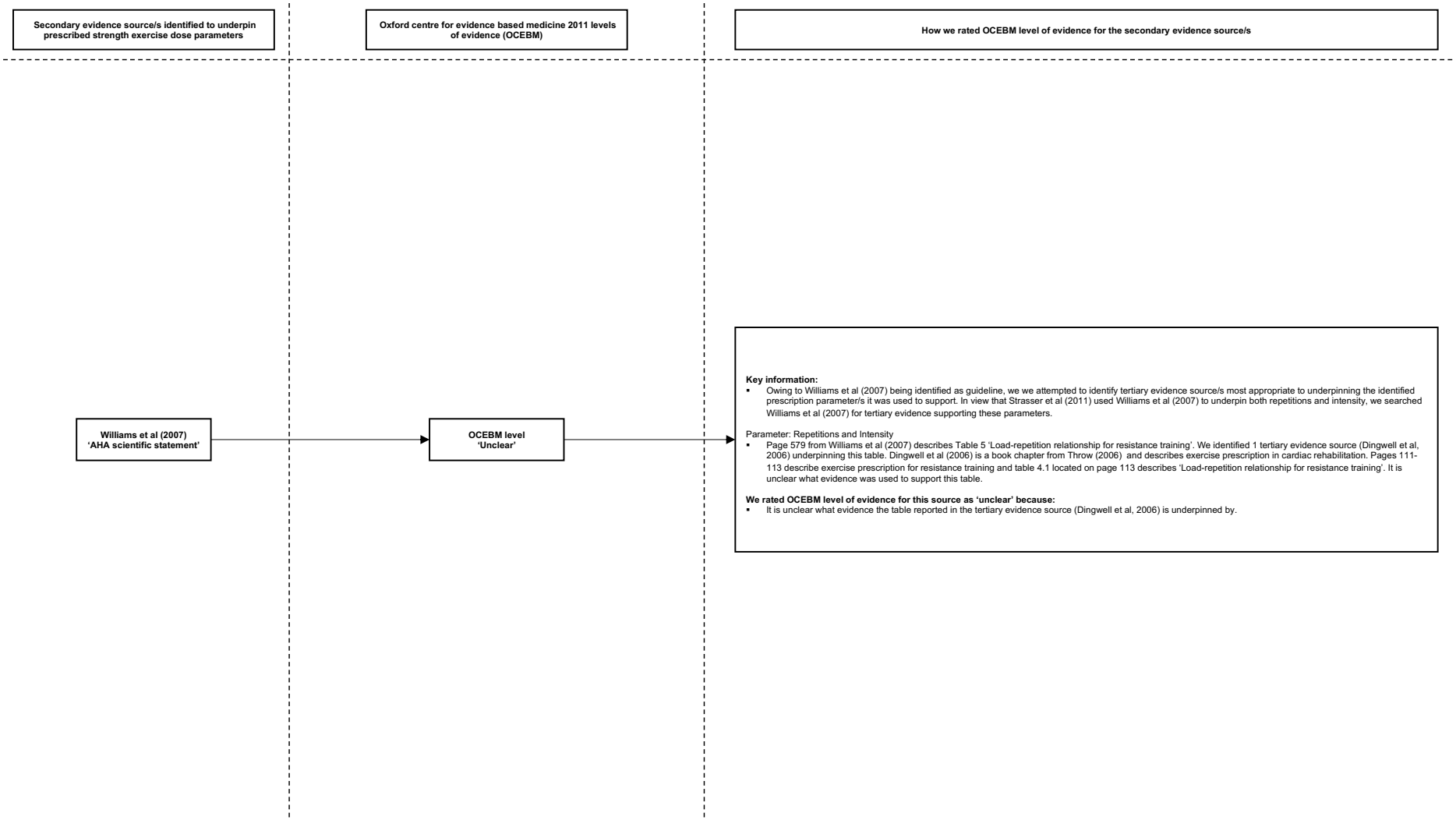

Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
Oxford centre for evidence based medicine 2011 levels of evidence (OCEBM)
How we rated OCEBM level of evidence for the secondary evidence source/s
ACSM (2002) 'Position stand
OCEBM level '2-5'
Key information:
Owing to ACSM (2002) being identified as a guideline, we attempted to identify tertiary evidence source/s most appropriate to underpinning the identified prescription parameter/s it was used to support. In view that Lemmey et al (2009) used ACSM (2002) to underpin volume and intensity optimal for muscle hypertrophy we searched ACSM (2002) for tertiary evidence supporting these parameters.
Parameter: Volume and Intensity
We refined our search by focusing on evidence underpinning muscle hypertrophy owing to Lemmey et al (2009) describing this when citing ACSM (2002). We located a section titled 'Programme design recommendations for increasing muscle hypertrophy' and cautiously identified 19 tertiary evidence sources underpinning the approach considered optimal for inducing muscle hypertrophy. We identified 10 cohort studies, 4 non-randomised controlled trials, 3 RCTs, 1 article with describing a mix of RCTs and cohort studies and 1 book.
We rated OCEBM level of evidence for this source as '2-5' (Randomised trial or observational study with dramatic effect to mechanism-based reasoning) because:
The tertiary evidence underpinning training volumes and intensities considered optimal for inducing muscle hypertrophy ranged between these two levels of evidence.
Marcora (2005) 'Non-randomised pilot study'
OCEBM level '2-5'
Key information:
Owing to Marcora et al (2005) being identified as the pilot study, we attempted to identify tertiary evidence source/s most appropriate to underpinning the identified prescription parameter/s it was used to support.. In view that Lemmey et al (2009) used Marcora et al (2005) to underpin the progressive resistance training (PRT) approach used, we searched Marcora et al (2005) for tertiary evidence supporting this parameter. We identified 1 tertiary evidence source/s underpinning prescription parameter/s it was used to support.
Parameter: Programme design (Progressive resistance training)
Page 1032 Marcora et al (2005) describes: 'Therefore, we designed the present controlled study to investigate whether a PRT program prescribed for optimal stimulation of muscle hypertrophy (ACSM, 2002) is feasible and tolerable in mildly disabled patients with well-controlled RA, and to provide preliminary evidence for its efficacy as adjunct treatment of cachexia in this population'. We identified 10 cohort studies, 4 non-randomised controlled trials, 3 RCTs, 1 article with describing a mix of RCTs and cohort studies and 1 book.
We rated OCEBM level of evidence for this source as '2-5' (Randomised trial or observational study with dramatic effect to mechanism-based reasoning) because:
Marcora et al (2005) is a non-randomised 2-group, matched, parallel, controlled, pretest-posttest study
The tertiary evidence underpinning training volumes and intensities considered optimal for inducing muscle hypertrophy ranged between these two levels of evidence.

Dose parameter / Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Lemmey et al (2009)	1. Chest press, 2. Seated leg extension, 3. Rowing, 4. Bicep curl, 5. Triceps extension, 6. Leg press, 7. Leg curl, 8. Standing calf raises	2-3 sets	Weeks 1-4: 15 repetitions Weeks 5-6: 12 repetitions Weeks 7-24: 8 repetitions	Insufficiently described	Weeks 1-4: 60%1RM Weeks 5-6: 70%1RM Weeks 7-24: 80%1RM	1-2 minutes between sets	1RM reassessed every 4 weeks	2 x week	24 weeks	Exercise type: n/a Sets: Consistent Repetitions: Inconsistent Load: n/a Intensity: Inconsistent Recovery: n/a Progression: Unclear Frequency: n/a Duration: n/a
ACSM (2002)	Citation not used to support parameter	1-3 sets for novice or intermediate individuals	8-12 repetitions for novice or intermediate individuals	Citation not used to support parameter	70-85%1RM for novice or intermediate individuals	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	

Dose parameter / Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Lemmey et al (2009)	1. Chest press 2. Seated leg extension 3. Rowing 4. Bicep curl 5. Triceps extension 6. Leg press 7. Leg curl 8. Standing calf raises	2-3 sets	Weeks 1-4: 15 repetitions Weeks 5-6: 12 repetitions Weeks 7-24: 8 repetitions	Insufficiently described	Weeks 1-4: 60%1RM Weeks 5-6: 70%1RM Weeks 7-24: 80%1RM	1-2 minutes between sets	1RM reassessed every 4 weeks	2 x week	24 weeks	Exercise type: Consistent Sets: Inconsistent Repetitions: Inconsistent Load: Unclear Intensity: Inconsistent Recovery: Consistent Progression: Inconsistent Frequency: Inconsistent Duration: Inconsistent
Marcora et al (2005)	1. Chest press 2. Seated leg extension 3. Rowing 4. Bicep curl 5. Triceps extension 6. Leg press 7. Leg curl 8. Standing calf raises	4 sets	Set 1: 15 repetitions Sets 2-4: 8 repetitions (Repetition velocity: 1-2 seconds concentric/ eccentric)	Insufficiently described	Set 1: 40%1RM Sets 2-4: 80%1RM	1-2 minutes between sets and exercises	1RM reassessed at end of week 0, then every 2 weeks	3 x week	12 weeks	

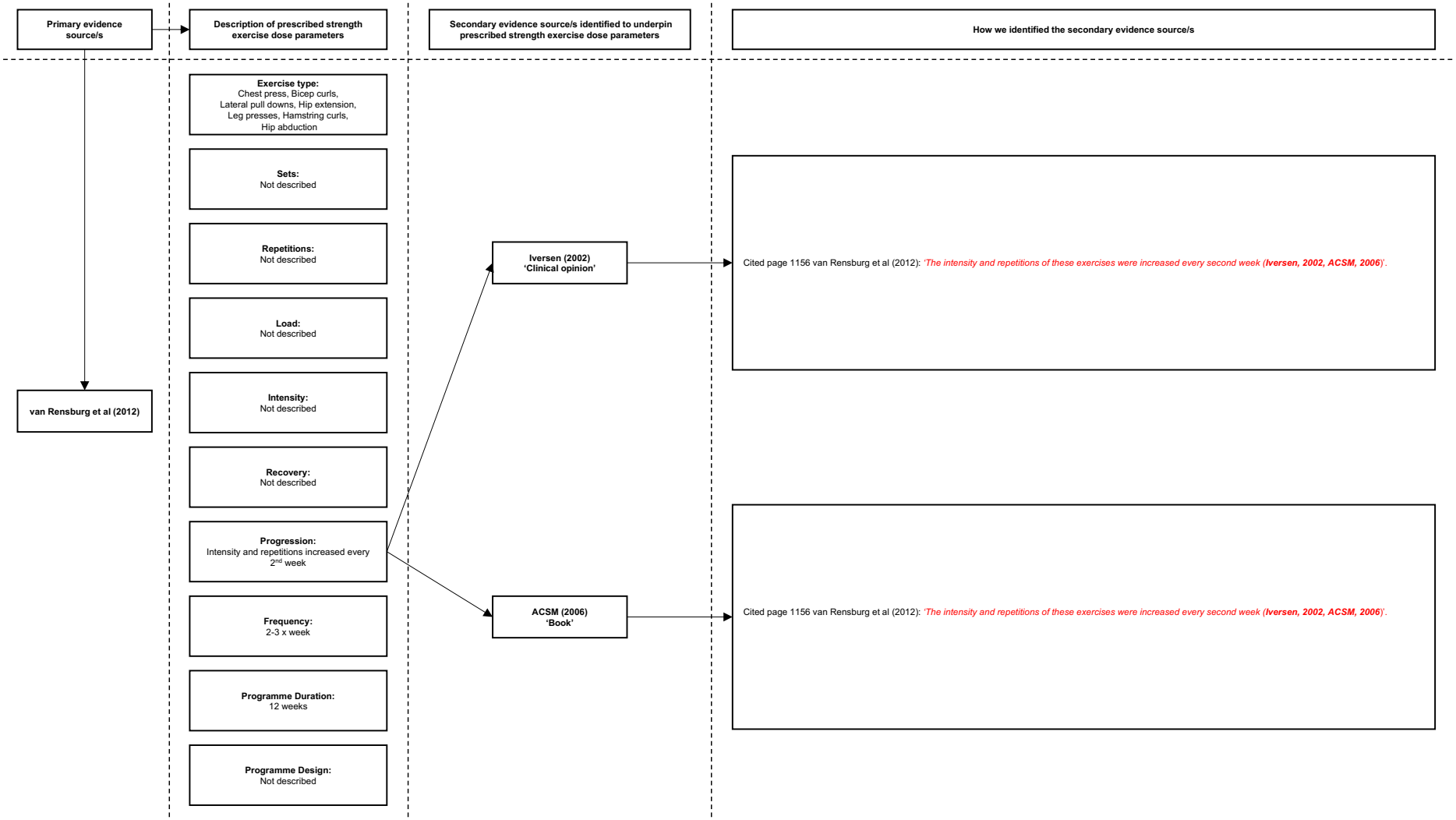
Strasser et al (2007)

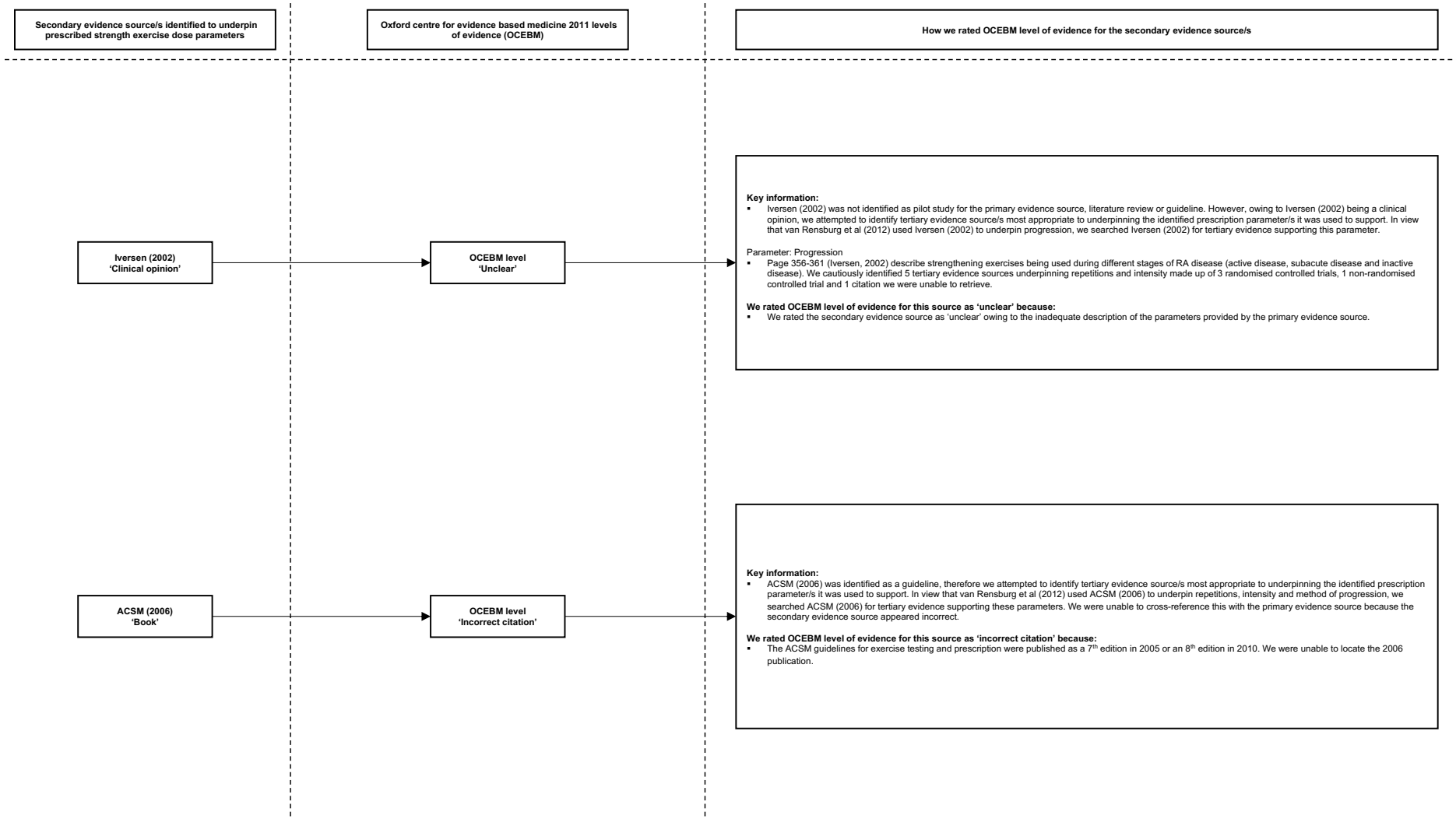

Primary evidence source/s
Description of prescribed strength exercise dose parameters
Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
How we identified the secondary evidence source/s
Exercise type:
Bench press, Chest cross, Shoulder press, Pull downs, Bicep curls, Triceps extension, Leg press, Abdominal exercises
Sets:
Week 1-2: Unclear,
Week 3 onwards: 2 progressing up to 4 sets by the end of the programme
Repetitions:
10-15
Load:
Not described
Intensity:
1st set 40%1RM, 2nd and 3rd sets 80%1RM
Recovery:
3 seconds between repetitions
Non-consecutive days of the week
Progression:
Load increased once 15reps successfully performed, weight was increased that permitted 10reps to be performed. Sets progressed systematically every 6weeks from 2 at beginning to 4 at the end of the programme
Frequency:
2 x week
Programme Duration:
6 months
Programme Design:
Not described.
Strasser et al (2011)
Williams et al (2007)
'AHA scientific statement'
Cited page 626 Strasser et al (2011): 'The ten to 15 repetitions maximum is equivalent to 70% 1RM for most exercises (Williams, 2007)'.


Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
Oxford centre for evidence based medicine 2011 levels of evidence (OCEBM)
How we rated OCEBM level of evidence for the secondary evidence source/s
Williams et al (2007) 'AHA scientific statement'
OCEBM level 'Unclear'
Key information:
Owing to Williams et al (2007) being identified as guideline, we we attempted to identify tertiary evidence source/s most appropriate to underpinning the identified prescription parameter/s it was used to support. In view that Strasser et al (2011) used Williams et al (2007) to underpin both repetitions and intensity, we searched Williams et al (2007) for tertiary evidence supporting these parameters.
Parameter: Repetitions and Intensity
Page 579 from Williams et al (2007) describes Table 5 'Load-repetition relationship for resistance training'. We identified 1 tertiary evidence source (Dingwell et al, 2006) underpinning this table. Dingwell et al (2006) is a book chapter from Throw (2006) and describes exercise prescription in cardiac rehabilitation. Pages 111-113 describe exercise prescription for resistance training and table 4.1 located on page 113 describes 'Load-repetition relationship for resistance training'. It is unclear what evidence was used to support this table.
We rated OCEBM level of evidence for this source as 'unclear' because:
It is unclear what evidence the table reported in the tertiary evidence source (Dingwell et al, 2006) is underpinned by.

Dose parameter / Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Strasser et al (2011)	1. Bench press 2. Chest cross 3. Shoulder press 4. Pull downs 5. Bicep curls 6. Triceps extension 7. Leg press 8. Abdominal exercises	Week 1-2: Unclear Week 3 onwards: 2 sets progressing up to 4 sets by the end of the programme	10-15 repetitions	Insufficiently described	1st set 40%1RM 2nd and 3rd sets 80%1RM	3 seconds between repetitions. Non-consecutive days of the week	Load increased once 15reps successfully performed, weight was increased that permitted 10reps to be performed. Sets progressed systematically every 6weeks from 2 at beginning to 4 at the end of the programme.	2 x week	6 months	Exercise type: n/a Sets: n/a Repetitions: Consistent Load: n/a Intensity: Consistent Recovery: n/a Progression: n/a Frequency: n/a Duration: n/a
Williams et al (2007)	Citation not used to support parameter	Citation not used to support parameter	8-12 repetitions per set for healthy sedentary adults or 10-15 repetitions at a low level of resistance, for example, <40% of 1RM, for older (>50-60 years of age), more frail persons, or cardiac patients	Citation not used to support parameter	40%1RM unclear for repetitions 80%1RM 8 repetitions	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	

van Rensburg et al (2012)

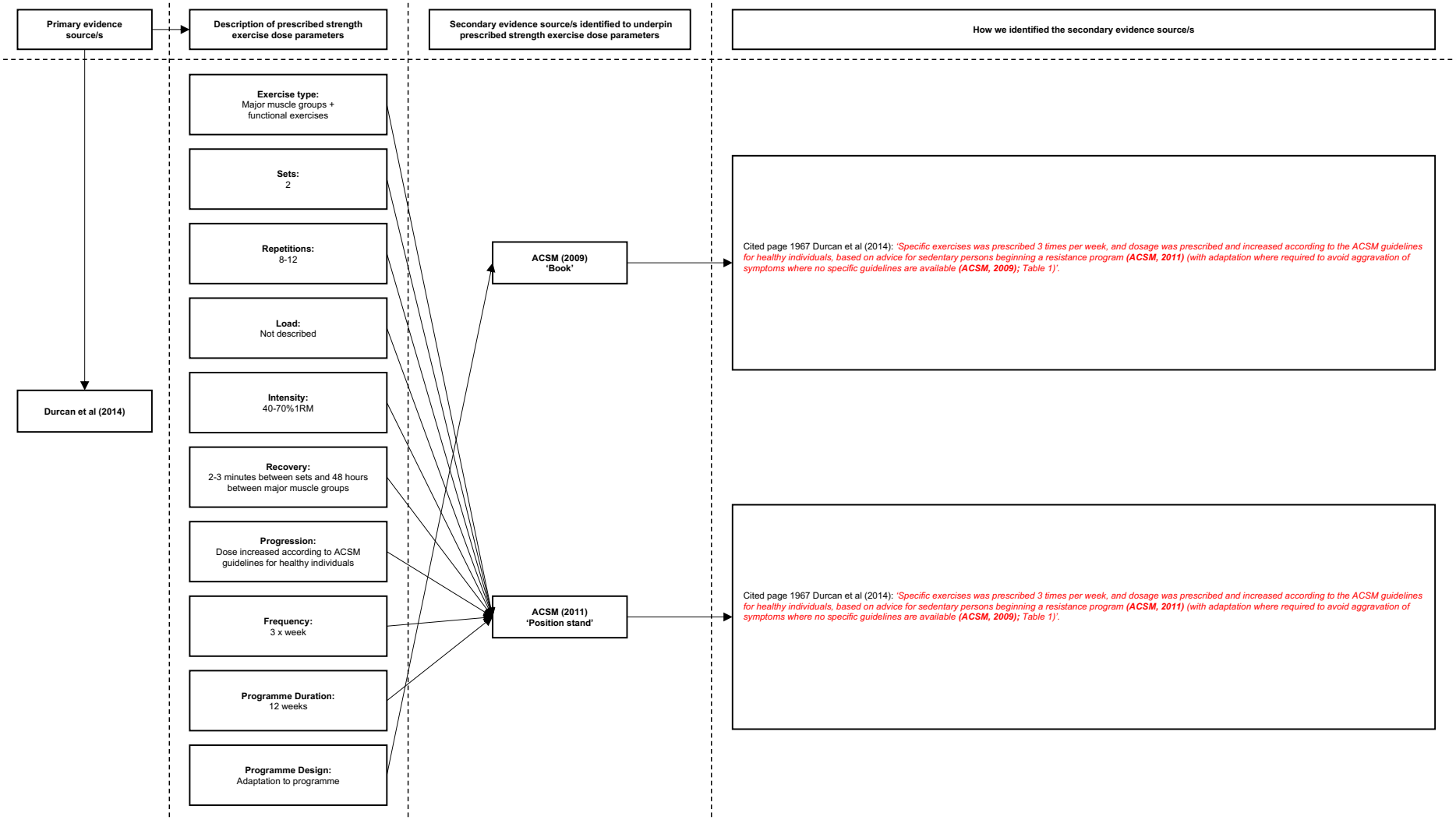

Primary evidence source/s
Description of prescribed strength exercise dose parameters
Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
How we identified the secondary evidence source/s
van Rensburg et al (2012)
Exercise type: Chest press, Bicep curls, Lateral pull downs, Hip extension, Leg presses, Hamstring curls, Hip abduction
Sets: Not described
Repetitions: Not described
Load: Not described
Intensity: Not described
Recovery: Not described
Progression: Intensity and repetitions increased every 2nd week
Frequency: 2-3 x week
Programme Duration: 12 weeks
Programme Design: Not described
Iversen (2002) 'Clinical opinion'
ACSM (2006) 'Book'
Cited page 1156 van Rensburg et al (2012): 'The intensity and repetitions of these exercises were increased every second week (Iversen, 2002, ACSM, 2006)'.
Cited page 1156 van Rensburg et al (2012): 'The intensity and repetitions of these exercises were increased every second week (Iversen, 2002, ACSM, 2006)'.

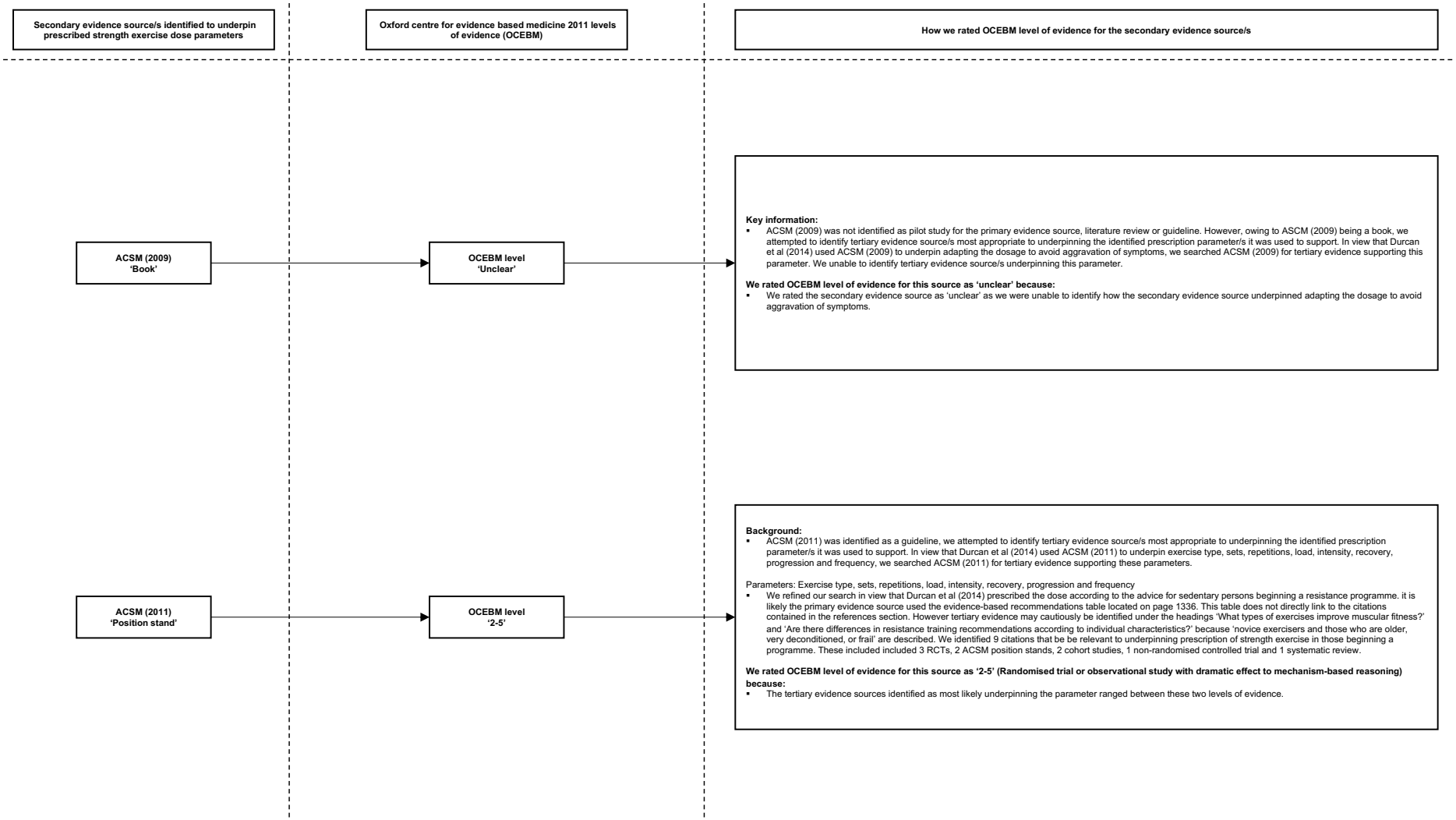

Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
Oxford centre for evidence based medicine 2011 levels of evidence (OCEBM)
How we rated OCEBM level of evidence for the secondary evidence source/s
Iversen (2002) 'Clinical opinion'
OCEBM level 'Unclear'
Key information:
Iversen (2002) was not identified as pilot study for the primary evidence source, literature review or guideline. However, owing to Iversen (2002) being a clinical opinion, we attempted to identify tertiary evidence source/s most appropriate to underpinning the identified prescription parameter/s it was used to support. In view that van Rensburg et al (2012) used Iversen (2002) to underpin progression, we searched Iversen (2002) for tertiary evidence supporting this parameter.
Parameter: Progression
Page 356-361 (Iversen, 2002) describe strengthening exercises being used during different stages of RA disease (active disease, subacute disease and inactive disease). We cautiously identified 5 tertiary evidence sources underpinning repetitions and intensity made up of 3 randomised controlled trials, 1 non-randomised controlled trial and 1 citation we were unable to retrieve.
We rated OCEBM level of evidence for this source as 'unclear' because:
We rated the secondary evidence source as 'unclear' owing to the inadequate description of the parameters provided by the primary evidence source.
ACSM (2006) 'Book'
OCEBM level 'Incorrect citation'
Key information:
ACSM (2006) was identified as a guideline, therefore we attempted to identify tertiary evidence source/s most appropriate to underpinning the identified prescription parameter/s it was used to support. In view that van Rensburg et al (2012) used ACSM (2006) to underpin repetitions, intensity and method of progression, we searched ACSM (2006) for tertiary evidence supporting these parameters. We were unable to cross-reference this with the primary evidence source because the secondary evidence source appeared incorrect.
We rated OCEBM level of evidence for this source as 'incorrect citation' because:
The ACSM guidelines for exercise testing and prescription were published as a 7th edition in 2005 or an 8th edition in 2010. We were unable to locate the 2006 publication.

Dose parameter / Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
van Rensburg et al (2012)	1. Chest press 2. Bicep curls 3. Lateral pull downs 4. Hip extension 5. Leg presses 6. Hamstring curls 7. Hip abduction	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	Intensity and repetitions increased every 2nd week	2 x week	12 weeks	Exercise type: n/a Sets: n/a Repetitions: n/a Load: n/a Intensity: n/a Recovery: n/a Progression: Inconsistent Frequency: n/a Duration: n/a
Iversen (2002)	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Isometric exercises are continued and the number of repetitions and sets can be increased as tolerated. Dynamic exercises with light resistance are now incorporated into the exercise regimen	Citation not used to support parameter	Citation not used to support parameter	

Dose parameter / Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
van Rensburg et al (2012)	1. Chest press 2. Bicep curls 3. Lateral pull downs 4. Hip extension 5. Leg presses 6. Hamstring curls 7. Hip abduction	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	Intensity and repetitions increased every 2nd week	2 x week	12 weeks	Exercise type: n/a Sets: n/a Repetitions: n/a Load: n/a Intensity: n/a Recovery: n/a Progression: Unclear Frequency: n/a Duration: n/a
ACSM (2006)	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Unclear	Citation not used to support parameter	Citation not used to support parameter	

Durcan et al (2014)

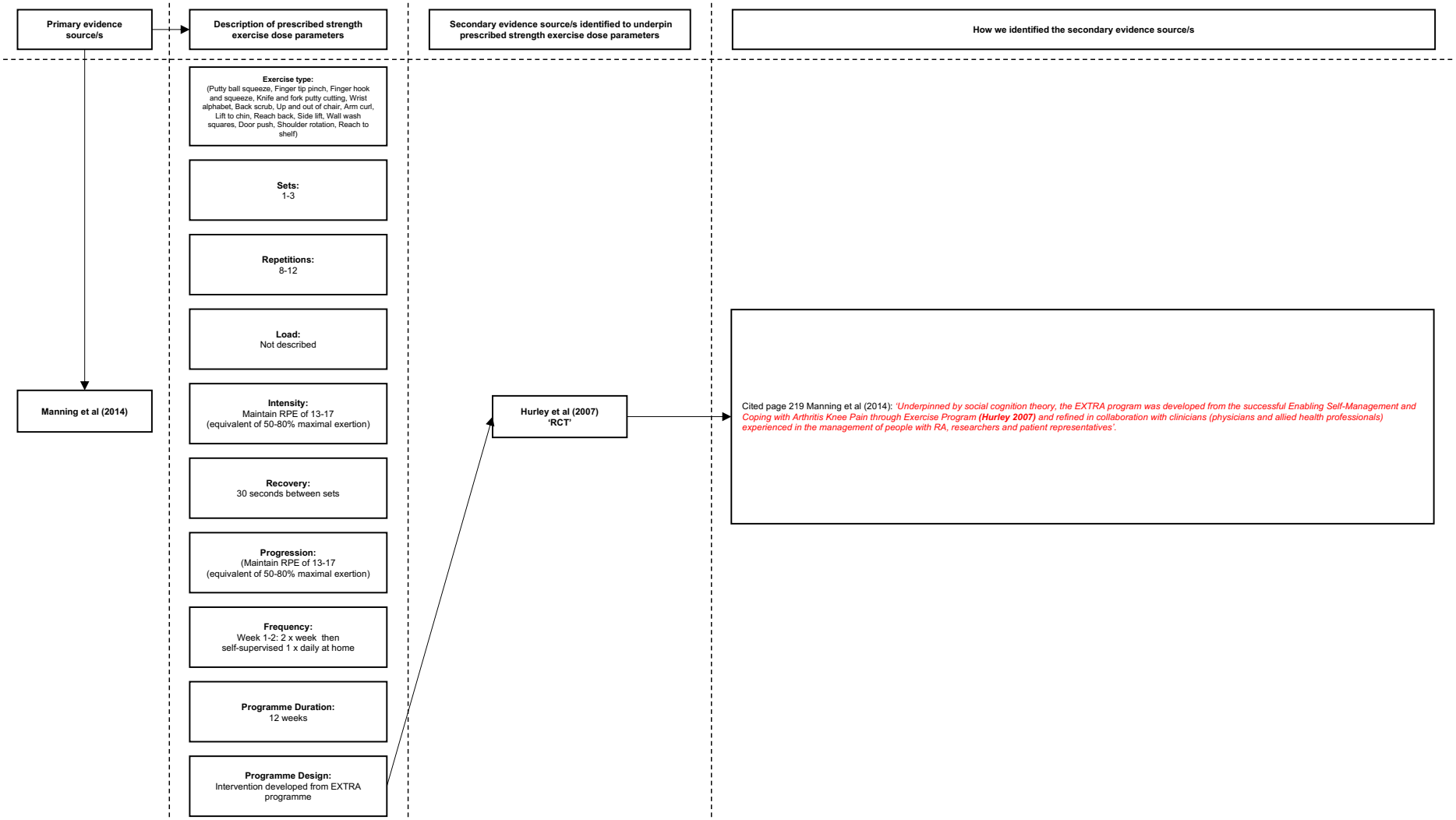

Primary evidence source/s
Description of prescribed strength exercise dose parameters
Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
How we identified the secondary evidence source/s
Durcan et al (2014)
Exercise type: Major muscle groups + functional exercises
Sets: 2
Repetitions: 8-12
Load: Not described
Intensity: 40-70%1RM
Recovery: 2-3 minutes between sets and 48 hours between major muscle groups
Progression: Dose increased according to ACSM guidelines for healthy individuals
Frequency: 3 x week
Programme Duration: 12 weeks
Programme Design: Adaptation to programme
ACSM (2009) 'Book'
ACSM (2011) 'Position stand'
Cited page 1967 Durcan et al (2014): 'Specific exercises was prescribed 3 times per week, and dosage was prescribed and increased according to the ACSM guidelines for healthy individuals, based on advice for sedentary persons beginning a resistance program (ACSM, 2011) (with adaptation where required to avoid aggravation of symptoms where no specific guidelines are available (ACSM, 2009); Table 1)'.
Cited page 1967 Durcan et al (2014): 'Specific exercises was prescribed 3 times per week, and dosage was prescribed and increased according to the ACSM guidelines for healthy individuals, based on advice for sedentary persons beginning a resistance program (ACSM, 2011) (with adaptation where required to avoid aggravation of symptoms where no specific guidelines are available (ACSM, 2009); Table 1)'.

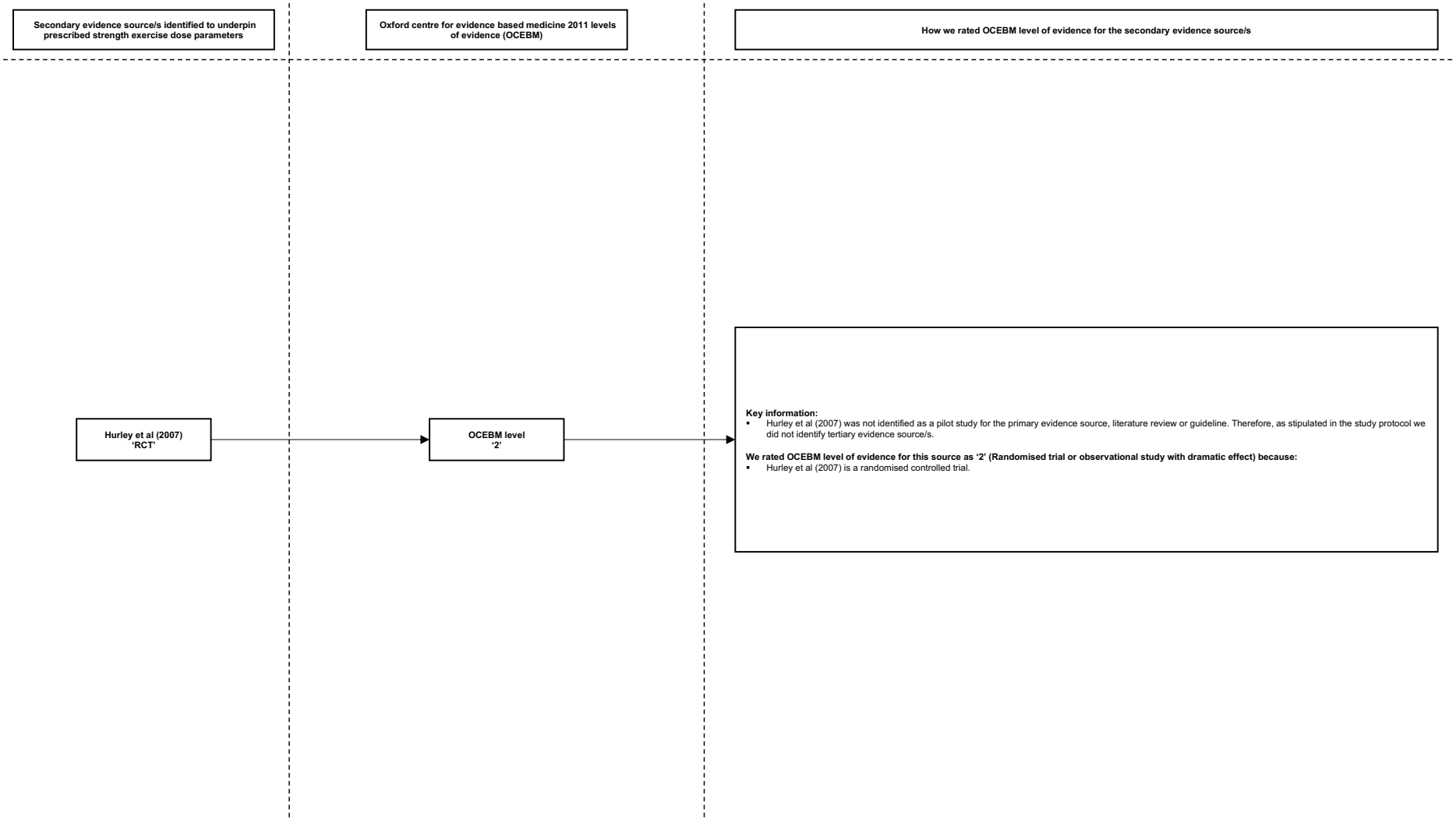

Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
Oxford centre for evidence based medicine 2011 levels of evidence (OCEBM)
How we rated OCEBM level of evidence for the secondary evidence source/s
ACSM (2009) 'Book'
OCEBM level 'Unclear'
Key information:
ACSM (2009) was not identified as pilot study for the primary evidence source, literature review or guideline. However, owing to ASCM (2009) being a book, we attempted to identify tertiary evidence source/s most appropriate to underpinning the identified prescription parameter/s it was used to support. In view that Durcan et al (2014) used ACSM (2009) to underpin adapting the dosage to avoid aggravation of symptoms, we searched ACSM (2009) for tertiary evidence supporting this parameter. We unable to identify tertiary evidence source/s underpinning this parameter.
We rated OCEBM level of evidence for this source as 'unclear' because:
We rated the secondary evidence source as 'unclear' as we were unable to identify how the secondary evidence source underpinned adapting the dosage to avoid aggravation of symptoms.
ACSM (2011) 'Position stand'
OCEBM level '2-5'
Background:
ACSM (2011) was identified as a guideline, we attempted to identify tertiary evidence source/s most appropriate to underpinning the identified prescription parameter/s it was used to support. In view that Durcan et al (2014) used ACSM (2011) to underpin exercise type, sets, repetitions, load, intensity, recovery, progression and frequency, we searched ACSM (2011) for tertiary evidence supporting these parameters.
Parameters: Exercise type, sets, repetitions, load, intensity, recovery, progression and frequency
We refined our search in view that Durcan et al (2014) prescribed the dose according to the advice for sedentary persons beginning a resistance programme. it is likely the primary evidence source used the evidence-based recommendations table located on page 1336. This table does not directly link to the citations contained in the references section. However tertiary evidence may cautiously be identified under the headings 'What types of exercises improve muscular fitness?' and 'Are there differences in resistance training recommendations according to individual characteristics?' because 'novice exercisers and those who are older, very deconditioned, or frail' are described. We identified 9 citations that be be relevant to underpinning prescription of strength exercise in those beginning a programme. These included included 3 RCTs, 2 ACSM position stands, 2 cohort studies, 1 non-randomised controlled trial and 1 systematic review.
We rated OCEBM level of evidence for this source as '2-5' (Randomised trial or observational study with dramatic effect to mechanism-based reasoning) because:
The tertiary evidence sources identified as most likely underpinning the parameter ranged between these two levels of evidence.

Dose parameter / Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Durcan et al (2014)	Major muscle groups + functional exercises	2 sets	8-12 repetitions	Insufficiently described	40-70%1RM	2-3 minutes between sets and 48 hours between major muscle groups	Dose increased according to ACSM guidelines for healthy individuals	3 x week	12 weeks	Exercise type: Unclear Sets: Unclear Repetitions: Consistent Load: Unclear Intensity: Unclear Recovery: Unclear Progression: Unclear Frequency: Unclear Duration: Unclear
ACSM (2009)	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	

Dose parameter / Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Durcan et al (2014)	Major muscle groups + functional exercises	2 sets	8-12 repetitions	Insufficiently described	40-70%1RM	2-3 minutes between sets and 48 hours between major muscle groups	Dose increased according to ACSM guidelines for healthy individuals	3 x week	12 weeks	Exercise type: Consistent Sets: Consistent Repetitions: Consistent Load: Unclear Intensity: Consistent Recovery: Consistent Progression: Consistent Frequency: Consistent Duration: Unclear
ACSM (2011)	Resistance exercise involving each major muscle group are recommended. A variety of exercise equipment and/or body weight can be used to perform these exercises.	1-4 sets	8-20 repetitions	Unclear	40-≥80%1RM	Rest intervals of 2-3minutes between each set of repetitions are effective. A rest of ≥48 hours between sessions for any single muscle group is recommended	A gradual progression of greater resistance and/or more repetitions per set and/or increasing frequency is recommended.	Each major muscle group should be trained on 2-3 x week.	No specific duration of training has been identified for effectiveness.	

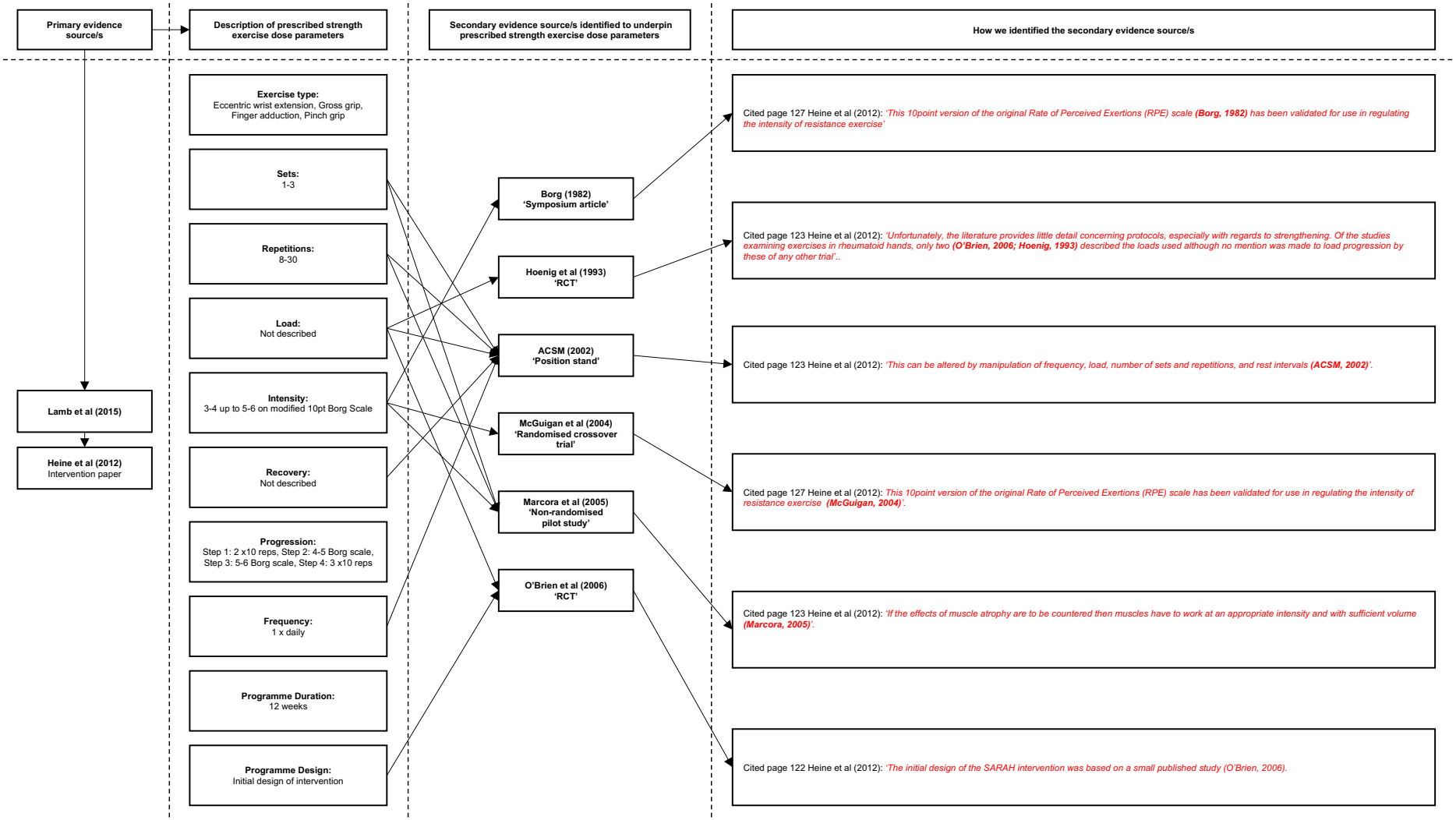
Manning et al (2014)

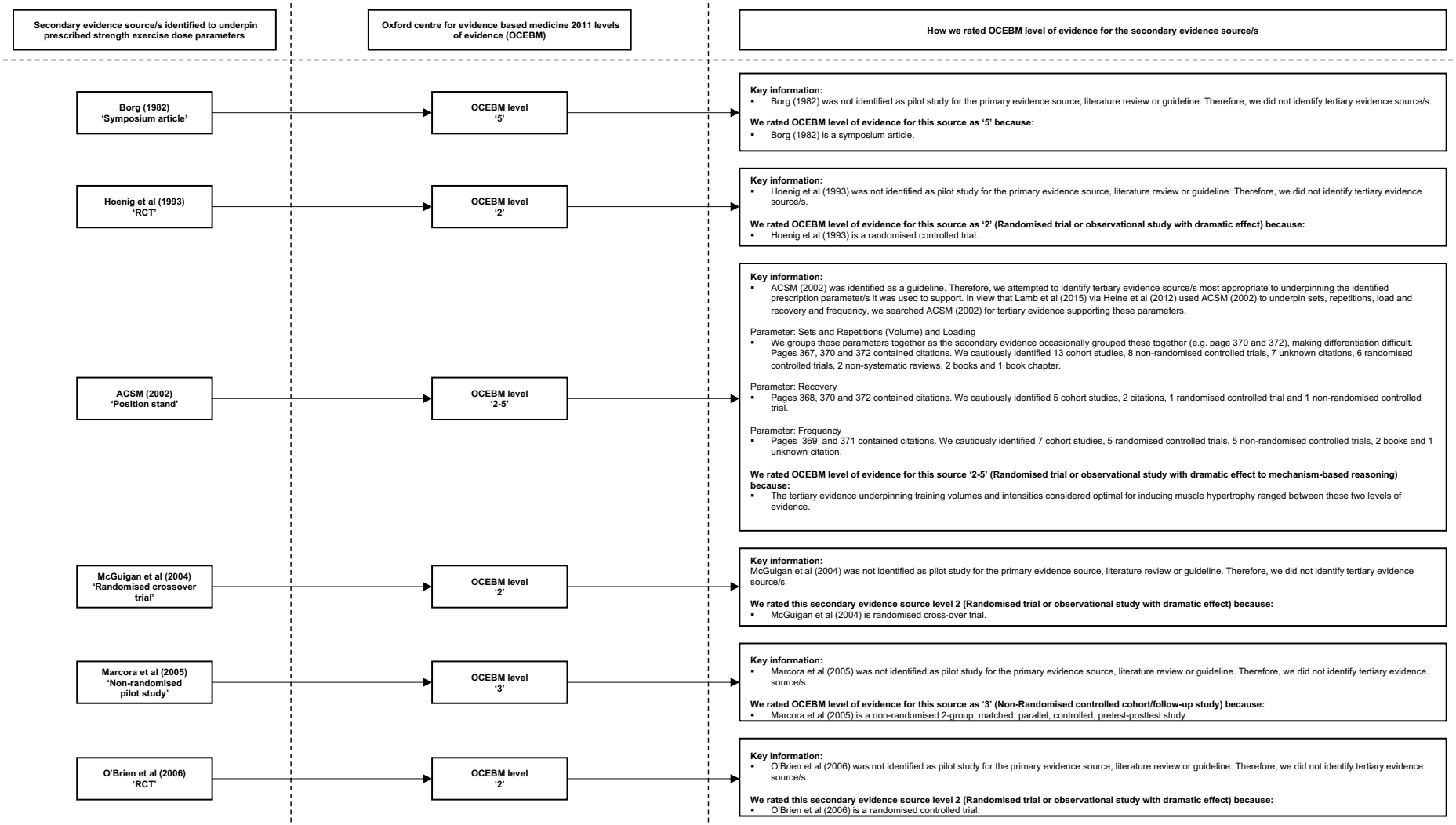

Primary evidence source/s
Description of prescribed strength exercise dose parameters
Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
How we identified the secondary evidence source/s
Exercise type:
(Putty ball squeeze, Finger tip pinch, Finger hook and squeeze, Knife and fork putty cutting, Wrist alphabet, Back scrub, Up and out of chair, Arm curl, Lift to chin, Reach back, Side lift, Wall wash squares, Door push, Shoulder rotation, Reach to shelf)
Sets:
1-3
Repetitions:
8-12
Load:
Not described
Intensity:
Maintain RPE of 13-17
(equivalent of 50-80% maximal exertion)
Recovery:
30 seconds between sets
Progression:
(Maintain RPE of 13-17
(equivalent of 50-80% maximal exertion)
Frequency:
Week 1-2: 2 x week then
self-supervised 1 x daily at home
Programme Duration:
12 weeks
Programme Design:
Intervention developed from EXTRA programme
Manning et al (2014)
Hurley et al (2007)
'RCT'
Cited page 219 Manning et al (2014): 'Underpinned by social cognition theory, the EXTRA program was developed from the successful Enabling Self-Management and Coping with Arthritis Knee Pain through Exercise Program (Hurley 2007) and refined in collaboration with clinicians (physicians and allied health professionals) experienced in the management of people with RA, researchers and patient representatives'.


Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
Oxford centre for evidence based medicine 2011 levels of evidence (OCEBM)
How we rated OCEBM level of evidence for the secondary evidence source/s
Hurley et al (2007) 'RCT'
OCEBM level '2'
Key information:
Hurley et al (2007) was not identified as a pilot study for the primary evidence source, literature review or guideline. Therefore, as stipulated in the study protocol we did not identify tertiary evidence source/s.
We rated OCEBM level of evidence for this source as '2' (Randomised trial or observational study with dramatic effect) because:
Hurley et al (2007) is a randomised controlled trial.

Dose parameter Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Manning et al (2014)	1. (Putty ball squeeze 2. Finger tip pinch 3. Finger hook and squeeze 4. Knife and fork putty cutting 5. Wrist alphabet 6. Back scrub 7. Up and out of chair 8. Arm curl 9. Lift to chin 10. Reach back 11. Side lift 12. Wall wash squares 13. Door push 14. Shoulder rotation 15. Reach to shelf	1-3 sets	8-12 repetitions	Insufficiently described	Maintain RPE of 13-17 (equivalent of 50-80% maximal exertion)	30 seconds between sets	(Maintain RPE of 13-17 (equivalent of 50-80% maximal exertion	Week 1-2: 2 x week then self-supervised 1 x daily at home	12 weeks	Exercise type: Inconsistent Sets: Unclear Repetitions: Inconsistent Load: Unclear Intensity: Unclear Recovery: Unclear Progression: Inconsistent Frequency: Inconsistent Duration: Inconsistent
Hurley et al (2007)	1. Exercise bike 2. Quadriceps bench 3. Theraband 4. Sit to stand 5. Step ups 6. Wall squats 7. Step downs 8. Knee wedge	1. Unclear 2. Unclear 3. Unclear 4. Unclear 5. Unclear 6. Unclear 7. Unclear 8. Unclear	1. 5 minutes 2. 24 reps 3. 2 minutes 4. 2 minutes 5. 1 minute 6. 1 minute 7. 1 minute 8. 1 minute	1. Unclear 2. Unclear 3. Light/mode rate/heavy 4. Unclear 5. Unclear 6. Unclear 7. Unclear 8. 0-5kg	1. Unclear 2. Unclear 3. Unclear 4. Unclear 5. Unclear 6. Unclear 7. Unclear 8. Unclear	1. Unclear 2. 5 secs 3. Unclear 4. Unclear 5. Unclear 6. Unclear 7. Unclear 8. Unclear	1. Increase time or resistance 2. Increase repetitions 3. Increase time or resistance 4. Increase time or decrease seat height 5. Increase time or step height (low, medium, high) 6. Increase time 7. Progression of exercise 6, increase time 8. Increase load 9. Unclear	2 x week	6 weeks	

Lamb et al (2015)


Primary evidence source/s
Description of prescribed strength exercise dose parameters
Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
How we identified the secondary evidence source/s
Lamb et al (2015)
Heine et al (2012) Intervention paper
Exercise type: Eccentric wrist extension, Gross grip, Finger adduction, Pinch grip
Sets: 1-3
Repetitions: 8-30
Load: Not described
Intensity: 3-4 up to 5-6 on modified 10pt Borg Scale
Recovery: Not described
Progression: Step 1: 2 x10 reps, Step 2: 4-5 Borg scale, Step 3: 5-6 Borg scale, Step 4: 3 x10 reps
Frequency: 1 x daily
Programme Duration: 12 weeks
Programme Design: Initial design of intervention
Borg (1982) 'Symposium article'
Hoenig et al (1993) 'RCT'
ACSM (2002) 'Position stand'
McGuigan et al (2004) 'Randomised crossover trial'
Marcora et al (2005) 'Non-randomised pilot study'
O'Brien et al (2006) 'RCT'
Cited page 127 Heine et al (2012): 'This 10point version of the original Rate of Perceived Exertions (RPE) scale (Borg, 1982) has been validated for use in regulating the intensity of resistance exercise'
Cited page 123 Heine et al (2012): 'Unfortunately, the literature provides little detail concerning protocols, especially with regards to strengthening. Of the studies examining exercises in rheumatoid hands, only two (O'Brien, 2006; Hoenig, 1993) described the loads used although no mention was made to load progression by these of any other trial'..
Cited page 123 Heine et al (2012): 'This can be altered by manipulation of frequency, load, number of sets and repetitions, and rest intervals (ACSM, 2002)'.
Cited page 127 Heine et al (2012): This 10point version of the original Rate of Perceived Exertions (RPE) scale has been validated for use in regulating the intensity of resistance exercise (McGuigan, 2004)'.
Cited page 123 Heine et al (2012): 'If the effects of muscle atrophy are to be countered then muscles have to work at an appropriate intensity and with sufficient volume (Marcora, 2005)'.
Cited page 122 Heine et al (2012): 'The initial design of the SARAH intervention was based on a small published study (O'Brien, 2006).


Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
Oxford centre for evidence based medicine 2011 levels of evidence (OCEBM)
How we rated OCEBM level of evidence for the secondary evidence source/s
Borg (1982) 'Symposium article'
OCEBM level '5'
Key information:
Borg (1982) was not identified as pilot study for the primary evidence source, literature review or guideline. Therefore, we did not identify tertiary evidence source/s.
We rated OCEBM level of evidence for this source as '5' because:
Borg (1982) is a symposium article.
Hoenig et al (1993) 'RCT'
OCEBM level '2'
Key information:
Hoenig et al (1993) was not identified as pilot study for the primary evidence source, literature review or guideline. Therefore, we did not identify tertiary evidence source/s.
We rated OCEBM level of evidence for this source as '2' (Randomised trial or observational study with dramatic effect) because:
Hoenig et al (1993) is a randomised controlled trial.
ACSM (2002) 'Position stand'
OCEBM level '2-5'
Key information:
ACSM (2002) was identified as a guideline. Therefore, we attempted to identify tertiary evidence source/s most appropriate to underpinning the identified prescription parameter/s it was used to support. In view that Lamb et al (2015) via Heine et al (2012) used ACSM (2002) to underpin sets, repetitions, load and recovery and frequency, we searched ACSM (2002) for tertiary evidence supporting these parameters.
Parameter: Sets and Repetitions (Volume) and Loading
We groups these parameters together as the secondary evidence occasionally grouped these together (e.g. page 370 and 372), making differentiation difficult. Pages 367, 370 and 372 contained citations. We cautiously identified 13 cohort studies, 8 non-randomised controlled trials, 7 unknown citations, 6 randomised controlled trials, 2 non-systematic reviews, 2 books and 1 book chapter.
Parameter: Recovery
Pages 368, 370 and 372 contained citations. We cautiously identified 5 cohort studies, 2 citations, 1 randomised controlled trial and 1 non-randomised controlled trial.
Parameter: Frequency
Pages 369 and 371 contained citations. We cautiously identified 7 cohort studies, 5 randomised controlled trials, 5 non-randomised controlled trials, 2 books and 1 unknown citation.
We rated OCEBM level of evidence for this source '2-5' (Randomised trial or observational study with dramatic effect to mechanism-based reasoning) because:
The tertiary evidence underpinning training volumes and intensities considered optimal for inducing muscle hypertrophy ranged between these two levels of evidence.
McGuigan et al (2004) 'Randomised crossover trial'
OCEBM level '2'
Key information:
McGuigan et al (2004) was not identified as pilot study for the primary evidence source, literature review or guideline. Therefore, we did not identify tertiary evidence source/s
We rated this secondary evidence source level 2 (Randomised trial or observational study with dramatic effect) because:
McGuigan et al (2004) is randomised cross-over trial.
Marcora et al (2005) 'Non-randomised pilot study'
OCEBM level '3'
Key information:
Marcora et al (2005) was not identified as pilot study for the primary evidence source, literature review or guideline. Therefore, we did not identify tertiary evidence source/s.
We rated OCEBM level of evidence for this source as '3' (Non-Randomised controlled cohort/follow-up study) because:
Marcora et al (2005) is a non-randomised 2-group, matched, parallel, controlled, pretest-posttest study
O'Brien et al (2006) 'RCT'
OCEBM level '2'
Key information:
O'Brien et al (2006) was not identified as pilot study for the primary evidence source, literature review or guideline. Therefore, we did not identify tertiary evidence source/s.
We rated this secondary evidence source level 2 (Randomised trial or observational study with dramatic effect) because:
O'Brien et al (2006) is a randomised controlled trial.

Dose parameter / Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Lamb et al (2015)	1. Eccentric wrist extension 2. Gross grip 3. Finger adduction 4. Pinch grip	1-3 sets	8-30 repetitions	Insufficiently described	3-4 to 5-6 on modified Borg scale	Insufficiently described	Step 1: 2 x10 reps Step 2: 4-5 Borg scale Step 3: 5-6 Borg scale Step 4: 3 x10 reps	1 x daily	12 weeks	Exercise type: n/a Sets: n/a Repetitions: n/a Load: Unclear Intensity: Unclear Recovery: n/a Progression: n/a Frequency: n/a Duration: n/a
Borg (1982)	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Unclear	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	

Dose parameter Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Lamb et al (2015)	1. Eccentric wrist extension 2. Gross grip 3. Finger adduction 4. Pinch grip	1-3 sets	8-30 repetitions	Insufficiently described	3-4 to 5-6 on modified Borg scale	Insufficiently described	Step 1: 2 x10 reps Step 2: 4-5 Borg scale Step 3: 5-6 Borg scale Step 4: 3 x10 reps	1 x daily	12 weeks	Exercise type: n/a Sets: n/a Repetitions: n/a Load: Unclear Intensity: n/a Recovery: n/a Progression: n/a Frequency: n/a Duration: n/a
Hoenig et al (1993)	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Theraputty with a plasticity rating of 85 (medium soft grade/BeOK red)	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	

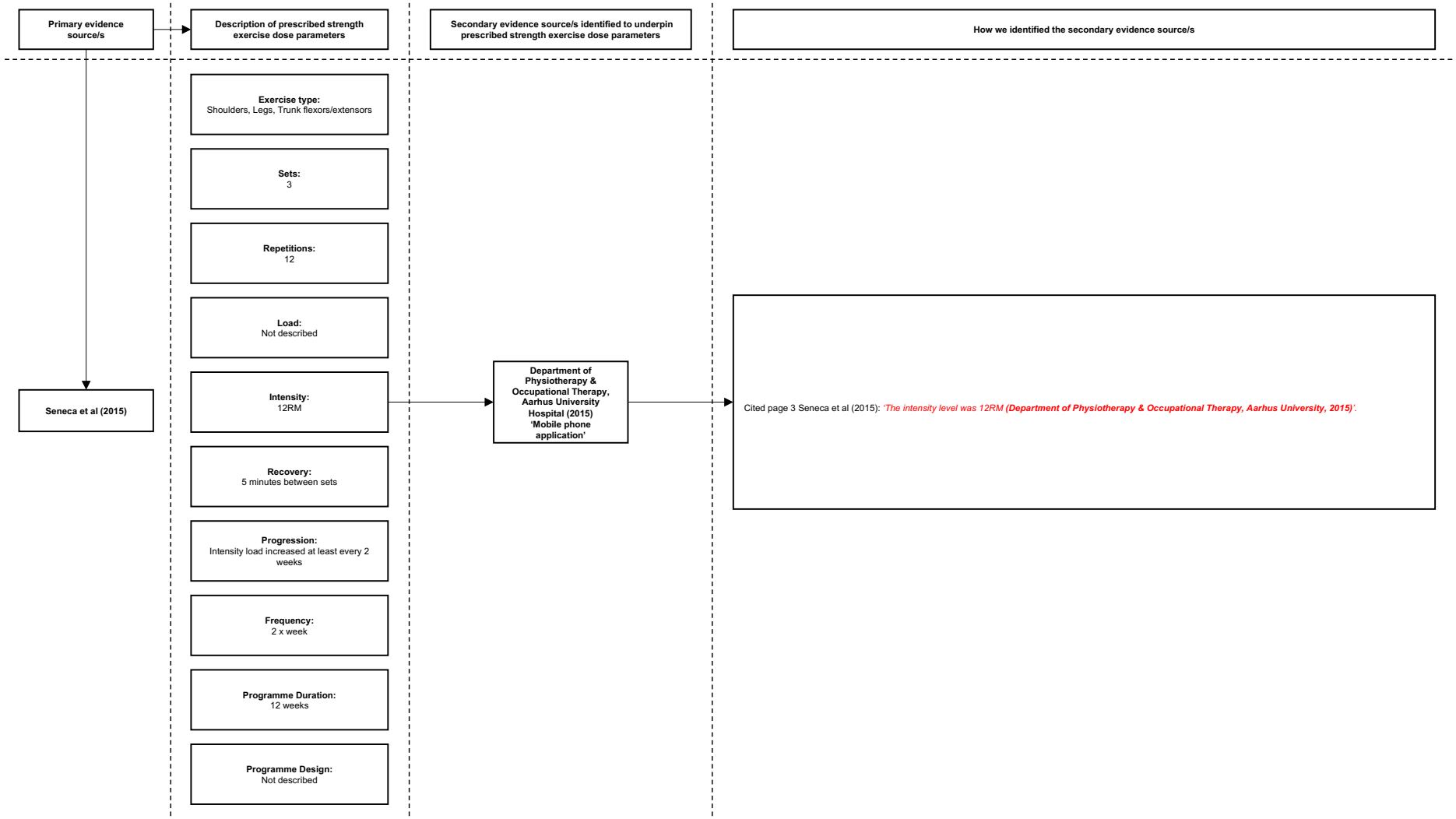
Dose parameter / Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Lamb et al (2015)	1. Eccentric wrist extension 2. Gross grip 3. Finger adduction 4. Pinch grip	1-3 sets	8-30 repetitions	Insufficiently described	3-4 to 5-6 on modified Borg scale	Insufficiently described	Step 1: 2 x10 reps Step 2: 4-5 Borg scale Step 3: 5-6 Borg scale Step 4: 3 x10 reps	1 x daily	12 weeks	Exercise type: n/a Sets: Consistent Repetitions: Consistent Load: Unclear Intensity: n/a Recovery: Unclear Progression: n/a Frequency: Inconsistent Duration: n/a
ACSM (2002)	Citation not used to support parameter	1-3	8-12	Novice 60-70%1RM	Citation not used to support parameter	2-3 minutes for core and 1-2 minutes for others	Citation not used to support parameter	Novice 2-3 x week Intermediate 2-4 x week Advanced 4-6 x week	Citation not used to support parameter	

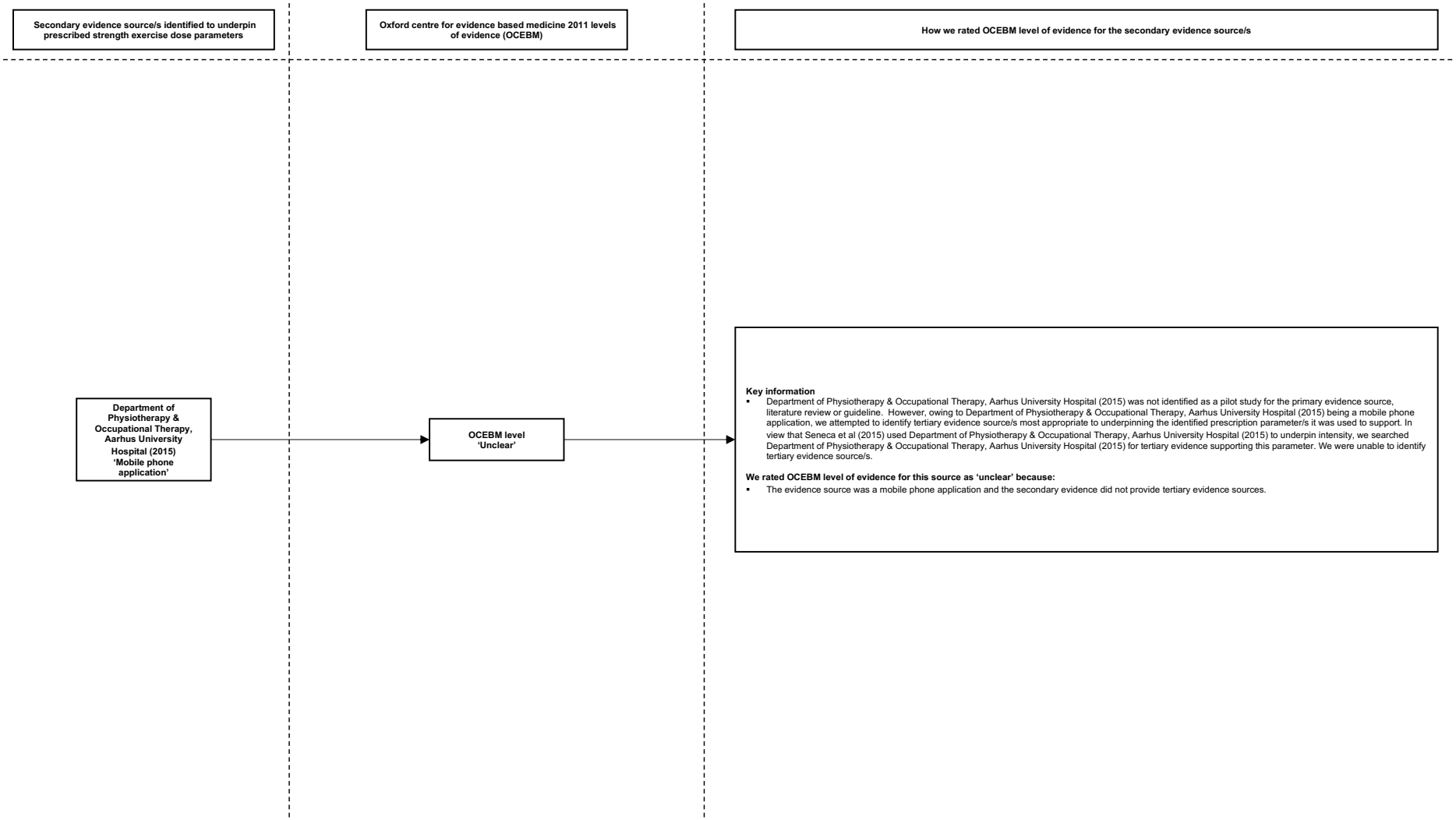
Dose parameter Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Lamb et al (2015)	1. Eccentric wrist extension 2. Gross grip 3. Finger adduction 4. Pinch grip	1-3 sets	8-30 repetitions	Insufficiently described	3-4 to 5-6 on modified Borg scale	Insufficiently described	Step 1: 2 x10 reps Step 2: 4-5 Borg scale Step 3: 5-6 Borg scale Step 4: 3 x10 reps	1 x daily	12 weeks	Exercise type: n/a Sets: n/a Repetitions: n/a Load: n/a Intensity: Unclear Recovery: n/a Progression: n/a Frequency: n/a Duration: n/a
McGuigan et al (2002)	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Unclear	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	

Dose parameter Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Lamb et al (2015)	1. Eccentric wrist extension 2. Gross grip 3. Finger adduction 4. Pinch grip	1-3 sets	8-30 repetitions	Insufficiently described	3-4 to 5-6 on modified Borg scale	Insufficiently described	Step 1: 2 x10 reps Step 2: 4-5 Borg scale Step 3: 5-6 Borg scale Step 4: 3 x10 reps	1 x daily	12 weeks	Exercise type: Inconsistent Sets: Inconsistent Repetitions: Inconsistent Load: n/a Intensity: Inconsistent Recovery: n/a Progression: n/a Frequency: n/a Duration: n/a
Marcora et al (2005)	1. Chest press 2. Seated leg extension 3. Seated row 4. Bicep curl 5. Triceps extension 6. Leg press 7. Leg curl 8. Standing calf raises	4 sets	Set 1: 15 repetitions Sets 2-4: 8 repetitions (Repetition velocity: 1-2 seconds concentric/ Eccentric)	Citation not used to support parameter	Set 1: 40%1RM Sets 2-4: 80%1RM	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	

Dose parameter / Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Lamb et al (2015)	1. Eccentric wrist extension 2. Gross grip 3. Finger adduction 4. Pinch grip	1-3 sets	8-30 repetitions	Insufficiently described	3-4 to 5-6 on modified Borg scale	Insufficiently described	Step 1: 2 x10 reps Step 2: 4-5 Borg scale Step 3: 5-6 Borg scale Step 4: 3 x10 reps	1 x daily	12 weeks	Exercise type: Consistent Sets: Unclear Repetitions: Inconsistent Load: Unclear Intensity: Unclear Recovery: Unclear Progression: Inconsistent Frequency: Inconsistent Duration: Inconsistent
O' Brien et al (2006)	1. Pinch grip using a towel 2. Wrist extension using theratube resistive band.	Unclear	Baseline: 5 repetitions 1 month: 10 repetitions 3 months: 20 repetitions	Unclear	Unclear	Unclear	Increase repetitions from 5 at baseline to 10 at 1 month and 20 repetitions of the exercises from 3 months onwards.	2 x daily	6 months	

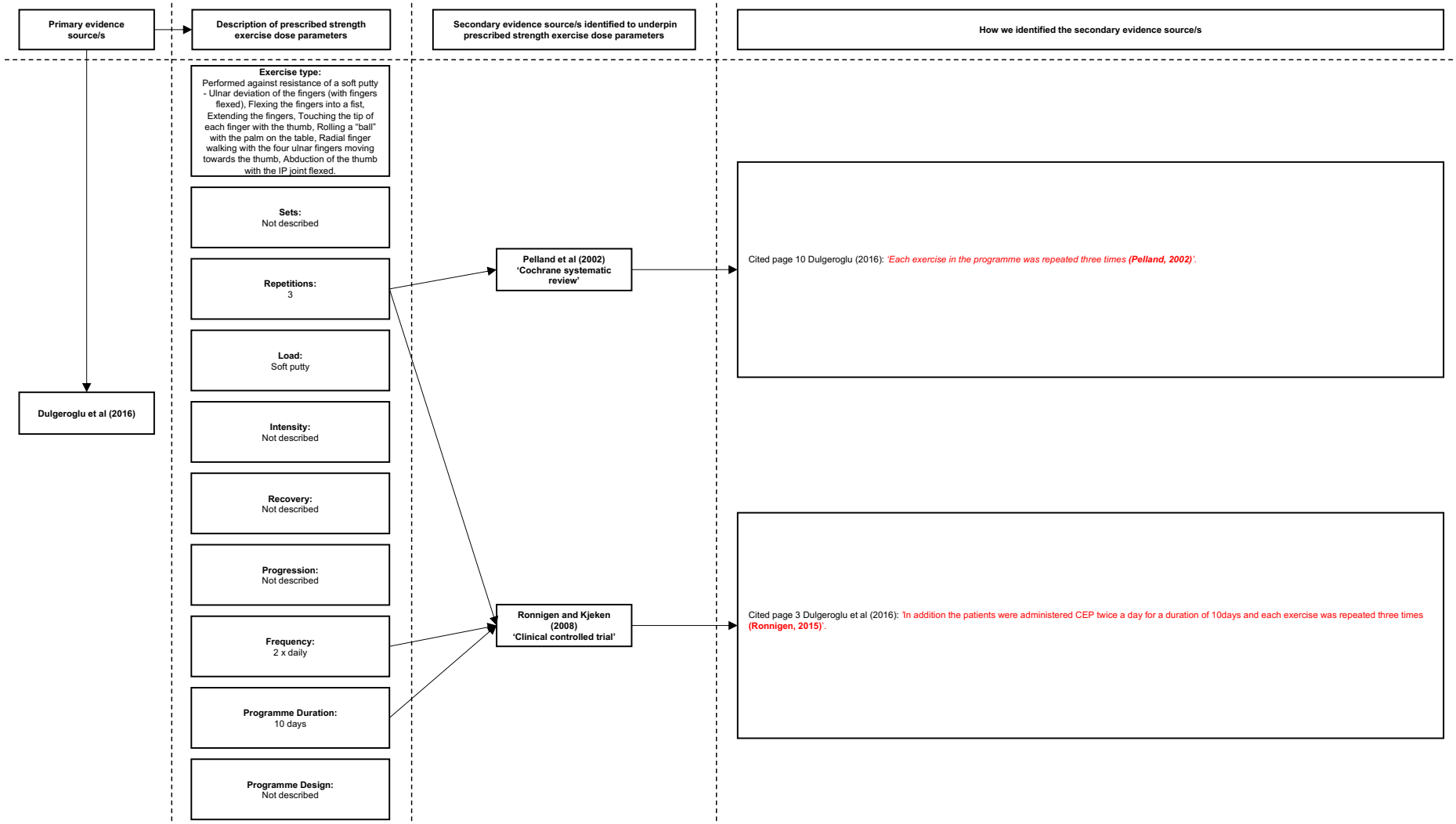
Seneca et al (2015)

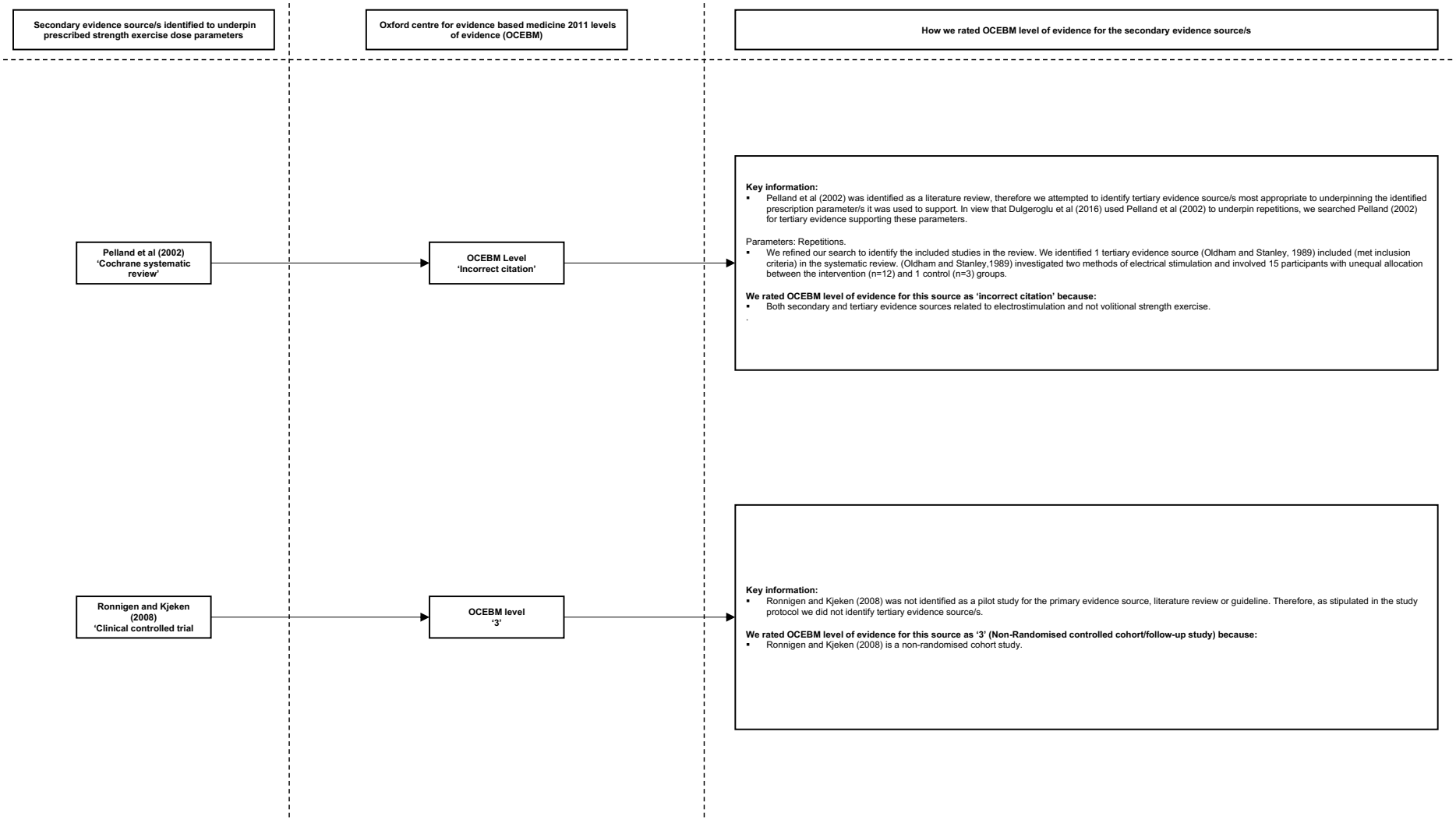

Primary evidence source/s
Description of prescribed strength exercise dose parameters
Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
How we identified the secondary evidence source/s
Exercise type: Shoulders, Legs, Trunk flexors/extensors
Sets: 3
Repetitions: 12
Load: Not described
Intensity: 12RM
Recovery: 5 minutes between sets
Progression: Intensity load increased at least every 2 weeks
Frequency: 2 x week
Programme Duration: 12 weeks
Programme Design: Not described
Seneca et al (2015)
Department of Physiotherapy & Occupational Therapy, Aarhus University Hospital (2015) 'Mobile phone application'
Cited page 3 Seneca et al (2015): 'The intensity level was 12RM (Department of Physiotherapy & Occupational Therapy, Aarhus University, 2015)'.


Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
Oxford centre for evidence based medicine 2011 levels of evidence (OCEBM)
How we rated OCEBM level of evidence for the secondary evidence source/s
Department of Physiotherapy & Occupational Therapy, Aarhus University Hospital (2015) 'Mobile phone application'
OCEBM level 'Unclear'
Key information
Department of Physiotherapy & Occupational Therapy, Aarhus University Hospital (2015) was not identified as a pilot study for the primary evidence source, literature review or guideline. However, owing to Department of Physiotherapy & Occupational Therapy, Aarhus University Hospital (2015) being a mobile phone application, we attempted to identify tertiary evidence source/s most appropriate to underpinning the identified prescription parameter/s it was used to support. In view that Seneca et al (2015) used Department of Physiotherapy & Occupational Therapy, Aarhus University Hospital (2015) to underpin intensity, we searched Department of Physiotherapy & Occupational Therapy, Aarhus University Hospital (2015) for tertiary evidence supporting this parameter. We were unable to identify tertiary evidence source/s.
We rated OCEBM level of evidence for this source as 'unclear' because:
The evidence source was a mobile phone application and the secondary evidence did not provide tertiary evidence sources.

Dose parameter Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Seneca et al (2015)	1. Shoulders 2. Legs 3. Trunk flexors/extensors	3 sets	12 repetitions	Insufficiently described	12RM (Repetition Maximum)	5 minutes between sets	Intensity load increased at least every 2 weeks	2 x week	12 weeks	Exercise type: n/a Sets: n/a Repetitions: Inconsistent Load: n/a Intensity: Consistent Recovery: n/a Progression: n/a Frequency: n/a Duration: n/a
Department of Physiotherapy & Occupational Therapy, Aarhus University Hospital (2015)	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	The right workout weight is the weight you can just lift 12 times.	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	

Dulgeroglu et al (2016)

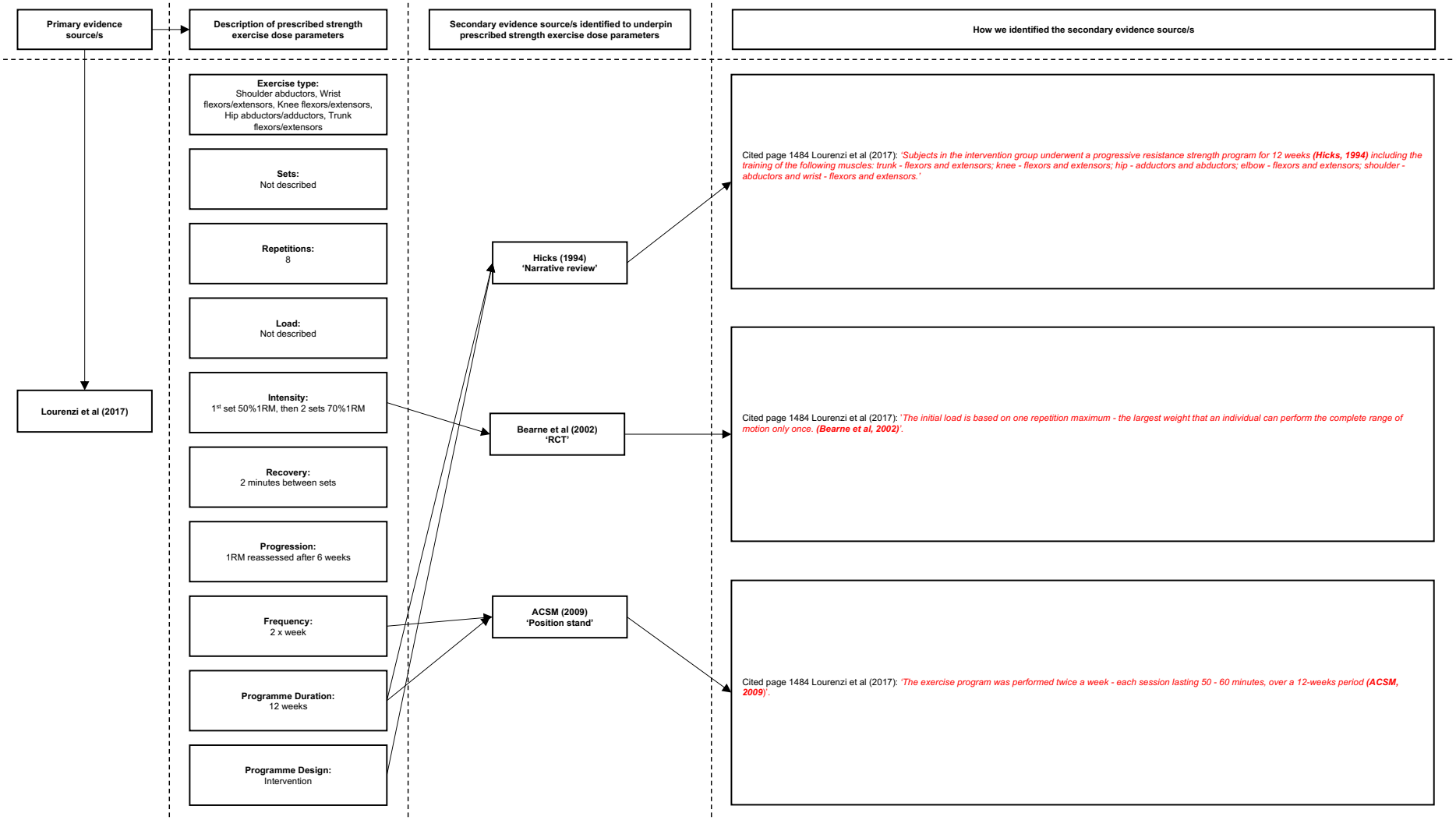

Primary evidence source/s
Description of prescribed strength exercise dose parameters
Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
How we identified the secondary evidence source/s
Dulgeroglu et al (2016)
Exercise type: Performed against resistance of a soft putty - Ulnar deviation of the fingers (with fingers flexed), Flexing the fingers into a fist, Extending the fingers, Touching the tip of each finger with the thumb, Rolling a "ball" with the palm on the table, Radial finger walking with the four ulnar fingers moving towards the thumb, Abduction of the thumb with the IP joint flexed.
Sets: Not described
Repetitions: 3
Load: Soft putty
Intensity: Not described
Recovery: Not described
Progression: Not described
Frequency: 2 x daily
Programme Duration: 10 days
Programme Design: Not described
Pelland et al (2002) 'Cochrane systematic review'
Ronnigen and Kjeken (2008) 'Clinical controlled trial'
Cited page 10 Dulgeroglu (2016): 'Each exercise in the programme was repeated three times (Pelland, 2002)'.
Cited page 3 Dulgeroglu et al (2016): 'In addition the patients were administered CEP twice a day for a duration of 10days and each exercise was repeated three times (Ronnigen, 2015)'.

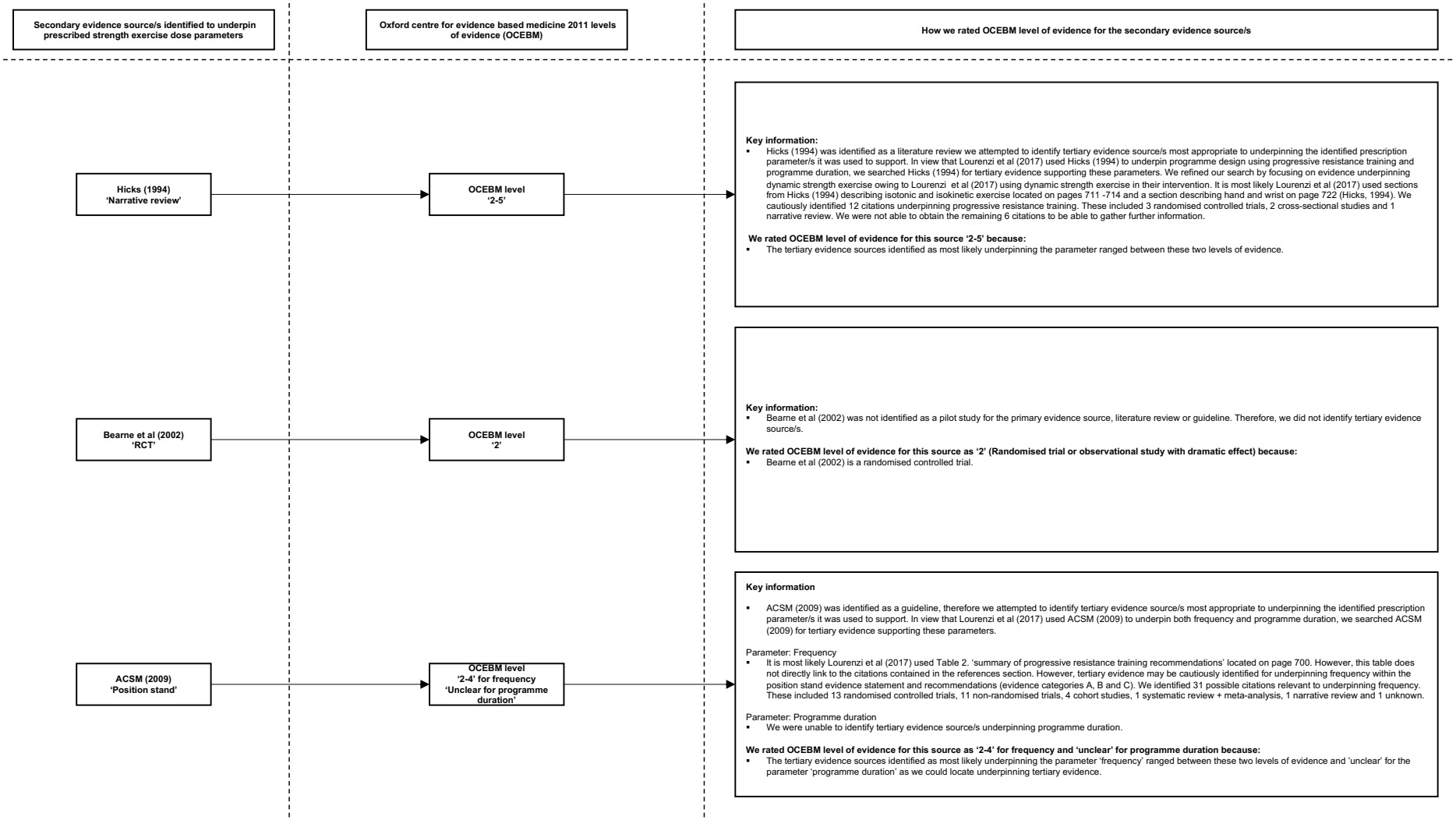

Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
Oxford centre for evidence based medicine 2011 levels of evidence (OCEBM)
How we rated OCEBM level of evidence for the secondary evidence source/s
Pelland et al (2002) 'Cochrane systematic review'
OCEBM Level 'Incorrect citation'
Key information:
Pelland et al (2002) was identified as a literature review, therefore we attempted to identify tertiary evidence source/s most appropriate to underpinning the identified prescription parameter/s it was used to support. In view that Dulgeroglu et al (2016) used Pelland et al (2002) to underpin repetitions, we searched Pelland (2002) for tertiary evidence supporting these parameters.
Parameters: Repetitions.
We refined our search to identify the included studies in the review. We identified 1 tertiary evidence source (Oldham and Stanley, 1989) included (met inclusion criteria) in the systematic review. (Oldham and Stanley,1989) investigated two methods of electrical stimulation and involved 15 participants with unequal allocation between the intervention (n=12) and 1 control (n=3) groups.
We rated OCEBM level of evidence for this source as 'incorrect citation' because:
Both secondary and tertiary evidence sources related to electrostimulation and not volitional strength exercise.
Ronnigen and Kjeken (2008) 'Clinical controlled trial
OCEBM level '3'
Key information:
Ronnigen and Kjeken (2008) was not identified as a pilot study for the primary evidence source, literature review or guideline. Therefore, as stipulated in the study protocol we did not identify tertiary evidence source/s.
We rated OCEBM level of evidence for this source as '3' (Non-Randomised controlled cohort/follow-up study) because:
Ronnigen and Kjeken (2008) is a non-randomised cohort study.

Dose parameter / Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Dulgeroglu et al (2016)	1. Ulnar deviation of the fingers (with fingers flexed) 2. Flexing the fingers into a fist, 3. Extending the fingers 4. Touching the tip of each finger with the thumb 5. Rolling a "ball" with the palm on the table 6. Radial finger walking with the four ulnar fingers moving towards the thumb, Abduction of the thumb with the IP joint flexed.	Insufficiently described	3 repetitions	Soft putty	Insufficiently described	Insufficiently described	Insufficiently described	2 x daily	10 days	Exercise type: n/a Sets: n/a Repetitions: Inconsistent Load: n/a Intensity: n/a Recovery: n/a Progression: n/a Frequency: n/a Duration: n/a
Pelland et al (2002)	Citation not used to support parameter	Citation not used to support parameter	Unclear	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	

Dose parameter / Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Dulgeroglu et al (2016)	1. Ulnar deviation of the fingers (with fingers flexed) 2. Flexing the fingers into a fist, 3. Extending the fingers 4. Touching the tip of each finger with the thumb 5. Rolling a "ball" with the palm on the table 6. Radial finger walking with the four ulnar fingers moving towards the thumb, 7. Abduction of the thumb with the IP joint flexed.	Insufficiently described	3 repetitions	Soft putty	Insufficiently described	Insufficiently described	Insufficiently described	2 x daily	10 days	Exercise type: n/a Sets: n/a Repetitions: Consistent Load: n/a Intensity: n/a Recovery: n/a Progression: n/a Frequency: Inconsistent Duration: Inconsistent
Ronnigen and Kjeken et al (2008)	Citation not used to support parameter	Citation not used to support parameter	3 repetitions	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Participants in the conservative hand exercise programme instructed to exercise to usual training regimes	14 weeks	

Lourenzi et al (2017)


Primary evidence source/s
Description of prescribed strength exercise dose parameters
Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
How we identified the secondary evidence source/s
Lourenzi et al (2017)
Exercise type: Shoulder abductors, Wrist flexors/extensors, Knee flexors/extensors, Hip abductors/adductors, Trunk flexors/extensors
Sets: Not described
Repetitions: 8
Load: Not described
Intensity: 1st set 50%1RM, then 2 sets 70%1RM
Recovery: 2 minutes between sets
Progression: 1RM reassessed after 6 weeks
Frequency: 2 x week
Programme Duration: 12 weeks
Programme Design: Intervention
Hicks (1994) 'Narrative review'
Bearne et al (2002) 'RCT'
ACSM (2009) 'Position stand'
Cited page 1484 Lourenzi et al (2017): 'Subjects in the intervention group underwent a progressive resistance strength program for 12 weeks (Hicks, 1994) including the training of the following muscles: trunk - flexors and extensors; knee - flexors and extensors; hip - adductors and abductors; elbow - flexors and extensors; shoulder - abductors and wrist - flexors and extensors.'
Cited page 1484 Lourenzi et al (2017): 'The initial load is based on one repetition maximum - the largest weight that an individual can perform the complete range of motion only once. (Bearne et al, 2002)'.
Cited page 1484 Lourenzi et al (2017): 'The exercise program was performed twice a week - each session lasting 50 - 60 minutes, over a 12-weeks period (ACSM, 2009)'.

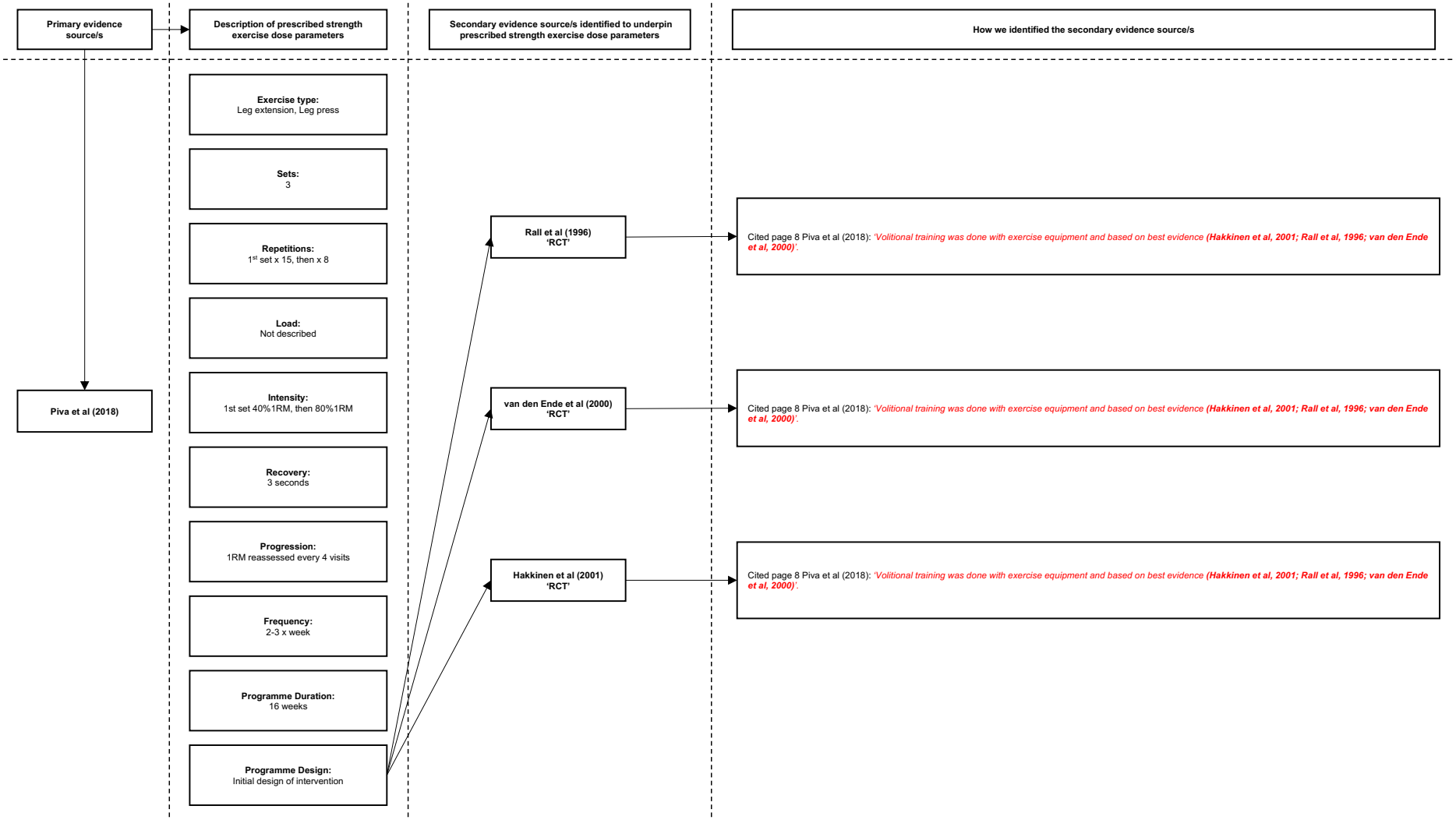

Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
Oxford centre for evidence based medicine 2011 levels of evidence (OCEBM)
How we rated OCEBM level of evidence for the secondary evidence source/s
Hicks (1994) 'Narrative review'
OCEBM level '2-5'
Key information:
Hicks (1994) was identified as a literature review we attempted to identify tertiary evidence source/s most appropriate to underpinning the identified prescription parameter/s it was used to support. In view that Lourenzi et al (2017) used Hicks (1994) to underpin programme design using progressive resistance training and programme duration, we searched Hicks (1994) for tertiary evidence supporting these parameters. We refined our search by focusing on evidence underpinning dynamic strength exercise owing to Lourenzi et al (2017) using dynamic strength exercise in their intervention. It is most likely Lourenzi et al (2017) used sections from Hicks (1994) describing isotonic and isokinetic exercise located on pages 711 -714 and a section describing hand and wrist on page 722 (Hicks, 1994). We cautiously identified 12 citations underpinning progressive resistance training. These included 3 randomised controlled trials, 2 cross-sectional studies and 1 narrative review. We were not able to obtain the remaining 6 citations to be able to gather further information.
We rated OCEBM level of evidence for this source '2-5' because:
The tertiary evidence sources identified as most likely underpinning the parameter ranged between these two levels of evidence.
Bearne et al (2002) 'RCT'
OCEBM level '2'
Key information:
Bearne et al (2002) was not identified as a pilot study for the primary evidence source, literature review or guideline. Therefore, we did not identify tertiary evidence source/s.
We rated OCEBM level of evidence for this source as '2' (Randomised trial or observational study with dramatic effect) because:
Bearne et al (2002) is a randomised controlled trial.
ACSM (2009) 'Position stand'
OCEBM level '2-4' for frequency 'Unclear for programme duration'
Key information
ACSM (2009) was identified as a guideline, therefore we attempted to identify tertiary evidence source/s most appropriate to underpinning the identified prescription parameter/s it was used to support. In view that Lourenzi et al (2017) used ACSM (2009) to underpin both frequency and programme duration, we searched ACSM (2009) for tertiary evidence supporting these parameters.
Parameter: Frequency
It is most likely Lourenzi et al (2017) used Table 2. 'summary of progressive resistance training recommendations' located on page 700. However, this table does not directly link to the citations contained in the references section. However, tertiary evidence may be cautiously identified for underpinning frequency within the position stand evidence statement and recommendations (evidence categories A, B and C). We identified 31 possible citations relevant to underpinning frequency. These included 13 randomised controlled trials, 11 non-randomised trials, 4 cohort studies, 1 systematic review + meta-analysis, 1 narrative review and 1 unknown.
Parameter: Programme duration
We were unable to identify tertiary evidence source/s underpinning programme duration.
We rated OCEBM level of evidence for this source as '2-4' for frequency and 'unclear' for programme duration because:
The tertiary evidence sources identified as most likely underpinning the parameter 'frequency' ranged between these two levels of evidence and 'unclear' for the parameter 'programme duration' as we could locate underpinning tertiary evidence.

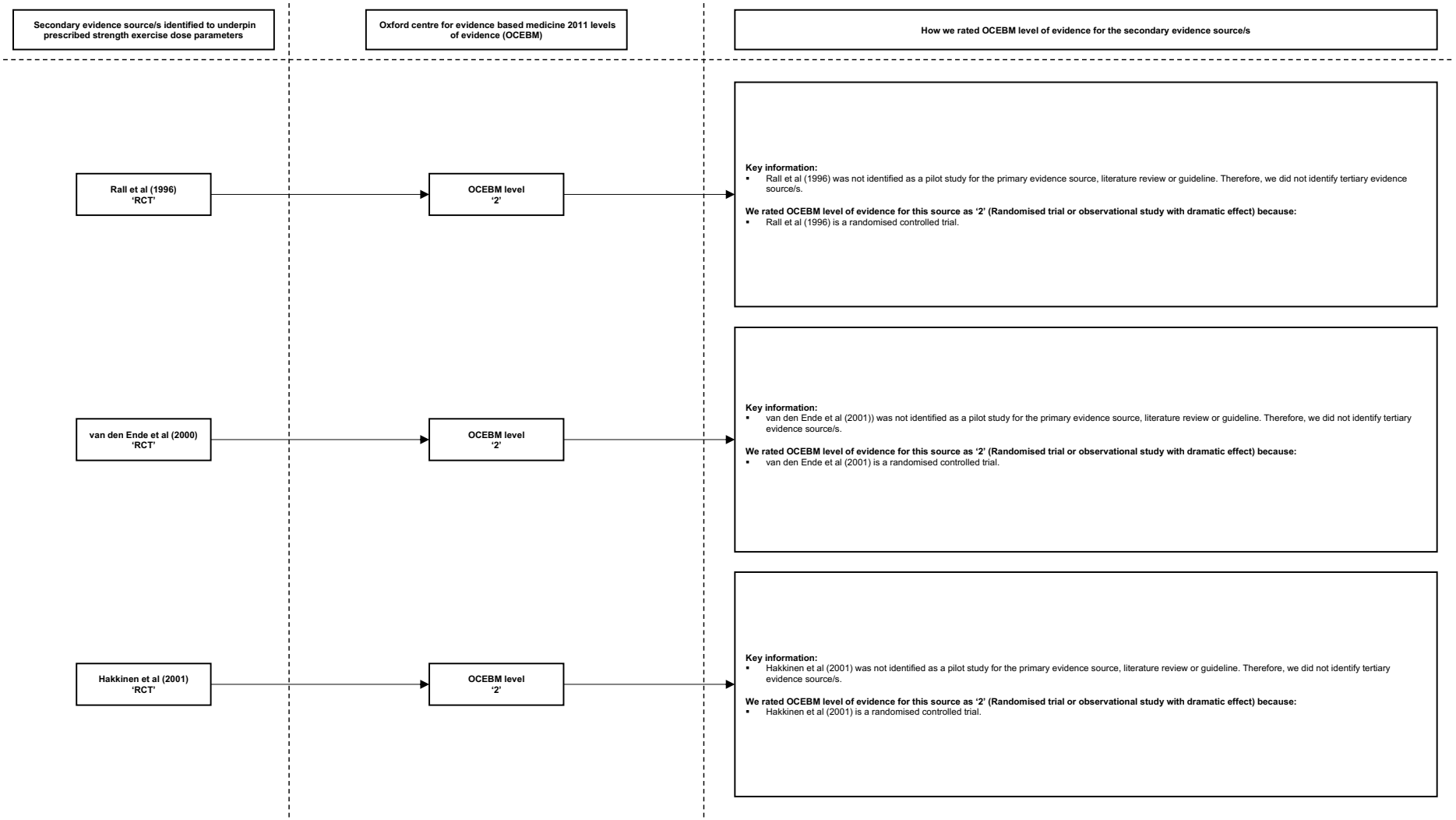
Dose parameter Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Lourenzi et al (2017)	1. Shoulder abductors 2. Wrist flexors/extensors 3. Knee flexors/extensors 4. Hip abductors/adductors 5. Trunk flexors/extensors	Insufficiently described	8 repetitions	Insufficiently described	1st set 50%1RM then 2 sets 70%1RM	2 minutes between sets	1RM reassessed after 6 weeks	2 x week	12 weeks	Exercise type: Unclear Sets: Unclear Repetitions: Inconsistent Load: Unclear Intensity: Unclear Recovery: Inconsistent Progression: Inconsistent Frequency: Consistent
Hicks (1994)	1. Isometric 2. Isotonic 3. Isokinetic	Unclear	10 repetitions	1-2 pounds	Unclear	Isometric exercise 20 seconds rest between contractions Isometric exercise Unclear	After 1 month of isometric exercises the patient can be advanced to an isotonic exercise program	The exercise program is done 3 x week for each muscle group to be exercised.	Programs usually require 12-weeks duration.	

Dose parameter / Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Lourenzi et al (2017)	1. Shoulder abductors 2. Wrist flexors/extensors 3. Knee flexors/extensors 4. Hip abductors/adductors 5. Trunk flexors/extensors	Insufficiently described	8 repetitions	Insufficiently described	1st set 50%1RM then 2 sets 70%1RM	2 minutes between sets	1RM reassessed after 6 weeks	2 x week	12 weeks	Exercise type: n/a Sets: n/a Repetitions: n/a Load: n/a Intensity: Inconsistent Recovery: n/a Progression: n/a Frequency: n/a Duration: n/a
Bearne et al (2002)	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Isometric MVC Functional 1-5 minutes recording number of repetitions	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	

Dose parameter / Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Lourenzi et al (2017)	1. Shoulder abductors 2. Wrist flexors/extensors 3. Knee flexors/extensors 4. Hip abductors/adductors 5. Trunk flexors/extensors	Insufficiently described	8 repetitions	Insufficiently described	1st set 50%1RM then 2 sets 70%1RM	2 minutes between sets	1RM reassessed after 6 weeks	2 x week	12 weeks	Exercise type: n/a Sets: n/a Repetitions: n/a Load: n/a Intensity: n/a Recovery: n/a Progression: n/a Frequency: Consistent Duration: Unclear
ACSM (2009)	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Novice 2 -3 x week Intermediate 3-4 x week Advanced 4-6 x week	Unclear	

Piva et al (2018)


Primary evidence source/s
Description of prescribed strength exercise dose parameters
Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
How we identified the secondary evidence source/s
Piva et al (2018)
Exercise type: Leg extension, Leg press
Sets: 3
Repetitions: 1st set x 15, then x 8
Load: Not described
Intensity: 1st set 40%1RM, then 80%1RM
Recovery: 3 seconds
Progression: 1RM reassessed every 4 visits
Frequency: 2-3 x week
Programme Duration: 16 weeks
Programme Design: Initial design of intervention
Rall et al (1996) 'RCT'
van den Ende et al (2000) 'RCT'
Hakkinen et al (2001) 'RCT'
Cited page 8 Piva et al (2018): 'Volitional training was done with exercise equipment and based on best evidence (Hakkinen et al, 2001; Rall et al, 1996; van den Ende et al, 2000)'.
Cited page 8 Piva et al (2018): 'Volitional training was done with exercise equipment and based on best evidence (Hakkinen et al, 2001; Rall et al, 1996; van den Ende et al, 2000)'.
Cited page 8 Piva et al (2018): 'Volitional training was done with exercise equipment and based on best evidence (Hakkinen et al, 2001; Rall et al, 1996; van den Ende et al, 2000)'.


Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
Oxford centre for evidence based medicine 2011 levels of evidence (OCEBM)
How we rated OCEBM level of evidence for the secondary evidence source/s
Rall et al (1996) 'RCT'
OCEBM level '2'
Key information:
Rall et al (1996) was not identified as a pilot study for the primary evidence source, literature review or guideline. Therefore, we did not identify tertiary evidence source/s.
We rated OCEBM level of evidence for this source as '2' (Randomised trial or observational study with dramatic effect) because:
Rall et al (1996) is a randomised controlled trial.
van den Ende et al (2000) 'RCT'
OCEBM level '2'
Key information:
van den Ende et al (2001)) was not identified as a pilot study for the primary evidence source, literature review or guideline. Therefore, we did not identify tertiary evidence source/s.
We rated OCEBM level of evidence for this source as '2' (Randomised trial or observational study with dramatic effect) because:
van den Ende et al (2001) is a randomised controlled trial.
Hakkinen et al (2001) 'RCT'
OCEBM level '2'
Key information:
Hakkinen et al (2001) was not identified as a pilot study for the primary evidence source, literature review or guideline. Therefore, we did not identify tertiary evidence source/s.
We rated OCEBM level of evidence for this source as '2' (Randomised trial or observational study with dramatic effect) because:
Hakkinen et al (2001) is a randomised controlled trial.

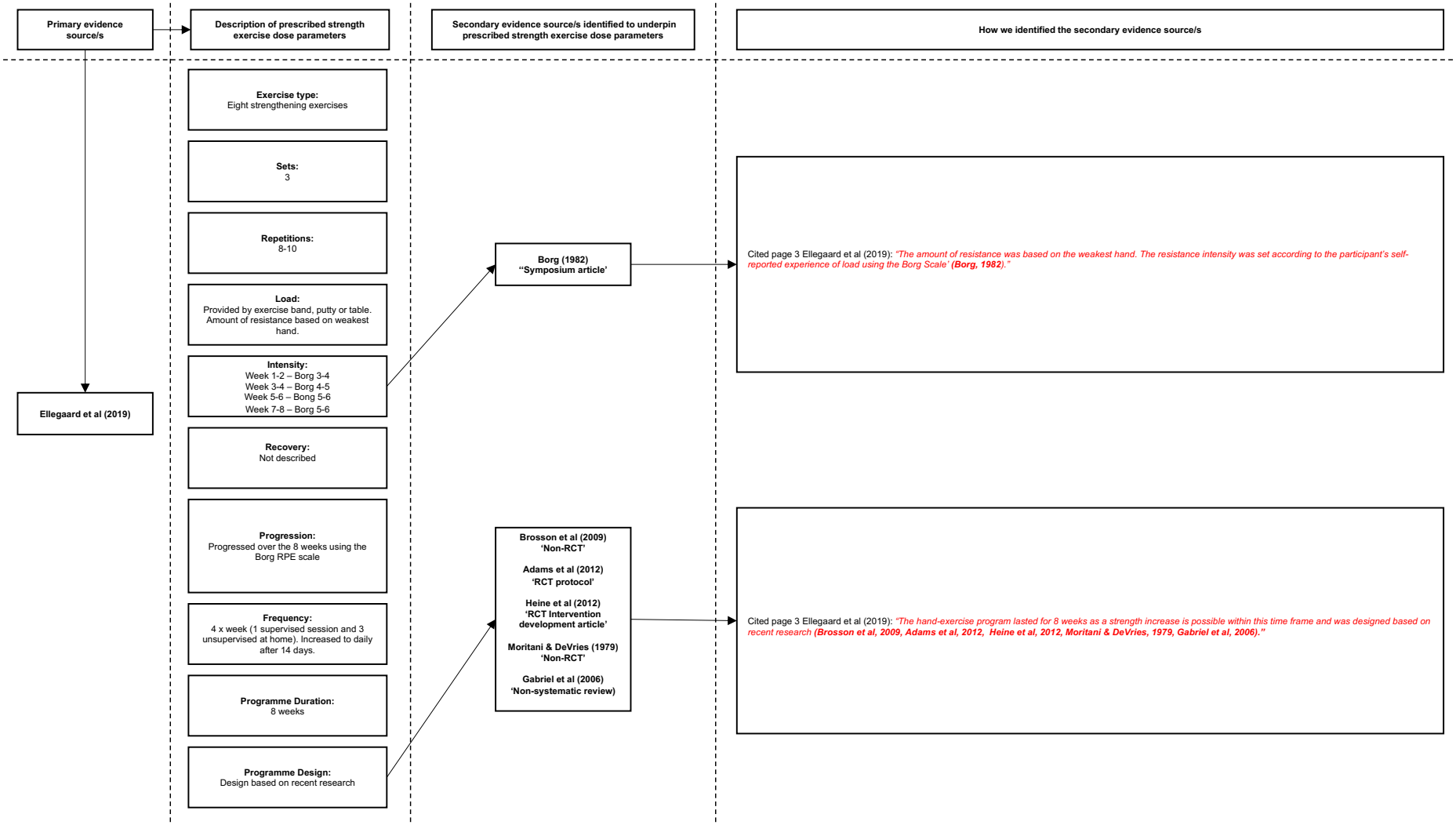
Dose parameter Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Piva et al (2018)	1. Leg extension 2. Leg press	3 sets	1st set 15 repetitions 2nd and 3rd sets 8 repetitions	Insufficiently described	1st set 40%1RM then 80%1RM	3 seconds	1RM reassessed every 4 visits	2-3 x week	16 weeks	Exercise type: Consistent Sets: Consistent Repetitions: Inconsistent Load: Unclear Intensity: Inconsistent Recovery: Inconsistent Progression: Inconsistent Frequency: Inconsistent Duration: Inconsistent
Rall et al (1996)	Major muscle groups using chest press, leg press, leg extension, back extension and abdominal curl machines.	3 sets	8 repetitions	Unclear	80%1RM	2-3 seconds rest between repetitions and 2 minutes rest between sets. Training sessions separated by 2-3 days rest	Strength testing performed at baseline and every 2 weeks to maintain a constant training intensity of 80% as strength improved.	2 x week	12 weeks	

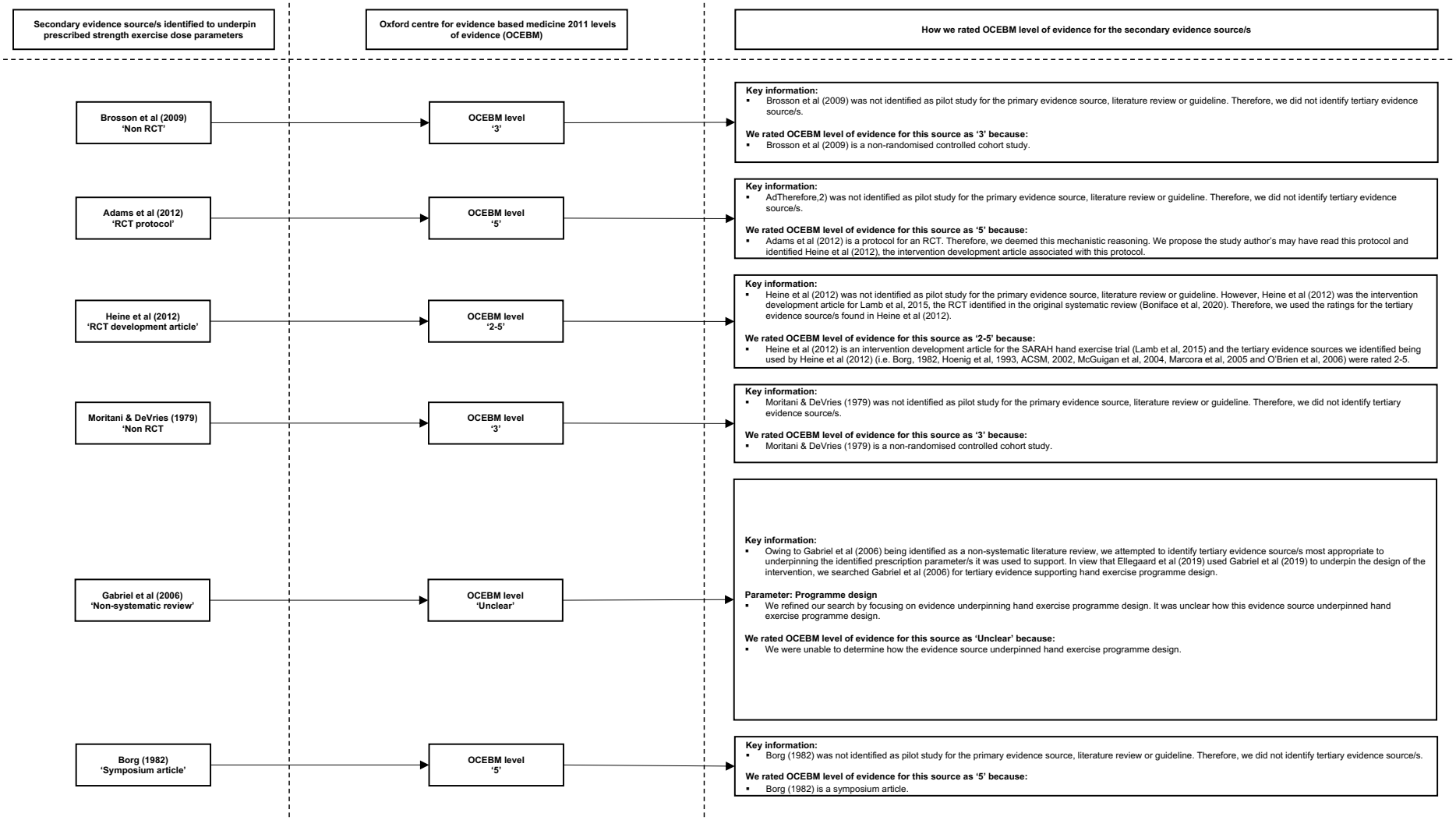
Dose parameter / Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Piva et al (2018)	1. Leg extension 2. Leg press	3 sets	1st set 15 repetitions 2nd and 3rd sets 8 repetitions	Insufficiently described	1st set 40%1RM then 80%1RM	3 seconds	1RM reassessed every 4 visits	2-3 x week	16 weeks	Exercise type: Inconsistent Sets: Consistent Repetitions: Inconsistent Load: Unclear Intensity: Inconsistent Recovery: Inconsistent Progression: Inconsistent Frequency: Inconsistent Duration: Inconsistent
van den Ende et al (2000)	1. Isometric knee extension 2. Isometric knee flexion 3. Isometric shoulder girdle muscles 4. Isometric larger joints 5. Isokinetic knee extension 6. Isokinetic knee flexion	Isometric: 3 sets Isokinetic: 3 sets Isometric shoulder: 1 set	Isometric: 5 repetitions Isokinetic: 8 repetitions Isometric shoulder: 6 repetitions	Unclear	Isometric: 70% MVC for 6 seconds at 45° flexion Isokinetic: 70% MVC at angular velocity 60°/s Isometric shoulder: 6 seconds	Isometric: 30 seconds between sets Isokinetic: unclear Isometric: unclear	MVC determined every week by exercise therapist	5 x week	24 weeks	

Dose parameter / Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Piva et al (2018)	1. Leg extension 2. Leg press	3 sets	1st set 15 repetitions 2nd and 3rd sets 8 repetitions	Insufficiently described	1st set 40%1RM then 80%1RM	3 seconds	1RM reassessed every 4 visits	2-3 x week	16 weeks	Exercise type: Unclear Sets: Inconsistent Repetitions: Inconsistent Load: Unclear Intensity: Inconsistent Recovery: Unclear Progression: Inconsistent Frequency: Inconsistent Duration: Inconsistent
Hakkinen et al (2001)	1. Upper limb exercises 2. Lower limb exercises 3. Abdominal exercises 4. Back exercises	2 sets	8-12 repetitions	Upper limb: Elastic bands Lower limb: Elastic bands Abdominal: Dumbbells Back: Dumbbells	50-70%1RM	Insufficiently described	Intensity of strength training re-evaluated every 6 months	2 x week	24 months	

APPENDIX 5. STUDY ONE. ADDENDUM.UNDERPINNING EVIDENCE IDENTIFIED DURING UPDATE SEARCH.

Ellegaard et al (2019)


Primary evidence source/s
Description of prescribed strength exercise dose parameters
Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
How we identified the secondary evidence source/s
Ellegaard et al (2019)
Exercise type:
Eight strengthening exercises
Sets:
3
Repetitions:
8-10
Load:
Provided by exercise band, putty or table. Amount of resistance based on weakest hand.
Intensity:
Week 1-2 – Borg 3-4
Week 3-4 – Borg 4-5
Week 5-6 – Bong 5-6
Week 7-8 – Borg 5-6
Recovery:
Not described
Progression:
Progressed over the 8 weeks using the Borg RPE scale
Frequency:
4 x week (1 supervised session and 3 unsupervised at home). Increased to daily after 14 days.
Programme Duration:
8 weeks
Programme Design:
Design based on recent research
Borg (1982)
''Symposium article'
Brosson et al (2009)
'Non-RCT'
Adams et al (2012)
'RCT protocol'
Heine et al (2012)
'RCT Intervention development article'
Moritani & DeVries (1979)
'Non-RCT'
Gabriel et al (2006)
'Non-systematic review)
Cited page 3 Ellegaard et al (2019): "The amount of resistance was based on the weakest hand. The resistance intensity was set according to the participant's self-reported experience of load using the Borg Scale' (Borg, 1982)."
Cited page 3 Ellegaard et al (2019): "The hand-exercise program lasted for 8 weeks as a strength increase is possible within this time frame and was designed based on recent research (Brosson et al, 2009, Adams et al, 2012, Heine et al, 2012, Moritani & DeVries, 1979, Gabriel et al, 2006)."


Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
Oxford centre for evidence based medicine 2011 levels of evidence (OCEBM)
How we rated OCEBM level of evidence for the secondary evidence source/s
Brosson et al (2009) 'Non RCT'
OCEBM level '3'
Key information:
Brosson et al (2009) was not identified as pilot study for the primary evidence source, literature review or guideline. Therefore, we did not identify tertiary evidence source/s.
We rated OCEBM level of evidence for this source as '3' because:
Brosson et al (2009) is a non-randomised controlled cohort study.
Adams et al (2012) 'RCT protocol'
OCEBM level '5'
Key information:
AdTherefore,2) was not identified as pilot study for the primary evidence source, literature review or guideline. Therefore, we did not identify tertiary evidence source/s.
We rated OCEBM level of evidence for this source as '5' because:
Adams et al (2012) is a protocol for an RCT. Therefore, we deemed this mechanistic reasoning. We propose the study author's may have read this protocol and identified Heine et al (2012), the intervention development article associated with this protocol.
Heine et al (2012) 'RCT development article'
OCEBM level '2-5'
Key information:
Heine et al (2012) was not identified as pilot study for the primary evidence source, literature review or guideline. However, Heine et al (2012) was the intervention development article for Lamb et al, 2015, the RCT identified in the original systematic review (Boniface et al, 2020). Therefore, we used the ratings for the tertiary evidence source/s found in Heine et al (2012).
We rated OCEBM level of evidence for this source as '2-5' because:
Heine et al (2012) is an intervention development article for the SARAH hand exercise trial (Lamb et al, 2015) and the tertiary evidence sources we identified being used by Heine et al (2012) (i.e. Borg, 1982, Hoenig et al, 1993, ACSM, 2002, McGuigan et al, 2004, Marcora et al, 2005 and O'Brien et al, 2006) were rated 2-5.
Moritani & DeVries (1979) 'Non RCT
OCEBM level '3'
Key information:
Moritani & DeVries (1979) was not identified as pilot study for the primary evidence source, literature review or guideline. Therefore, we did not identify tertiary evidence source/s.
We rated OCEBM level of evidence for this source as '3' because:
Moritani & DeVries (1979) is a non-randomised controlled cohort study.
Gabriel et al (2006) 'Non-systematic review'
OCEBM level 'Unclear'
Key information:
Owing to Gabriel et al (2006) being identified as a non-systematic literature review, we attempted to identify tertiary evidence source/s most appropriate to underpinning the identified prescription parameter/s it was used to support. In view that Ellegaard et al (2019) used Gabriel et al (2019) to underpin the design of the intervention, we searched Gabriel et al (2006) for tertiary evidence supporting hand exercise programme design.
Parameter: Programme design
We refined our search by focusing on evidence underpinning hand exercise programme design. It was unclear how this evidence source underpinned hand exercise programme design.
We rated OCEBM level of evidence for this source as 'Unclear' because:
We were unable to determine how the evidence source underpinned hand exercise programme design.
Borg (1982) 'Symposium article'
OCEBM level '5'
Key information:
Borg (1982) was not identified as pilot study for the primary evidence source, literature review or guideline. Therefore, we did not identify tertiary evidence source/s.
We rated OCEBM level of evidence for this source as '5' because:
Borg (1982) is a symposium article.

RCT Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Ellegaard et al (2019)	1. Gross grip with exercise putty. 2. Finger pinch with exercise putty. 3. Finger adduction with exercise putty. 4. Wrist extension with exercise band. 5. Wrist flexions with resistance from a table. 6. Biceps curls with exercise band. 7. Triceps extensions with exercise band.	3	8-10	Provided by exercise band, exercise putty or a table. Three putties and bands are available (low, moderate or hard) For the hand specific exercises, isometric holds ranging between 2-5 seconds were used.	Week 1-2 Borg 3-4 Week 3-4 Borg 4-5 Week 5-6 Borg 5-6 Week 7-8 Borg 5-6	Not described	Frequency increased from 4 x week to daily after 14 days. Progressed over the 8 weeks using the Borg RPE scale	4 x week (1 supervised session and 3 unsupervised at home). Increased to daily after 14 days.	8 weeks	Exercise type: Inconsistent Sets: Inconsistent Repetitions: Inconsistent Load: Consistent Intensity: Inconsistent Recovery: Unclear Progression: Inconsistent Frequency: Inconsistent Duration: Inconsistent
Brosson et al (2009) 'Non-RCT'	1. Gross grip with exercise putty. 2. Finger pinch with exercise putty. 3. Finger flexion with exercise putty. 4. Rolling hand forwards over putty (sausage shape) on table.	1	10	85grams of exercise putty. Participants were free to choose soft, medium or firm putty. Isometric holds ranging between 3-5 seconds were used.	Maximal effort.	20 seconds between repetitions. Each session separated by at least one day.	Not described Doesn't appear exercise programme was progressed.	5 x week	12 weeks	

RCT Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Ellegaard et al (2019)	1. Gross grip with exercise putty. 2. Finger pinch with exercise putty. 3. Finger adduction with exercise putty. 4. Wrist extension with exercise band. 5. Wrist flexions with resistance from a table. 6. Biceps curls with exercise band. 7. Triceps extensions with exercise band.	3	8-10	Provided by exercise band, exercise putty or a table. Three putties and bands are available (low, moderate or hard) For the hand specific exercises, isometric holds ranging between 2-5 seconds were used.	Week 1-2 Borg 3-4 Week 3-4 Borg 4-5 Week 5-6 Borg 5-6 Week 7-8 Borg 5-6	Insufficiently described	Frequency increased from 4 x week to daily after 14 days. Progressed over the 8 weeks using the Borg RPE scale	4 x week (1 supervised session and 3 unsupervised at home). Increased to daily after 14 days.	8 weeks	Exercise type: Unclear Sets: Unclear Repetitions: Unclear Load: Unclear Intensity: Unclear Recovery: Unclear Progression: Unclear Frequency: Inconsistent Duration: Inconsistent
Adams et al (2012) 'RCT protocol'	Not described.	Not described.	Not described.	Exercise putty, band or ball.	A modified Borg scale of perceived exertion will be used to regulate the intensity of resistance exercise.	Not described.	The intervention will use a standardised protocol of progression and, if necessary, regression of exercise intensity.	Five exercise sessions supervised by a therapist supported by a home exercise programme performed daily.	12 weeks	

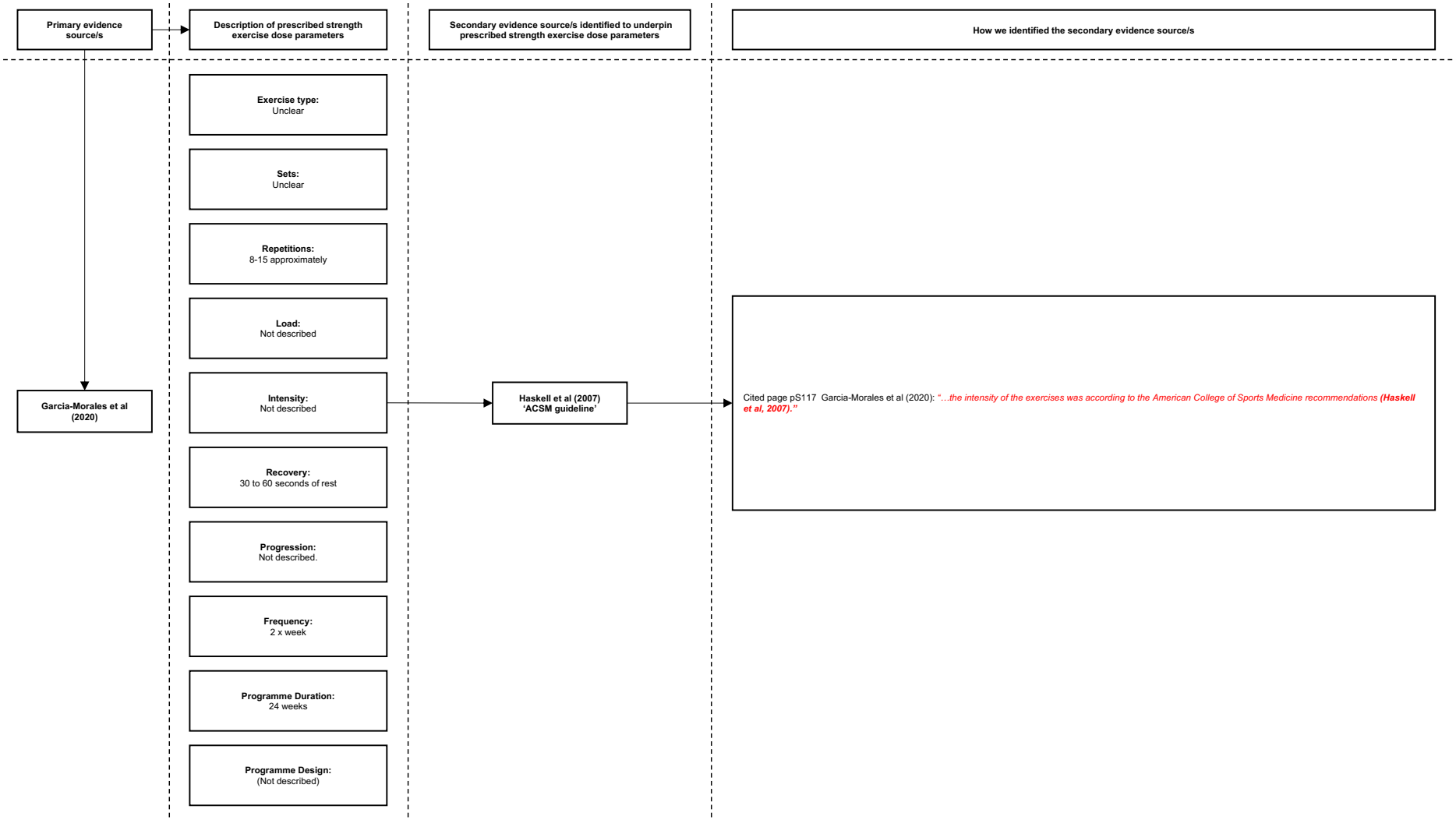
RCT Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Ellegaard et al (2019)	1. Gross grip with exercise putty. 2. Finger pinch with exercise putty. 3. Finger adduction with exercise putty. 4. Wrist extension with exercise band. 5. Wrist flexions with resistance from a table. 6. Biceps curls with exercise band. 7. Triceps extensions with exercise band.	3	8-10	Provided by exercise band, exercise putty or a table. Three putties and bands are available (low, moderate or hard) For the hand specific exercises, isometric holds ranging between 2-5 seconds were used.	Week 1-2 Borg 3-4 Week 3-4 Borg 4-5 Week 5-6 Borg 5-6 Week 7-8 Borg 5-6	Insufficiently described	Frequency increased from 4 x week to daily after 14 days. Progressed over the 8 weeks using the Borg RPE scale	4 x week (1 supervised session and 3 unsupervised at home). Increased to daily after 14 days.	8 weeks	Exercise type: Inconsistent Sets: Consistent Repetitions: Consistent Load: Unclear Intensity: Consistent Recovery: Unclear Progression: Inconsistent Frequency: Inconsistent Duration: Inconsistent
Heine et al (2012) 'RCT Intervention development article'	1. Gross grip with exercise putty. 2. Finger pinch with exercise putty. 3. Finger adduction with exercise putty. 4. Eccentric wrist extension with exercise band.	1-3 set	8-30	insufficiently described	3-4 to 5-6 on modified Borg scale	Insufficiently described	Step 1: 2 x10 reps Step 2: 4-5 Borg scale Step 3: 5-6 Borg scale Step 4: 3 x10 reps	1 x day	12 weeks	

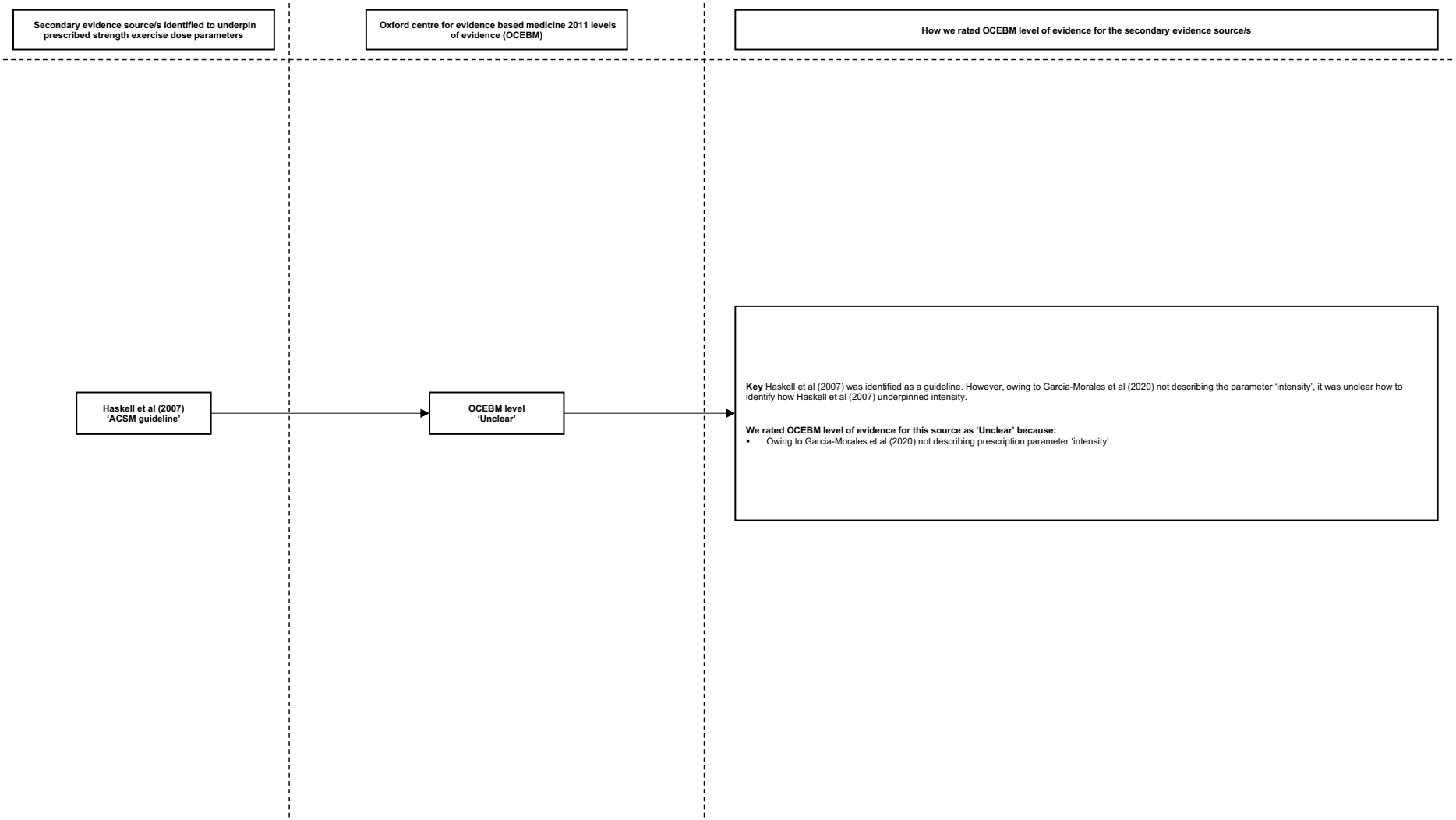
RCT Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Ellegaard et al (2019)	1. Gross grip with exercise putty. 2. Finger pinch with exercise putty. 3. Finger adduction with exercise putty. 4. Wrist extension with exercise band. 5. Wrist flexions with resistance from a table. 6. Biceps curls with exercise band. 7. Triceps extensions with exercise band.	3	8-10	Provided by exercise band, exercise putty or a table. Three putties and bands are available (low, moderate or hard) For the hand specific exercises, isometric holds ranging between 2-5 seconds were used.	Week 1-2 Borg 3-4 Week 3-4 Borg 4-5 Week 5-6 Borg 5-6 Week 7-8 Borg 5-6	Insufficiently described	Frequency increased from 4 x week to daily after 14 days. Progressed over the 8 weeks using the Borg RPE scale	4 x week (1 supervised session and 3 unsupervised at home). Increased to daily after 14 days.	8 weeks	Exercise type: Inconsistent Sets: Inconsistent Repetitions: Inconsistent Load: Inconsistent Intensity: Inconsistent Recovery: Unclear Progression: Inconsistent Frequency: Inconsistent Duration: Consistent
Moritani & DeVries (1979) 'Non-RCT'	Elbow flexor dumbbell training.	2	10	Dumbbell	2/3rd of maximum	Not described	Maximal strength tested at two-week intervals and training workload was adjusted to maintain 2/3rds maximal load.	3 x week	8 weeks	

RCT Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Ellegaard et al (2019)	1. Gross grip with exercise putty. 2. Finger pinch with exercise putty. 3. Finger adduction with exercise putty. 4. Wrist extension with exercise band. 5. Wrist flexions with resistance from a table. 6. Biceps curls with exercise band. 7. Triceps extensions with exercise band.	3	8-10	Provided by exercise band, exercise putty or a table. Three putties and bands are available (low, moderate or hard) For the hand specific exercises, isometric holds ranging between 2-5 seconds were used.	Week 1-2 Borg 3-4 Week 3-4 Borg 4-5 Week 5-6 Borg 5-6 Week 7-8 Borg 5-6	Insufficiently described	Frequency increased from 4 x week to daily after 14 days. Progressed over the 8 weeks using the Borg RPE scale	4 x week (1 supervised session and 3 unsupervised at home). Increased to daily after 14 days.	8 weeks	Exercise type: Unclear Sets: Unclear Repetitions: Unclear Load: Unclear Intensity: Unclear Recovery: Unclear Progression: Unclear Frequency: Unclear Duration: Unclear
Gabriel et al (2006) 'Non-systematic review'	Not described	Not described	Not described	Not described	Not described	Not described	Not described	Not described	Not described	

Dose parameter Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Ellegaard et al (2019)	1. Gross grip with exercise putty. 2. Finger pinch with exercise putty. 3. Finger adduction with exercise putty. 4. Wrist extension with exercise band. 5. Wrist flexions with resistance from a table. 6. Biceps curls with exercise band. 7. Triceps extensions with exercise band.	3	8-10	Provided by exercise band, exercise putty or a table. Three putties and bands are available (low, moderate or hard) For the hand specific exercises, isometric holds ranging between 2-5 seconds were used.	Week 1-2 Borg 3-4 Week 3-4 Borg 4-5 Week 5-6 Borg 5-6 Week 7-8 Borg 5-6	Insufficiently described	Progressed over the 8 weeks using the Borg RPE scale	4 x week (1 supervised session and 3 unsupervised at home). Increased to daily after 14 days.	8 weeks	Exercise type: n/a Sets: n/a Repetitions: n/a Load: n/a Intensity: Unclear Recovery: n/a Progression: n/a Frequency: n/a Duration: n/a
Borg (1982)	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Unclear	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	

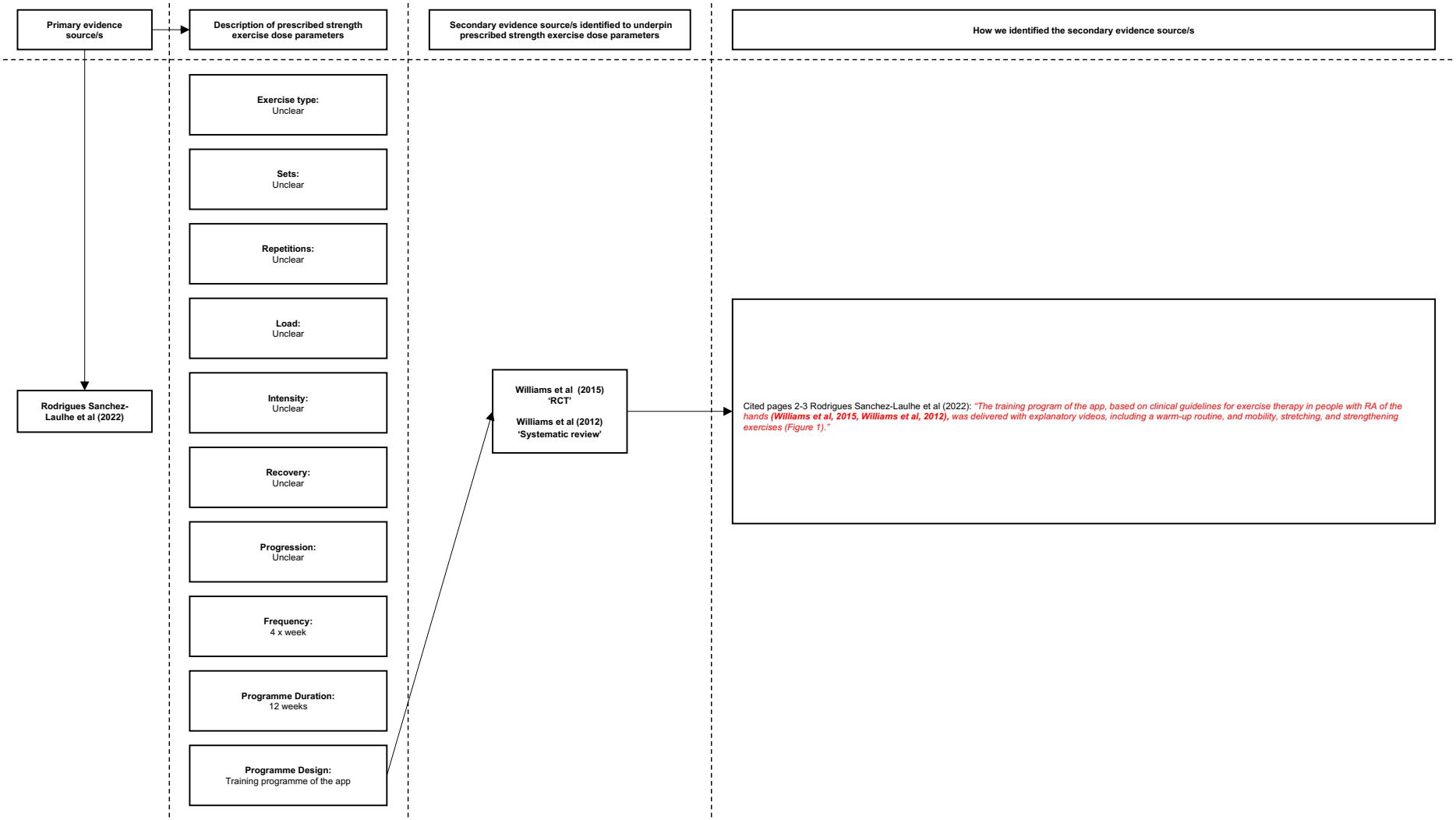
Garcia-Morales et al (2020)

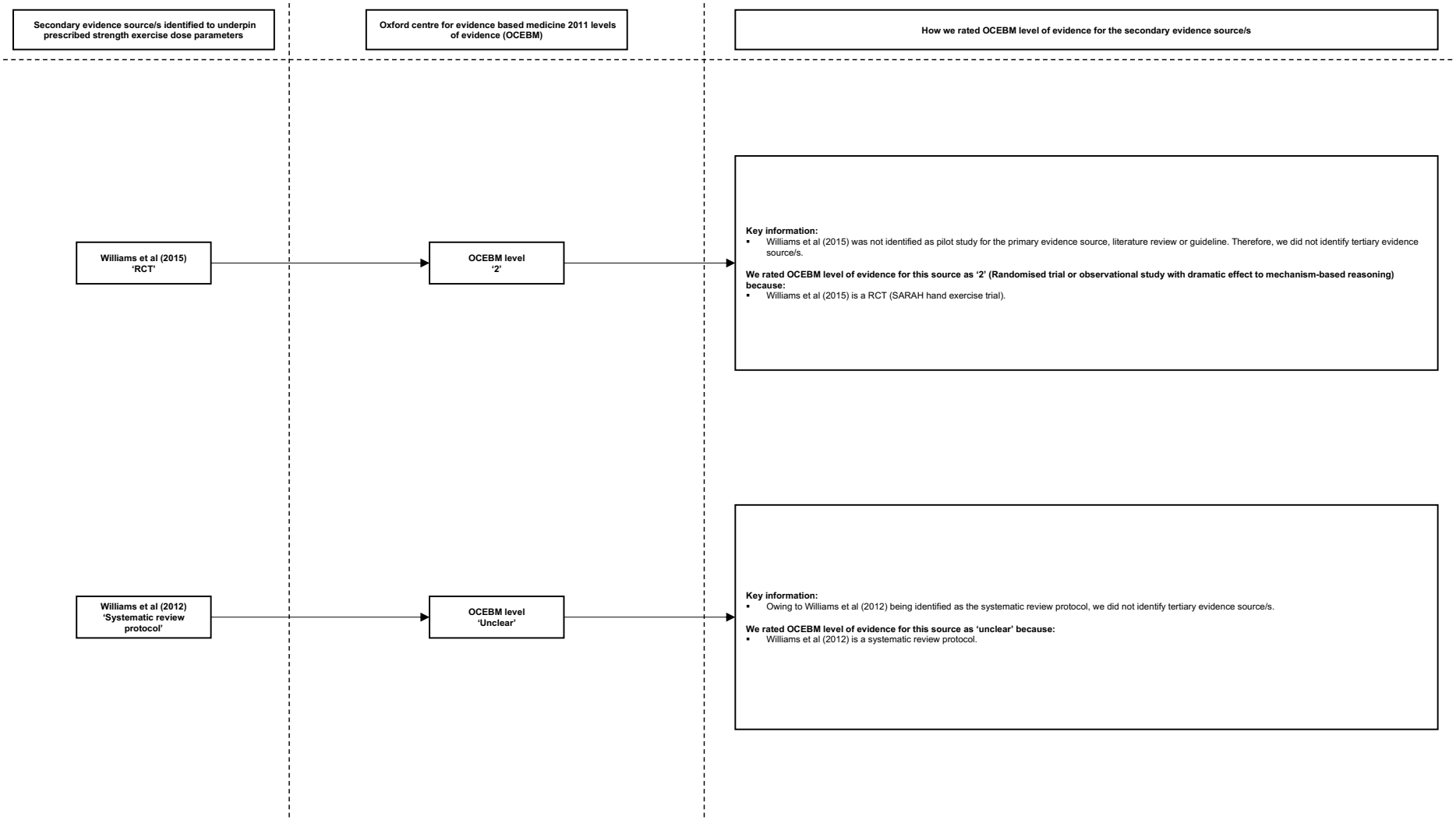

Primary evidence source/s
Description of prescribed strength exercise dose parameters
Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
How we identified the secondary evidence source/s
Exercise type: Unclear
Sets: Unclear
Repetitions: 8-15 approximately
Load: Not described
Intensity: Not described
Recovery: 30 to 60 seconds of rest
Progression: Not described.
Frequency: 2 x week
Programme Duration: 24 weeks
Programme Design: (Not described)
Garcia-Morales et al (2020)
Haskell et al (2007) 'ACSM guideline'
Cited page pS117 Garcia-Morales et al (2020): "…the intensity of the exercises was according to the American College of Sports Medicine recommendations (Haskell et al, 2007)."


Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
Oxford centre for evidence based medicine 2011 levels of evidence (OCEBM)
How we rated OCEBM level of evidence for the secondary evidence source/s
Haskell et al (2007) 'ACSM guideline'
OCEBM level 'Unclear'
Key Haskell et al (2007) was identified as a guideline. However, owing to Garcia-Morales et al (2020) not describing the parameter 'intensity', it was unclear how to identify how Haskell et al (2007) underpinned intensity.
We rated OCEBM level of evidence for this source as 'Unclear' because:
Owing to Garcia-Morales et al (2020) not describing prescription parameter 'intensity'.

Dose parameter / Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Garcia-Morales et al (2020)	Insufficiently described	1	8-15 repetitions approximately	Insufficiently described	Insufficiently described	30 to 60 seconds of rest	Insufficiently described	2 x week	24 weeks	Exercise type: n/a Sets: n/a Repetitions: n/a Load: n/a Intensity: Unclear Recovery: n/a Progression: n/a Frequency: n/a Duration: n/a
Haskell et al (2007)	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Unclear	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	

Rodrigues Sanchez-Laulhe et al (2022)

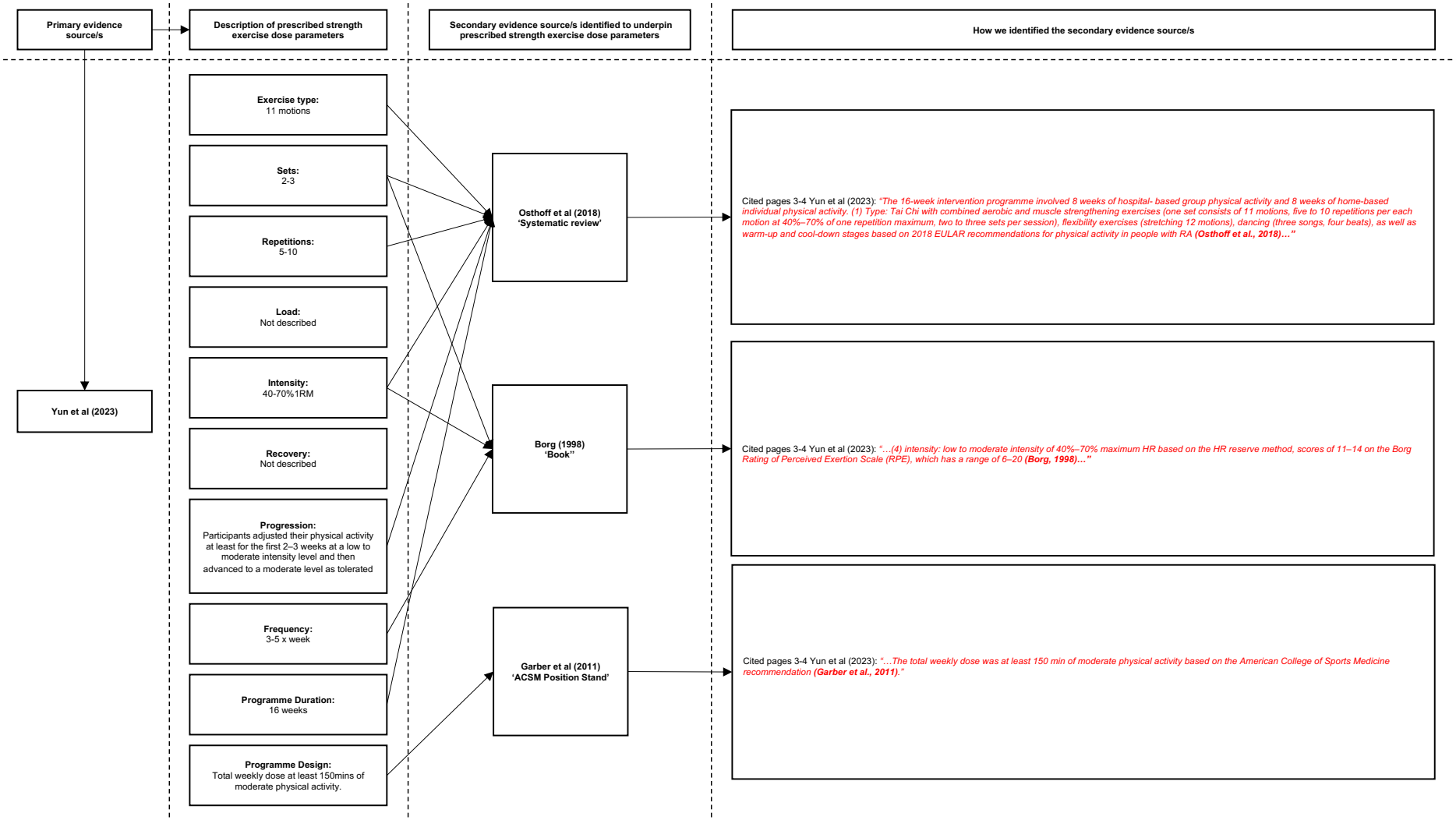

Primary evidence source/s
Description of prescribed strength exercise dose parameters
Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
How we identified the secondary evidence source/s
Exercise type: Unclear
Sets: Unclear
Repetitions: Unclear
Load: Unclear
Intensity: Unclear
Recovery: Unclear
Progression: Unclear
Frequency: 4 x week
Programme Duration: 12 weeks
Programme Design: Training programme of the app
Rodrigues Sanchez-Laulhe et al (2022)
Williams et al (2015) 'RCT'
Williams et al (2012) 'Systematic review'
Cited pages 2-3 Rodrigues Sanchez-Laulhe et al (2022): "The training program of the app, based on clinical guidelines for exercise therapy in people with RA of the hands (Williams et al, 2015, Williams et al, 2012), was delivered with explanatory videos, including a warm-up routine, and mobility, stretching, and strengthening exercises (Figure 1)."

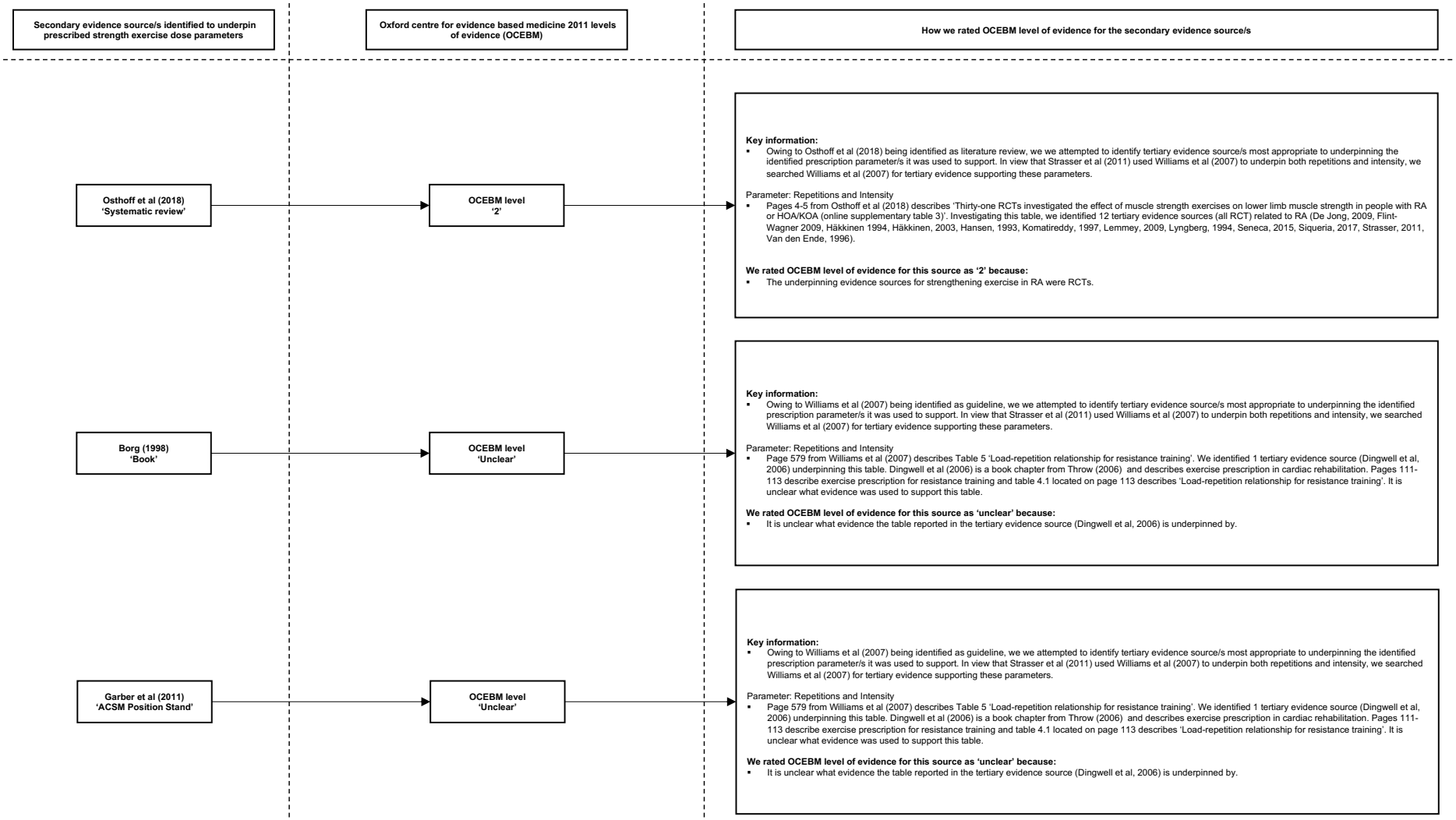

Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
Oxford centre for evidence based medicine 2011 levels of evidence (OCEBM)
How we rated OCEBM level of evidence for the secondary evidence source/s
Williams et al (2015) 'RCT'
OCEBM level '2'
Key information:
Williams et al (2015) was not identified as pilot study for the primary evidence source, literature review or guideline. Therefore, we did not identify tertiary evidence source/s.
We rated OCEBM level of evidence for this source as '2' (Randomised trial or observational study with dramatic effect to mechanism-based reasoning) because:
Williams et al (2015) is a RCT (SARAH hand exercise trial).
Williams et al (2012) 'Systematic review protocol'
OCEBM level 'Unclear'
Key information:
Owing to Williams et al (2012) being identified as the systematic review protocol, we did not identify tertiary evidence source/s.
We rated OCEBM level of evidence for this source as 'unclear' because:
Williams et al (2012) is a systematic review protocol.

Dose parameter Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Rodrigues Sanchez-Laulhe et al (2022)	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	4 x week	12 weeks	Exercise type: Unclear Sets: Unclear Repetitions: Unclear Load: Unclear Intensity: Unclear Recovery: Unclear Progression: Unclear Frequency: Inconsistent Duration: Consistent
Williams et al (2015)	1. Eccentric wrist extension 2. Gross grip 3. Finger adduction 4. Pinch grip	1-3 sets	8-30 repetitions	Insufficiently described	3-4 to 5-6 on modified Borg scale	Insufficiently described	Step 1: 2 x10 reps Step 2: 4-5 Borg scale Step 3: 5-6 Borg scale Step 4: 3 x10 reps	1 x daily	12 weeks	

Dose parameter / Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Rodrigues Sanchez-Laulhe et al (2022)	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	Insufficiently described	4 x week	12 weeks	Exercise type: Unclear Sets: Unclear Repetitions: Unclear Load: Unclear Intensity: Unclear Recovery: Unclear Progression: Unclear Frequency: Unclear Duration: Unclear
Williams et al (2012)	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	

Yun et al (2023)


Primary evidence source/s
Description of prescribed strength exercise dose parameters
Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
How we identified the secondary evidence source/s
Yun et al (2023)
Exercise type: 11 motions
Sets: 2-3
Repetitions: 5-10
Load: Not described
Intensity: 40-70%1RM
Recovery: Not described
Progression: Participants adjusted their physical activity at least for the first 2–3 weeks at a low to moderate intensity level and then advanced to a moderate level as tolerated
Frequency: 3-5 x week
Programme Duration: 16 weeks
Programme Design: Total weekly dose at least 150mins of moderate physical activity.
Osthoff et al (2018) 'Systematic review'
Borg (1998) 'Book''
Garber et al (2011) 'ACSM Position Stand'
Cited pages 3-4 Yun et al (2023): "The 16-week intervention programme involved 8 weeks of hospital- based group physical activity and 8 weeks of home-based individual physical activity. (1) Type: Tai Chi with combined aerobic and muscle strengthening exercises (one set consists of 11 motions, five to 10 repetitions per each motion at 40%–70% of one repetition maximum, two to three sets per session), flexibility exercises (stretching 12 motions), dancing (three songs, four beats), as well as warm-up and cool-down stages based on 2018 EULAR recommendations for physical activity in people with RA (Osthoff et al., 2018)…"
Cited pages 3-4 Yun et al (2023): "…(4) intensity: low to moderate intensity of 40%–70% maximum HR based on the HR reserve method, scores of 11–14 on the Borg Rating of Perceived Exertion Scale (RPE), which has a range of 6–20 (Borg, 1998)…"
Cited pages 3-4 Yun et al (2023): "…The total weekly dose was at least 150 min of moderate physical activity based on the American College of Sports Medicine recommendation (Garber et al., 2011)."

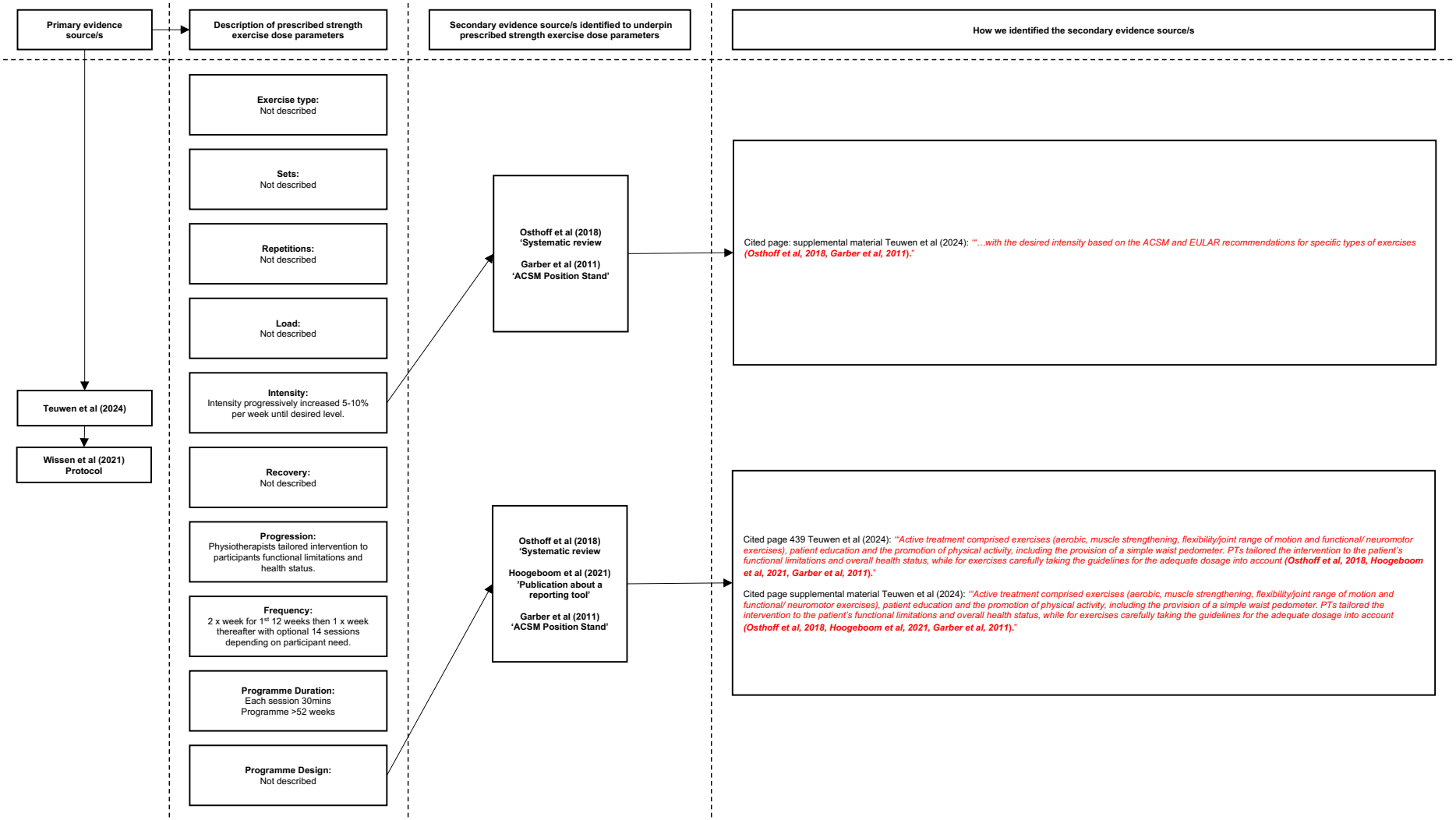

Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
Oxford centre for evidence based medicine 2011 levels of evidence (OCEBM)
How we rated OCEBM level of evidence for the secondary evidence source/s
Osthoff et al (2018) 'Systematic review'
OCEBM level '2'
Key information:
Owing to Osthoff et al (2018) being identified as literature review, we we attempted to identify tertiary evidence source/s most appropriate to underpinning the identified prescription parameter/s it was used to support. In view that Strasser et al (2011) used Williams et al (2007) to underpin both repetitions and intensity, we searched Williams et al (2007) for tertiary evidence supporting these parameters.
Parameter: Repetitions and Intensity
Pages 4-5 from Osthoff et al (2018) describes 'Thirty-one RCTs investigated the effect of muscle strength exercises on lower limb muscle strength in people with RA or HOA/KOA (online supplementary table 3)'. Investigating this table, we identified 12 tertiary evidence sources (all RCT) related to RA (De Jong, 2009, Flint-Wagner 2009, Häkkinen 1994, Häkkinen, 2003, Hansen, 1993, Komatireddy, 1997, Lemmey, 2009, Lyngberg, 1994, Seneca, 2015, Siqueria, 2017, Strasser, 2011, Van den Ende, 1996).
We rated OCEBM level of evidence for this source as '2' because:
The underpinning evidence sources for strengthening exercise in RA were RCTs.
Borg (1998) 'Book'
OCEBM level 'Unclear'
Key information:
Owing to Williams et al (2007) being identified as guideline, we we attempted to identify tertiary evidence source/s most appropriate to underpinning the identified prescription parameter/s it was used to support. In view that Strasser et al (2011) used Williams et al (2007) to underpin both repetitions and intensity, we searched Williams et al (2007) for tertiary evidence supporting these parameters.
Parameter: Repetitions and Intensity
Page 579 from Williams et al (2007) describes Table 5 'Load-repetition relationship for resistance training'. We identified 1 tertiary evidence source (Dingwell et al, 2006) underpinning this table. Dingwell et al (2006) is a book chapter from Throw (2006) and describes exercise prescription in cardiac rehabilitation. Pages 111-113 describe exercise prescription for resistance training and table 4.1 located on page 113 describes 'Load-repetition relationship for resistance training'. It is unclear what evidence was used to support this table.
We rated OCEBM level of evidence for this source as 'unclear' because:
It is unclear what evidence the table reported in the tertiary evidence source (Dingwell et al, 2006) is underpinned by.
Garber et al (2011) 'ACSM Position Stand'
OCEBM level 'Unclear'
Key information:
Owing to Williams et al (2007) being identified as guideline, we we attempted to identify tertiary evidence source/s most appropriate to underpinning the identified prescription parameter/s it was used to support. In view that Strasser et al (2011) used Williams et al (2007) to underpin both repetitions and intensity, we searched Williams et al (2007) for tertiary evidence supporting these parameters.
Parameter: Repetitions and Intensity
Page 579 from Williams et al (2007) describes Table 5 'Load-repetition relationship for resistance training'. We identified 1 tertiary evidence source (Dingwell et al, 2006) underpinning this table. Dingwell et al (2006) is a book chapter from Throw (2006) and describes exercise prescription in cardiac rehabilitation. Pages 111-113 describe exercise prescription for resistance training and table 4.1 located on page 113 describes 'Load-repetition relationship for resistance training'. It is unclear what evidence was used to support this table.
We rated OCEBM level of evidence for this source as 'unclear' because:
It is unclear what evidence the table reported in the tertiary evidence source (Dingwell et al, 2006) is underpinned by.

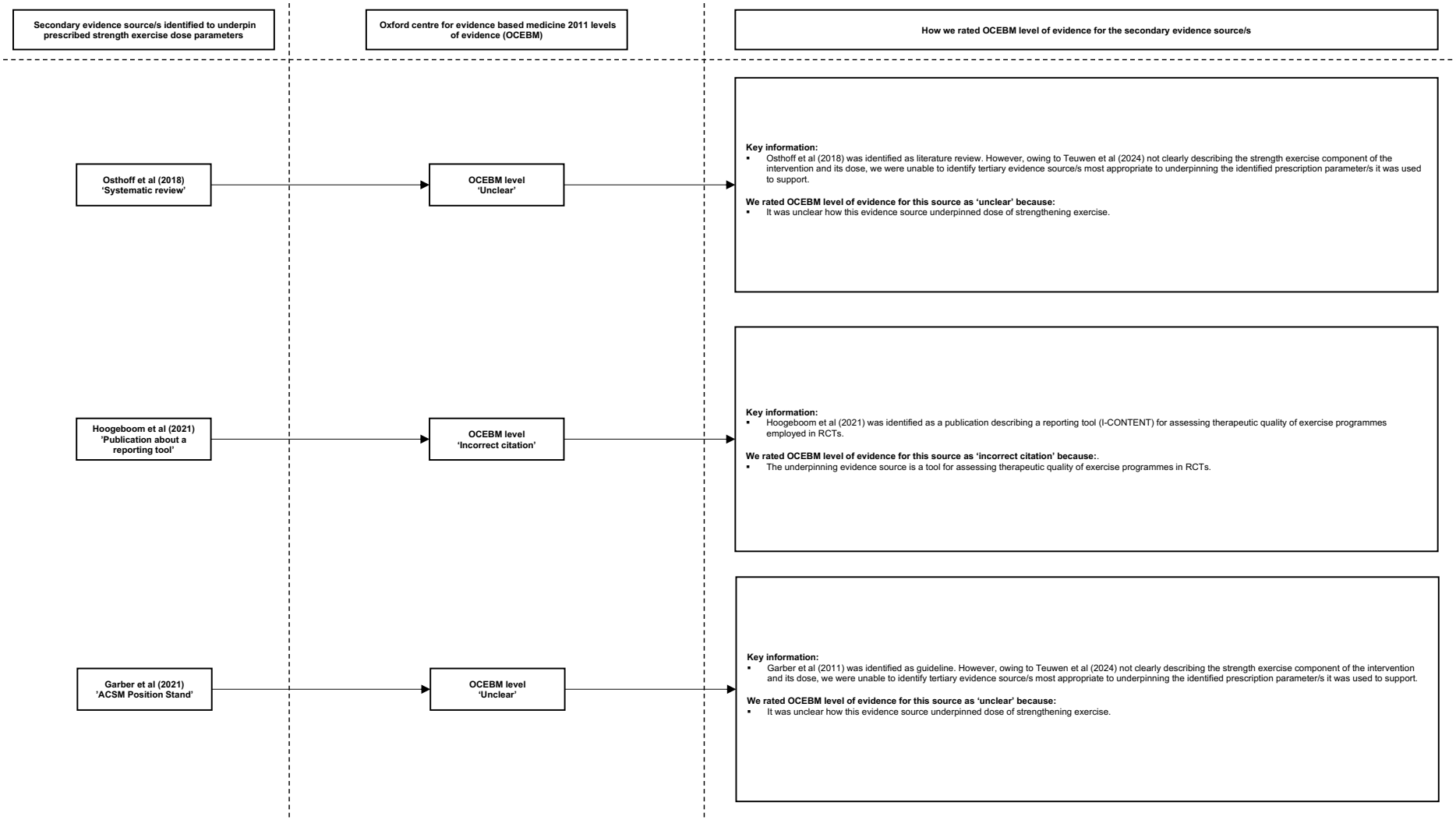
Dose parameter Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Yun et al (2023)	11 motions	2-3 sets	5 -10 repetitions	Insufficiently described	40-70%1RM or low to moderate intensity of 40%–70% maximum HR based on the HR reserve method	Not described	Not described	3-5 x week	16 weeks	Exercise type: Unclear Sets: Unclear Repetitions: Unclear Load: Unclear Intensity: Unclear Recovery: Unclear Progression: n/a Frequency: Unclear Duration: Unclear
Osthoff et al (2018)	Review included 9 RCTs in meta-analysis (p4-5) investigating the effect of muscle strength exercises on lower limb muscle strength in people with RA.	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	

Dose parameter Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Yun et al (2023)	11 motions	2-3 sets	5 -10 repetitions	Insufficiently described	40-70%1RM or low to moderate intensity of 40%–70% maximum HR based on the HR reserve method	Not described	Not described	3-5 x week	16 weeks	Exercise type: n/a Sets: n/a Repetitions: n/a Load: n/a Intensity: Unclear Recovery: n/a Progression: n/a Frequency: n/a Duration: n/a
Borg et al (1998)	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Unclear	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	Citation not used to support parameter	

Dose parameter Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Yun et al (2023)	11 motions	2-3 sets	5 -10 repetitions	Insufficiently described	40-70%1RM or low to moderate intensity of 40%–70% maximum HR based on the HR reserve method	Not described	Not described	3-5 x week	16 weeks	Exercise type: Unclear Sets: Unclear Repetitions: Unclear Load: Unclear Intensity: Unclear Recovery: Unclear Progression: Unclear Frequency: Unclear Duration: Unclear
Garber et al (2011) 'ACSM Position Stand **Taken from table 2 p1336**	Each major muscle group should be trained	1 set 'Can be effective especially among older and novice exercisers'	10-15 reps 'Middle aged and older persons starting exercise'	Unclear	40-50% of 1RM Older and/or sedentary persons beginning a resistance training programme	2-3 minutes between each set A rest-interval of ≥48 hour between sessions for any single muscle group	Gradual progression of greater resistances, and/or more repetitions per set, and/or increasing frequency	2-3 x week	Unclear	

Teuwen et al (2024)


Primary evidence source/s
Description of prescribed strength exercise dose parameters
Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
How we identified the secondary evidence source/s
Teuwen et al (2024)
Wissen et al (2021) Protocol
Exercise type: Not described
Sets: Not described
Repetitions: Not described
Load: Not described
Intensity: Intensity progressively increased 5-10% per week until desired level.
Recovery: Not described
Progression: Physiotherapists tailored intervention to participants functional limitations and health status.
Frequency: 2 x week for 1st 12 weeks then 1 x week thereafter with optional 14 sessions depending on participant need.
Programme Duration: Each session 30mins Programme >52 weeks
Programme Design: Not described
Osthoff et al (2018) 'Systematic review
Garber et al (2011) 'ACSM Position Stand'
Osthoff et al (2018) 'Systematic review
Hoogeboom et al (2021) 'Publication about a reporting tool'
Garber et al (2011) 'ACSM Position Stand'
Cited page: supplemental material Teuwen et al (2024): "'…with the desired intensity based on the ACSM and EULAR recommendations for specific types of exercises (Osthoff et al, 2018, Garber et al, 2011)."
Cited page 439 Teuwen et al (2024): "'Active treatment comprised exercises (aerobic, muscle strengthening, flexibility/joint range of motion and functional/ neuromotor exercises), patient education and the promotion of physical activity, including the provision of a simple waist pedometer. PTs tailored the intervention to the patient's functional limitations and overall health status, while for exercises carefully taking the guidelines for the adequate dosage into account (Osthoff et al, 2018, Hoogeboom et al, 2021, Garber et al, 2011)."
Cited page supplemental material Teuwen et al (2024): "'Active treatment comprised exercises (aerobic, muscle strengthening, flexibility/joint range of motion and functional/ neuromotor exercises), patient education and the promotion of physical activity, including the provision of a simple waist pedometer. PTs tailored the intervention to the patient's functional limitations and overall health status, while for exercises carefully taking the guidelines for the adequate dosage into account (Osthoff et al, 2018, Hoogeboom et al, 2021, Garber et al, 2011)."


Secondary evidence source/s identified to underpin prescribed strength exercise dose parameters
Oxford centre for evidence based medicine 2011 levels of evidence (OCEBM)
How we rated OCEBM level of evidence for the secondary evidence source/s
Osthoff et al (2018) 'Systematic review'
OCEBM level 'Unclear'
Key information:
Osthoff et al (2018) was identified as literature review. However, owing to Teuwen et al (2024) not clearly describing the strength exercise component of the intervention and its dose, we were unable to identify tertiary evidence source/s most appropriate to underpinning the identified prescription parameter/s it was used to support.
We rated OCEBM level of evidence for this source as 'unclear' because:
It was unclear how this evidence source underpinned dose of strengthening exercise.
Hoogeboom et al (2021) 'Publication about a reporting tool'
OCEBM level 'Incorrect citation'
Key information:
Hoogeboom et al (2021) was identified as a publication describing a reporting tool (I-CONTENT) for assessing therapeutic quality of exercise programmes employed in RCTs.
We rated OCEBM level of evidence for this source as 'incorrect citation' because:.
The underpinning evidence source is a tool for assessing therapeutic quality of exercise programmes in RCTs.
Garber et al (2021) 'ACSM Position Stand'
OCEBM level 'Unclear'
Key information:
Garber et al (2011) was identified as guideline. However, owing to Teuwen et al (2024) not clearly describing the strength exercise component of the intervention and its dose, we were unable to identify tertiary evidence source/s most appropriate to underpinning the identified prescription parameter/s it was used to support.
We rated OCEBM level of evidence for this source as 'unclear' because:
It was unclear how this evidence source underpinned dose of strengthening exercise.

Dose parameter Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Teuwen et al (2024) **+** **Wissen et al (2021) Protocol**	Insufficiently described	Insufficiently described	Insufficiently described	With use of own weight, attributes or devices	Dose of exercise based on ASCM guidelines (Garber et al, 2011)	Insufficiently described	Physiotherapists tailored intervention to participants functional limitations and health status. Intensity progressively increased 5-10% per week until desired level.	Two supervised sessions per week for 1st 12 weeks then 1 x week thereafter with option of 14extra sessions depending on participant need.	>52 weeks	Exercise type: Unclear Sets: Unclear Repetitions: Unclear Load: Unclear Intensity: Unclear Recovery: Unclear Progression: Unclear Frequency: Unclear Duration: Unclear
Osthoff et al (2018) 'Systematic review	Review included 9 RCTs in meta-analysis (p4-5) investigating the effect of muscle strength exercises on lower limb muscle strength in people with RA.	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	

Dose parameter Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Teuwen et al (2024) **+** **Wissen et al (2021) Protocol**	Insufficiently described	Insufficiently described	Insufficiently described	With use of own weight, attributes or devices	Dose of exercise based on ASCM guidelines (Garber et al, 2011)	Insufficiently described	Physiotherapists tailored intervention to participants functional limitations and health status. Intensity progressively increased 5-10% per week until desired level.	Two supervised sessions per week for 1st 12 weeks then 1 x week thereafter with option of 14extra sessions depending on participant need.	>52 weeks	Exercise type: Unclear Sets: Unclear Repetitions: Unclear Load: Unclear Intensity: Unclear Recovery: Unclear Progression: Unclear Frequency: Unclear Duration: Unclear
Hoogeboom et al (2021) 'Publication about a reporting tool'	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	

Dose parameter Underpinning evidence	Type of strength exercise	Sets	Repetitions	Load	Intensity	Recovery	Method of progression	Frequency	Programme duration	Consistency rating
Teuwen et al (2024) + **Wissen et al (2021) Protocol**	Insufficiently described	Insufficiently described	Insufficiently described	With use of own weight, attributes or devices	Dose of exercise based on ASCM guidelines (Garber et al, 2011)	Insufficiently described	Physiotherapists tailored intervention to participants functional limitations and health status. Intensity progressively increased 5-10% per week until desired level.	Two supervised sessions per week for 1st 12 weeks then 1 x week thereafter with option of 14extra sessions depending on participant need.	>52 weeks	Exercise type: Unclear Sets: Unclear Repetitions: Unclear Load: Unclear Intensity: Consistent Recovery: Unclear Progression: Consistent Frequency: Inconsistent Duration: Unclear
Garber et al (2011) 'ACSM Position Stand **Taken from table 2 p1336**	Each major muscle group should be trained	1 set 'Can be effective especially among older and novice exercisers'	10-15 reps 'Middle aged and older persons starting exercise'	Unclear	40-50% of 1RM 'Older and/or sedentary persons beginning a resistance training programme'	2-3 minutes between each set A rest-interval of ≥48 hour between sessions for any single muscle group	Gradual progression of greater resistances, and/or more repetitions per set, and/or increasing frequency	2-3 x week	Unclear	

APPENDIX 6. STUDY TWO – FULL PUBLICATION.

Received: 28 April 2022 | Accepted: 2 May 2022

DOI: 10.1002/msc.1646

RESEARCH ARTICLE

WILEY

Understanding prescribed dose in hand strengthening exercise for rheumatoid arthritis: A secondary analysis of the SARAH trial

Graham Boniface[1] | Maria T. Sanchez-Santos[2] | Meriel Norris[1] | Neil OConnell[1] | Esther Williamson[2] | Sarah E. Lamb[2,3]

[1]Department of Health Sciences, Centre for Health and Wellbeing across the Lifecourse, Brunel University London, Uxbridge, UK

[2]Nuffield Department of Orthopaedics Rheumatology and Musculoskeletal Sciences (NDORMS), University of Oxford, Oxford, UK

[3]College of Medicine and Health, University of Exeter, Exeter, UK

Correspondence
Neil OConnell, Department of Health Sciences, Centre for Health and Wellbeing across the Lifecourse, Brunel University London, Uxbridge, United Kingdom.
Email: neil.oconnell@brunel.ac.uk

Abstract

Objective: 1) To identify therapist or participant characteristics associated with prescribed dose of hand strengthening exercise in adults with rheumatoid arthritis and 2) To determine the impact of dose prescribed on outcome (hand function and grip strength).

Methods: Overall dose was calculated using area under the curve (AUC). Analysis 1 assessed the association between therapist professional background, therapist grade, baseline participant physical and psychological characteristics and prescribed dose. Analyses 2 and 3 estimated the relationship between prescribed dose and overall hand function and grip strength. Generalised estimating equation linear regression analysis was used.

Results: Analysis 1: Being treated by an occupational therapist ($\beta = -297.0$, 95% CI −398.6, −195.4), metacarpophalangeal joint deformity ($\beta = -24.1$, 95% CI −42.3, −5.9), a higher number of swollen wrist/hand joints ($\beta = -11.4$, 95% CI −21.6, −1.2) and the participant feeling downhearted and low all of the time ($\beta = -293.6$, 95% CI −436.1, −151.1) were associated with being prescribed a lower dose. Being treated by a grade 6 therapist ($\beta = 159.1$, 95% CI 65.7, 252.5), higher baseline grip strength ($\beta = 0.15$, 95% CI 0.02, 0.28) and greater participant confidence to exercise without fear of making symptoms worse ($\beta = 18.9$, 95% CI 1.5, 36.3) were associated with being prescribed a higher dose. Analyses 2 and 3: Higher dose was associated with greater overall hand function ($\beta = 0.005$, 95% CI 0.001, 0.010) and full-hand grip strength ($\beta = 0.014$, 95% CI 0.000, 0.025) at 4-month.

Conclusion: Higher dose was associated with better clinical outcomes. Prescription of hand strengthening exercise is associated with both therapist and participant characteristics.

KEYWORDS
dose, hand, hand exercise, hand strength, rheumatoid arthritis, SARAH trial

APPENDIX 7. STUDY TWO – BRUNEL REC APPROVAL.

College of Health and Life Sciences Research Ethics Committee (DCS)
Brunel University London
Kingston Lane
Uxbridge
UB8 3PH
United Kingdom

www.brunel.ac.uk

19 February 2019

LETTER OF APPROVAL

Applicant: Mr Graham Boniface

Project Title: Stretching and Strengthening for People with Rheumatoid Arthritis of the Hands (SARAH) Trial: Secondary Data Analysis

Reference: 13763-LR-Jan/2019- 17357-1

Dear Mr Graham Boniface

The Research Ethics Committee has considered the above application recently submitted by you.

The Chair, acting under delegated authority has agreed that there is no objection on ethical grounds to the proposed study. Approval is given on the understanding that the conditions of approval set out below are followed:

- The agreed protocol must be followed. Any changes to the protocol will require prior approval from the Committee by way of an application for an amendment.

Please note that:

- Research Participant Information Sheets and (where relevant) flyers, posters, and consent forms should include a clear statement that research ethics approval has been obtained from the relevant Research Ethics Committee.
- The Research Participant Information Sheets should include a clear statement that queries should be directed, in the first instance, to the Supervisor (where relevant), or the researcher. Complaints, on the other hand, should be directed, in the first instance, to the Chair of the relevant Research Ethics Committee.
- Approval to proceed with the study is granted subject to receipt by the Committee of satisfactory responses to any conditions that may appear above, in addition to any subsequent changes to the protocol.
- The Research Ethics Committee reserves the right to sample and review documentation, including raw data, relevant to the studyYou may not undertake any research activity if you are not a registered student of Brunel University or if you cease to become registered, including abeyance or temporary withdrawal. As a deregistered student you would not be insured to undertake research activity. Research activity includes the recruitment of participants, undertaking consent procedures and collection of data. Breach of this requirement constitutes research misconduct and is a disciplinary offence.

Professor Christina Victor

Chair

College of Health and Life Sciences Research Ethics Committee (DCS)
Brunel University London

APPENDIX 8. STUDY THREE – FULL PUBLICATION.

Received: 13 November 2023 | Revised: 16 November 2023 | Accepted: 17 November 2023

DOI: 10.1002/msc.1849

WILEY

RESEARCH ARTICLE

Prescribing hand strengthening exercise for patients with rheumatoid arthritis; clinical cues influencing occupational therapists' and physiotherapists' judgements

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[2]Marie Curie Palliative Care Research Department, Division of Psychiatry, University College London, London, UK

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[4]Nuffield Department of Orthopaedics Rheumatology and Musculoskeletal Sciences (NDORMS), University of Oxford, Oxford, UK

[5]Centre for Applied Health and Social Care Research, Kingston University, Kingston, UK

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Email: neil.oconnell@brunel.ac.uk

Funding information
Brunel University London; National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care Oxford at Oxford Health NHS Foundation Trust; NIHR Biomedical Research Centre, Oxford

Abstract

Objective: To explore the clinical judgements of therapists in prescribing the intensity of hand strengthening exercise in rheumatoid arthritis (RA).

Methods: Phase I: Eleven therapists knowledgeable in treating patients with RA subjectively identified seven clinical cues. These were incorporated into 54 hypothetical patient case scenarios. Phase II: Therapists with ≥2 years post-registration experience and current or recent experience in treating patients with RA were asked to assess 69 case scenarios in total (54 + 15 repeats) and judge what intensity of hand strengthening exercise they would prescribe using the OMNI-Resistance Exercise Scale of perceived exertion. Using responses to the repeated cases, the Cochran-Weiss-Shanteau index of expertise was used to identify therapists who prescribed more consistently. Multiple regression was used to determine which clinical cues were most strongly associated with the intensity of exercise prescribed. A sub-group analysis explored differences between consistent and inconsistent prescribers.

Results: Fifty-three therapists took part. Thirty completed all 69 case scenarios. Across all therapists, the three most important clinical cues associated with lower intensity of exercise prescribed were (1) Patient's reported pain intensity whilst practising the exercise ($\beta = -1.150$, $p < 0.001$), (2) Disease activity ($\beta = -0.425$, $p < 0.001$) and (3) average hand pain over the last week ($\beta = -0.353$ $p < 0.001$). Twelve therapists were categorised as consistent prescribers. This group relied on fewer clinical cues (three vs. seven) when judging what intensity of exercise to prescribe.

Conclusion: This study provides insights into how therapists prescribe hand exercises. Intensity of hand strengthening exercise was influenced by three key clinical cues, including pain intensity and disease activity.

KEYWORDS
decision making, dose, hand exercise, judgement analysis, rheumatoid arthritis

APPENDIX *9*. STUDY THREE – BRUNEL REC APPROVAL.

Phase I – Initial Brunel REC approval.

College of Health, Medicine and Life Sciences Research Ethics Committee (DHS)
Brunel University London
Kingston Lane
Uxbridge
UB8 3PH
United Kingdom

www.brunel.ac.uk

10 May 2022

LETTER OF APPROVAL

APPROVAL HAS BEEN GRANTED FOR THIS STUDY TO BE CARRIED OUT BETWEEN 02/05/2022 AND 31/08/2022

Applicant (s): Mr Graham Boniface Dr Meriel Norris, Dr Neil O'Connell, Dr Esther Williamson, Dr Nicola White, Professor Priscilla Harries, Dr Christopher Tomlinson

Project Title: Decision making in prescribing hand strengthening exercise in rheumatoid arthritis: a judgement analysis

Reference: 36607-LR-May/2022- 39386-2

Dear Mr Graham Boniface

The Research Ethics Committee has considered the above application recently submitted by you.

The Chair, acting under delegated authority has agreed that there is no objection on ethical grounds to the proposed study. Approval is given on the understanding that the conditions of approval set out below are followed:

- **Approval is given for remote (online/telephone) research activity only. Face-to-face activity and/or travel will require approval by way of an amendment.**
- **The agreed protocol must be followed. Any changes to the protocol will require prior approval from the Committee by way of an application for an amendment.**
- **Please ensure that you monitor and adhere to all up-to-date local and national Government health advice for the duration of your project.**

Please note that:

- Research Participant Information Sheets and (where relevant) flyers, posters, and consent forms should include a clear statement that research ethics approval has been obtained from the relevant Research Ethics Committee.
- The Research Participant Information Sheets should include a clear statement that queries should be directed, in the first instance, to the Supervisor (where relevant), or the researcher. Complaints, on the other hand, should be directed, in the first instance, to the Chair of the relevant Research Ethics Committee.
- Approval to proceed with the study is granted subject to receipt by the Committee of satisfactory responses to any conditions that may appear above, in addition to any subsequent changes to the protocol.
- The Research Ethics Committee reserves the right to sample and review documentation, including raw data, relevant to the study.
- If your project has been approved to run for a duration longer than 12 months, you will be required to submit an annual progress report to the Research Ethics Committee. You will be contacted about submission of this report before it becomes due.

Professor Louise Mansfield

Chair of the College of Health, Medicine and Life Sciences Research Ethics Committee (DHS)

Brunel University London

Page 1 of 1

Phase I – Amendment Brunel REC approval.

College of Health, Medicine and Life Sciences Research Ethics Committee (DHS)
Brunel University London
Kingston Lane
Uxbridge
UB8 3PH
United Kingdom

www.brunel.ac.uk

28 June 2022

LETTER OF APPROVAL

APPROVAL HAS BEEN GRANTED FOR THIS STUDY TO BE CARRIED OUT BETWEEN 02/05/2022 AND 31/08/2022 31/08/2022 31/10/2022

Applicant (s): Mr Graham Boniface

Project Title: Decision making in prescribing hand strengthening exercise in rheumatoid arthritis: a judgement analysis

Reference: 36607-A-Jun/2022- 40324-1

Dear Mr Graham Boniface

The Research Ethics Committee has considered the above application recently submitted by you.

The Chair, acting under delegated authority has agreed that there is no objection on ethical grounds to the proposed study. Approval is given on the understanding that the conditions of approval set out below are followed:

- **B3 - PIS: What if something goes wrong? - Suggest you rewrite using the following: 'If you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. 'The person to be contacted if the participant wishes to complain about the experience should be the Chair of the relevant Research Ethics Committee (relevant contact details should be provided – see details at the end of this document).**
- **B3 - PIS: Please provide contact details for researcher and supervisor under 'Contact for further information and complaints'**
- **The agreed protocol must be followed. Any changes to the protocol will require prior approval from the Committee by way of an application for an amendment.**
- **Please ensure that you monitor and adhere to all up-to-date local and national Government health advice for the duration of your project.**

Please note that:

- Research Participant Information Sheets and (where relevant) flyers, posters, and consent forms should include a clear statement that research ethics approval has been obtained from the relevant Research Ethics Committee.
- The Research Participant Information Sheets should include a clear statement that queries should be directed, in the first instance, to the Supervisor (where relevant), or the researcher. Complaints, on the other hand, should be directed, in the first instance, to the Chair of the relevant Research Ethics Committee.
- Approval to proceed with the study is granted subject to receipt by the Committee of satisfactory responses to any conditions that may appear above, in addition to any subsequent changes to the protocol.
- The Research Ethics Committee reserves the right to sample and review documentation, including raw data, relevant to the study.
- If your project has been approved to run for a duration longer than 12 months, you will be required to submit an annual progress report to the Research Ethics Committee. You will be contacted about submission of this report before it becomes due.

Professor Louise Mansfield

Chair of the College of Health, Medicine and Life Sciences Research Ethics Committee (DHS)

Brunel University London

Phase II – Initial Brunel REC approval.

College of Health, Medicine and Life Sciences Research Ethics Committee (DHS)
Brunel University London
Kingston Lane
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United Kingdom

www.brunel.ac.uk

29 July 2022

LETTER OF APPROVAL

APPROVAL HAS BEEN GRANTED FOR THIS STUDY TO BE CARRIED OUT BETWEEN 01/09/2022 AND 31/08/2023

Applicant (s): Mr Graham Boniface Dr Meriel Norris, Dr Neil O'Connell, Dr Esther Williamson, Dr Nicola White, Professor Priscilla Harries, Dr Christopher Tomlinson

Project Title: Phase II of the DOSED study: Decision making in prescribing hand strengthening exercise in rheumatoid arthritis: a judgement analysis

Reference: 37041-LR-Jul/2022- 40789-1

Dear Mr Graham Boniface

The Research Ethics Committee has considered the above application recently submitted by you.

The Chair, acting under delegated authority has agreed that there is no objection on ethical grounds to the proposed study. Approval is given on the understanding that the conditions of approval set out below are followed:

- **Advert/poster - Please add that the study has been approved the the College of Health, Medicine and Life Sciences Research Ethics Committee**
- **The agreed protocol must be followed. Any changes to the protocol will require prior approval from the Committee by way of an application for an amendment.**
- **Please ensure that you monitor and adhere to all up-to-date local and national Government health advice for the duration of your project.**

Please note that:

- Research Participant Information Sheets and (where relevant) flyers, posters, and consent forms should include a clear statement that research ethics approval has been obtained from the relevant Research Ethics Committee.
- The Research Participant Information Sheets should include a clear statement that queries should be directed, in the first instance, to the Supervisor (where relevant), or the researcher. Complaints, on the other hand, should be directed, in the first instance, to the Chair of the relevant Research Ethics Committee.
- Approval to proceed with the study is granted subject to receipt by the Committee of satisfactory responses to any conditions that may appear above, in addition to any subsequent changes to the protocol.
- The Research Ethics Committee reserves the right to sample and review documentation, including raw data, relevant to the study.
- If your project has been approved to run for a duration longer than 12 months, you will be required to submit an annual progress report to the Research Ethics Committee. You will be contacted about submission of this report before it becomes due.
- You may not undertake any research activity if you are not a registered student of Brunel University or if you cease to become registered, including abeyance or temporary withdrawal. As a deregistered student you would not be insured to undertake research activity. Research activity includes the recruitment of participants, undertaking consent procedures and collection of data. Breach of this requirement constitutes research misconduct and is a disciplinary offence.

Professor Louise Mansfield

Chair of the College of Health, Medicine and Life Sciences Research Ethics Committee (DHS)

Brunel University London

Page 1 of 1

Phase II Amendment Brunel REC approval.

College of Health, Medicine and Life Sciences Research Ethics Committee (DHS)
Brunel University London
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10 February 2023

LETTER OF APPROVAL

APPROVAL HAS BEEN GRANTED FOR THIS STUDY TO BE CARRIED OUT BETWEEN 01/09/2022 AND 31/08/2023

Applicant (s): Mr Graham Boniface

Project Title: Phase II of the DOSED study: Decision making in prescribing hand strengthening exercise in rheumatoid arthritis: a judgement analysis

Reference: 37041-A-Feb/2023- 43653-1

Dear Mr Graham Boniface

The Research Ethics Committee has considered the above application recently submitted by you.

The Chair, acting under delegated authority has agreed that there is no objection on ethical grounds to the proposed study. Approval is given on the understanding that the conditions of approval set out below are followed:

- **Amendment - Change to rating of perceived exertion scale being used.**
- **The agreed protocol must be followed. Any changes to the protocol will require prior approval from the Committee by way of an application for an amendment.**
- **Please ensure that you monitor and adhere to all up-to-date local and national Government health advice for the duration of your project.**

Please note that:

- Research Participant Information Sheets and (where relevant) flyers, posters, and consent forms should include a clear statement that research ethics approval has been obtained from the relevant Research Ethics Committee.
- The Research Participant Information Sheets should include a clear statement that queries should be directed, in the first instance, to the Supervisor (where relevant), or the researcher. Complaints, on the other hand, should be directed, in the first instance, to the Chair of the relevant Research Ethics Committee.
- Approval to proceed with the study is granted subject to any conditions that may appear above.
- The Research Ethics Committee reserves the right to sample and review documentation, including raw data, relevant to the study.
- If your project has been approved to run for a duration longer than 12 months, you will be required to submit an annual progress report to the Research Ethics Committee. You will be contacted about submission of this report before it becomes due.
- You may not undertake any research activity if you are not a registered student of Brunel University or if you cease to become registered, including abeyance or temporary withdrawal. As a deregistered student you would not be insured to undertake research activity. Research activity includes the recruitment of participants, undertaking consent procedures and collection of data. Breach of this requirement constitutes research misconduct and is a disciplinary offence.

Professor Louise Mansfield

Chair of the College of Health, Medicine and Life Sciences Research Ethics Committee (DHS)

Brunel University London

APPENDIX 10. STUDY THREE. PARTICIPANT INFORMATION SHEET AND CONSENT FORMS

Phase I. Participant Information sheet and consent form.

PARTICIPANT INFORMATION SHEET

Research study title:

Decision making in prescribing hand strengthening exercise in rheumatoid arthritis: a clinical judgement analysis

Short title:

DOSED: **D**ecis**O**ns in **S**trength **E**xercise **D**ose

Invitation to take part:

You are being asked to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask me if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. Thank you for reading this.

Background to study:

Occupational therapists and physiotherapists (therapists) play a key role in the management of individuals with pain and dysfunction of the hands caused by rheumatoid arthritis (RA). NICE guidelines recommend therapists prescribe hand strengthening exercise, however, no information is offered about what dose to prescribe, only that it should be tailored to the individual. Identifying how therapists during the healthcare consultation, select, weight, and combine information when deciding what dose of hand exercise to prescribe may be helpful in reducing variation in prescribing practice, optimise clinical and cost effectiveness and inform future (more detailed) clinical guidelines.

What is the purpose of the study?

To explore therapists' judgements (decisions) prescribing hand strengthening exercise in rheumatoid arthritis. The study is comprised of two phases. Phase I involves identifying the information (cues) therapists use when deciding what dose of hand strengthening exercise to prescribe. Phase II involves therapists completing an online experiment, where they will be presented with hypothetical case scenarios and asked to decide about what intensity of hand strengthening exercise they would prescribe. This participant information sheet relates to phase I of the DOSED study.

Why have I been invited to participate?

In order to explore how therapists' judge what dose to prescribe in phase II, the study needs to identify the information (cues) most commonly used in clinical practice to prescribe hand strengthening exercise. These cues will be used to develop case scenarios that will be used in the phase II of this research study. In order to do this, we need expert therapists' who are 1) Registered with the Health and Care Professions Council, 2) Have five or more years post-registration experience, 3) Treat more than 5 patients with pain and dysfunction of the hands and wrists caused by RA per month and 4) Have undertaken post-graduate training (e.g., Masters/PhD) and/or specialist hand therapy training (e.g., British Association of Hand Therapists accreditation).

Do I have to take part?

Taking part is voluntary. You can withdraw at any time without consequence or pressure personally or professionally.

What will happen to me if I take part?

You will be asked to take part in a group meeting involving 5-12 other participants via an online meeting platform (e.g. Microsoft TEAMS). Prior to this meeting taking place we will first email you a data collection form from the study researcher's Brunel University email address. You will be asked to list all the information (cues) you use when making decisions about what dose of hand strengthening exercise to prescribe patients with pain and dysfunction of the hands caused by RA. We will ask you to complete this within 2 weeks of receiving the email. Should we not hear back from you, we will send to emails spaced one week apart, reminding you to complete the form. We will collate everyone's responses before sending you everyone's overall list of cues in a second email. This time we will ask you look at everyone's responses and add any further cues that come to mind. Again, we will ask you to complete a data collection form adding anymore cues that come to mind. We ask that you send the form back within 2 weeks. As before, we will send two reminder emails should we not hear from you. Once both these stages are complete, we will send a poll via email to arrange the online group meeting. The meeting will take approximately 2.5 hours and will involve group discussion about the cues collected. During the meeting we will ask you to add anymore cues that come to mind before being asked to rank the list of cues in order of importance. Once this is complete, this will end your involvement in this phase I of the DOSED study. We will ask if you are interested in hearing more about phase II. If so, we will send you further information about taking part.

Are there any lifestyle restrictions?

There are not expected to be any lifestyle restrictions.

What are the possible disadvantages and risks of taking part?

There are not expected to be any risks. However, this is a group-based task and in the online meeting you will be expected to engage with other participants. In addition, taking part will require you to set aside some time outside of normal work hours, which you may find a burden.

What are the possible benefits of taking part?

By taking part, you will be contributing towards improving our understanding about how therapists prescribe dose of hand strengthening exercise in RA.

What if something goes wrong?

Owing to the nature of the study, we do not anticipate anything going wrong. However, if you have questions or complaints, please direct these in the first instance to the principal investigator or PhD student supervisor (contact details below).

Will my taking part in this study be kept confidential?

All data related to this project will be kept safely according to GDPR policies. No identifying information will be shared outside of the group. We will also make it clear to the group that the participants and content should not be discussed outside of the meeting. However as this is a group discussion there is a risk that others in the group may share your involvement with the study.

Will I be recorded, and how will the recording be used?

The online group meeting will be audio and video recorded and saved to Brunel University London OneDrive. This is to allow the research team to look back on the information you provide after the meeting has finished. The recording will be deleted at the end of the PhD. This is expected in June 2024.

What will happen to the results of the research study?

We will use the results to inform the phase II of the study which will involve asking therapists to decide on what intensity of hand strengthening exercise they would prescribe when presented with different clinical case scenarios. We will report the results in via journal publication, conference and social media.

Who is organising and funding the research?

This work was supported by the National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care Oxford at Oxford Health NHS Foundation Trust, and supported by the NIHR Biomedical Research Centre, Oxford.

What are the indemnity arrangements?

Brunel University London provides appropriate insurance cover for research which has received ethical approval.

Who has reviewed the study?

The study has been reviewed by PhD student's supervisory team. Ethical approval has been granted by Brunel University.

Research Integrity

Brunel University London is committed to compliance with the Universities UK Research Integrity Concordat. You are entitled to expect the highest level of integrity from the researchers during the course of this research

Contact for further information and complaints:

Study researcher: Graham Boniface (graham.boniface@brunel.ac.uk)
PhD student supervisor: Dr Meriel Norris (meriel.norris@brunel.ac.uk)

For complaints:
College of Health and Life Sciences Research Ethics Committee
Chair: Professor Louise Mansfield (Louise.Mansfield@brunel.ac.uk)

CONSENT FORM

Decision making in prescribing hand strengthening exercise in rheumatoid arthritis: a clinical judgement analysis

Principal investigator: Graham Boniface

APPROVAL HAS BEEN GRANTED FOR THIS STUDY TO BE CARRIED OUT BETWEEN 02/05/2022 AND 31/08/2022

The participant should complete the whole of this sheet.		
	YES	NO
Have you read the above Participant Information Sheet?	☐	☐
Have you had an opportunity to ask questions and discuss this study?	☐	☐
Have you received satisfactory answers to all your questions?	☐	☐
Do you understand that you will not be referred to by name in any report concerning this study?	☐	☐
Do you understand that:		
• You are free to withdraw from this study at any time.	☐	☐
• You don't have to give any reason for withdrawing.	☐	☐
• Choosing not to participate or withdrawing will not affect your rights?	☐	☐
I agree to the online focus group being audio and video recorded.	☐	☐
I agree to the use of non-attributable quotes when the study is written up or published.	☐	☐
The procedures regarding confidentiality have been explained to me.	☐	☐
I agree that my anonymised data can be stored and shared with other researchers for use in future projects.	☐	☐
I agree to take part in this study.	☐	☐

Signature of research participant:	
Print name:	Date:

Phase II. Participant Information sheet and consent form.

PARTICIPANT INFORMATION SHEET

Research study title:

Decision making in prescribing hand strengthening exercise in rheumatoid arthritis: a clinical judgement analysis

Short title:

DOSED: **D**ecisi**O**ns in **S**trength **E**xercise **D**ose

Invitation to take part:

You are being asked to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask me if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. Thank you for reading this.

Background to study:

Occupational therapists and physiotherapists (therapists) play a key role in the management of individuals with pain and dysfunction of the hands caused by rheumatoid arthritis (RA). NICE guidelines recommend therapists prescribe hand strengthening exercise, however, no information is offered about what dose to prescribe, only that it should be tailored to the individual. Identifying how therapists during the healthcare consultation, select, weight and combine information when deciding what dose of hand exercise to prescribe may be helpful in reducing variation in prescribing practice, optimise clinical and cost effectiveness and inform future (more detailed) clinical guidelines.

What is the purpose of the study?

To explore therapists' judgements (decisions) prescribing hand strengthening exercise in rheumatoid arthritis. The study is comprised of two phases. Phase I involved identifying the information (cues) therapists use when deciding what dose of hand strengthening exercise to prescribe. Phase II involves therapists completing an online experiment, where they will be presented with hypothetical case scenarios and asked to decide about what intensity of hand strengthening exercise they would prescribe. This participant information sheet relates to phase II of the DOSED study.

Why have I been invited to participate?

In order to explore how therapists' judge what dose to prescribe, we need occupational therapists and physiotherapists who are 1) Registered with the Health and Care Professions Council, 2) Have 2 or more years post-registration experience and treat more than 5 patients with pain and dysfunction of the hands and wrists caused by RA per month.

Do I have to take part?

You have the right to decline or withdraw from the study without adverse effect to you personally or professionally. If you decide to take part, you will be given this information sheet to keep.

What will happen to me if I take part?

You will be asked to take part in an online experiment. We will ask you to review 75 hypothetical case scenarios involving patients with pain and dysfunction of the wrist and hand caused by rheumatoid arthritis. Each scenario will contain clinical details which at the end you will be asked to provide the intensity of hand strengthening exercise you would prescribe. To complete the set of case scenarios will take approximately 75 minutes. Should you need to stop and log out for whatever reason, your progress will be automatically saved. You will be able to log back in with your participant ID and password. If you don't log back in after 1-week, we will send you an automatic email reminding you and complete the experiment. The experiment will remain open for 3-months from the date you join the study. Once you complete all the case scenarios you will be sent a certificate of taking part for your CPD file and this will end your involvement in the DOSED study.

Are there any lifestyle restrictions?

There are not expected to be any lifestyle restrictions.

What are the possible disadvantages and risks of taking part?

There are not expected to be any risks. However, taking part will require you to set aside time outside of normal work hours to complete the study. You may find this a burden.

What are the possible benefits of taking part?

By taking part, you will be contributing towards improving our understanding about how therapists prescribe dose of hand strengthening exercise in RA.

What if something goes wrong?

Owing to the nature of the study, we do not anticipate anything going wrong. However, if you have questions or complaints, please direct these in the first instance to the principal investigator or PhD student supervisor (contact details below).

Will my taking part in this study be kept confidential?

All data related to this project will be kept safely according to GDPR policies.

Will I be recorded, and how will the recording be used?

No.

What will happen to the results of the research study?

We will use the results to inform future research centred on exercise prescription. We will report the results in via journal publication, conference and social media.

Who is organising and funding the research?

This work was supported by the National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care Oxford at Oxford Health NHS Foundation Trust, and supported by the NIHR Biomedical Research Centre, Oxford.

What are the indemnity arrangements?

Brunel University London provides appropriate insurance cover for research which has received ethical approval.

Who has reviewed the study?

The study has been reviewed by the College of health, Medicine and Life Sciences Research Ethics Committee.

Research Integrity

Brunel University London is committed to compliance with the Universities UK Research Integrity Concordat. You are entitled to expect the highest level of integrity from the researchers during the course of this research

Contact for further information and complaints:

Brunel University London is committed to compliance with the Universities UK Research Integrity Concordat. You are entitled to expect the highest level of integrity from the researchers during the course of this research

Contact for further information and complaints:

Professor Louise Mansfield, Chair College of Health, Medicine and Life Sciences Research Ethics Committee, Louise.Mansfield@brunel.ac.uk

Members of the research team:

Physiotherapist	Dr Meriel Norris Department of Health Sciences, Centre for Health and Wellbeing across the Lifecourse, Brunel University London, Uxbridge, United Kingdom
Physiotherapist	Dr Neil O'Connell Department of Health Sciences, Centre for Health and Wellbeing across the Lifecourse, Brunel University London, Uxbridge, United Kingdom
Physiotherapist	Dr Esther Williamson Nuffield Department of Orthopaedics Rheumatology and Musculoskeletal Sciences (NDORMS), University of Oxford, Oxford, United Kingdom.
Research associate	Dr Nicola White Marie Curie Palliative Care Research Department. Division of Psychiatry, University College London, United Kingdom
Occupational therapist	Professor Priscilla Harries Centre for Applied Health and Social Care Research, St George's, University of London, United Kingdom.

APPENDIX 11. STUDY THREE. PHASE I – INITIAL PARTICIPANT EMAIL INSTRUCTIONS.

Email subject: DOSED research study/Participant XX

Dear XX

Thank you for taking part in phase I of the above study. There are 3 key stages to this phase of the DOSED research study. Stage 1 and 2 centre on identifying the information (cues) you use to decide what dose of hand strengthening exercise to prescribe a patient with pain and dysfunction of the hands caused by rheumatoid arthritis. Stage 3 involves clarifying and ranking the cues participants have identified.

For this stage, please answer the following questions about yourself (please complete the table below) and complete and return the attached data collection form, trying not to take longer than 2 weeks. You will be sent two emails reminding you to complete this stage. Should you have any questions, please email graham.boniface@brunel.ac.uk

I look forward to receiving your email.

Graham Boniface
Chief Investigator

First name:	
Surname:	
Age (years):	
Gender (male/female/other/prefer not to say).	
Non-NHS email address:	
Professional background (occupational therapist or physiotherapist).	
Year of graduation as an occupational therapist or physiotherapist (year)	
Geographic work location (England, Northern Ireland, Scotland, Wales).	
Work environment (National Health Service, Private Sector, Both, Other – please state):	
Professional level (Agenda for Change job band 5, 6, 7, 8a, 8b, 8c, 8d, 9, Other- please state):	
Highest level of professional training (Undergraduate degree (e.g., BSc), post-graduate degree (e.g., MSc), PhD degree, Other – please state):	
Average RA patients treated per month (None, Less than 5, 5-10, 11-15, More than 15):	

DOSED_Phase 1_Email Instructions_Stage 1_V1.0_19Feb2022

APPENDIX 12. STUDY THREE. PHASE I – DATA COLLECTION FORM.

RESEARCH STUDY:

Decision making in prescribing hand strengthening exercise in rheumatoid arthritis: a

Participant instructions:

You have a patient with pain and dysfunction of the hands caused by rheumatoid arthritis. You decide to prescribe hand strengthening exercise. Please list all of the information (cues) gathered from the healthcare consultation to decide what exercise intensity to prescribe. **Please be as specific as possible.**

Cues
1.
2.
3.
4.
5.
6.
7.
8.
9.
10.
11.
12.
13.
14.
15.
16.
17.
18.
19.
20.

Please email back the completed form to graham.boniface@brunel.ac.uk

DOSED_Phase 1_Data Collection Form_V1.0_19Feb2022

APPENDIX 13. STUDY THREE. PHASE I – FOLLOW-UP PARTICIPANT EMAIL INSTRUCTIONS.

Email subject: DOSED research study

Dear XX

Thank you for emailing your list of cues.

We now attach everyone's responses. Please look at this list and think of any further cues that come to mind. Please complete and return the attached data collection form, trying not to take longer than 2 weeks. You will be sent two emails reminding you to complete this stage. Should you have any questions, please email graham.boniface@brunel.ac.uk

In addition to the above stage, you will shortly receive an email containing a poll to arrange the online group meeting. This meeting is expected to take place outside of work time. As with previous stages I will send two emails reminding you to complete the poll. The meeting is expected to take approximately 2 hours and will involve discussion about the cues collected. During this meeting we will collectively discuss the cues listed. The meeting will end with participants ranking the cues in order of importance.

Should you have any questions, please email graham.boniface@brunel.ac.uk

I look forward to receiving your email.

Graham Boniface
Project researcher

DOSED_Phase 1_Email Instructions_Stage 2_V1.0_19Feb2022

APPENDIX 14. STUDY THREE. PHASE I – TOP TEN CLINICAL CUES.

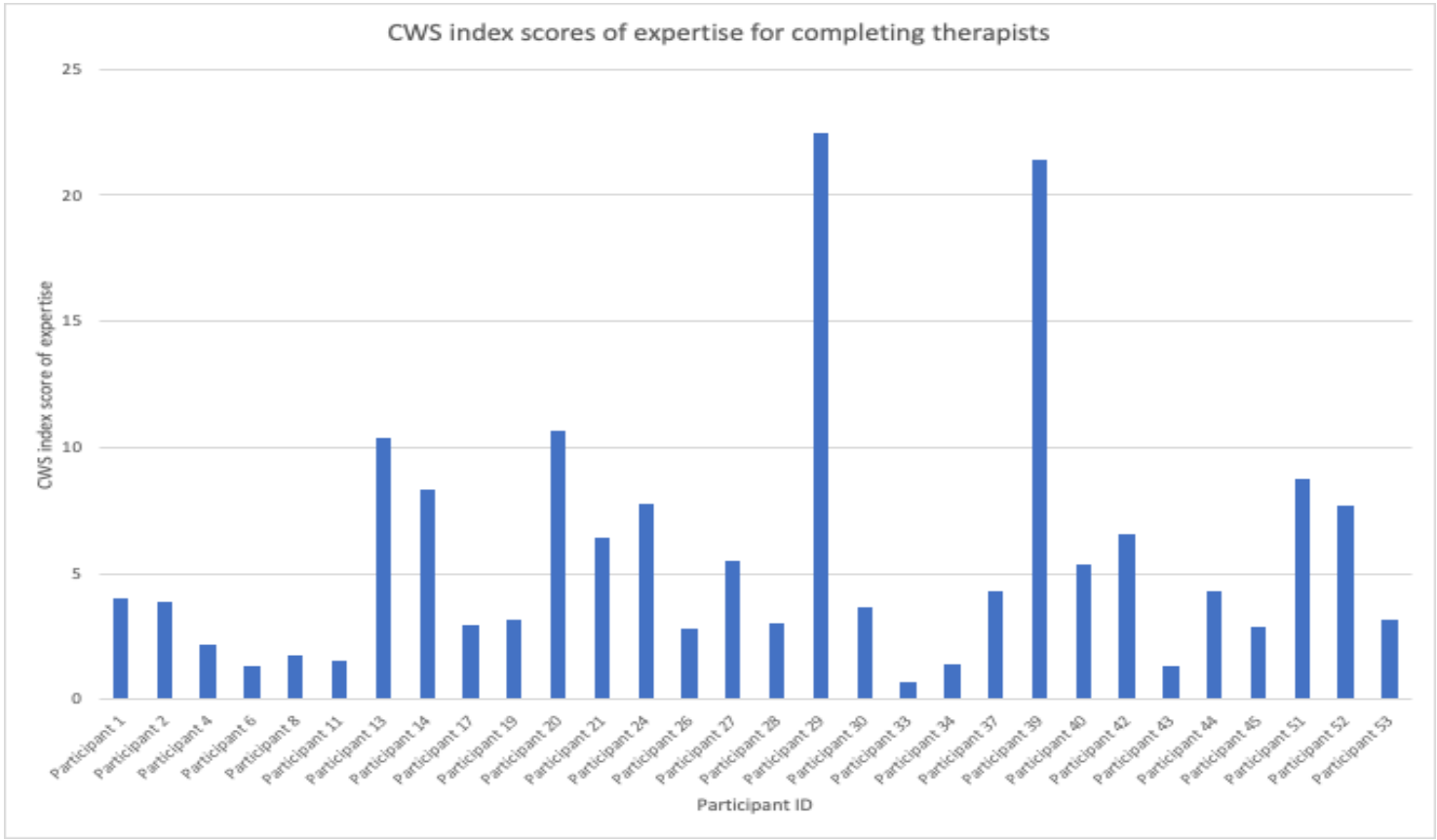
Clinical cues identified by therapists from phase I (Top 10 highlighted in grey).

Cue descriptor	Times cue descriptor mentioned (n=)	Participants suggesting cue (n=)
Pain	19	10
Current function	12	9
Current strength	12	8
Exercise performance during consultation	13	7
Joint ROM†	11	7
Joint deformity	9	7
Patient engagement	7	7
Patient goal	7	6
Joint swelling	7	5
Disease activity	8	4
Patient confidence in performing exercise without making pain worse	4	4
Co-morbidities	4	3
Patient time for exercise	3	3
Patient experience of following an exercise programme	2	2
Patient compliance	2	2
Previous response to exercise-based treatment	2	2
Patient use of splinting	2	2
Patient ability to modify dose of exercise during a flare-up	2	1
Availability of exercise equipment	2	1
Patient age	1	1
Contraindications to exercise	1	1
Exercise goal (motor relearning, hypertrophy, endurance)	1	1
Pain impacting carer responsibilities	1	1
Patient comprehension of the effects of exercise	1	1
Patient mood	1	1
Therapist type (OT or PT)‡	1	1
Hand fatigue doing activities	1	1
Psychosocial issues	1	1
Function required by patient	1	1
Patient dexterity	1	1
Joint stiffness/Contracture	1	1
Sensory deficits	1	1
Surgery (past/planned)	1	1

† ROM = Range of movement.

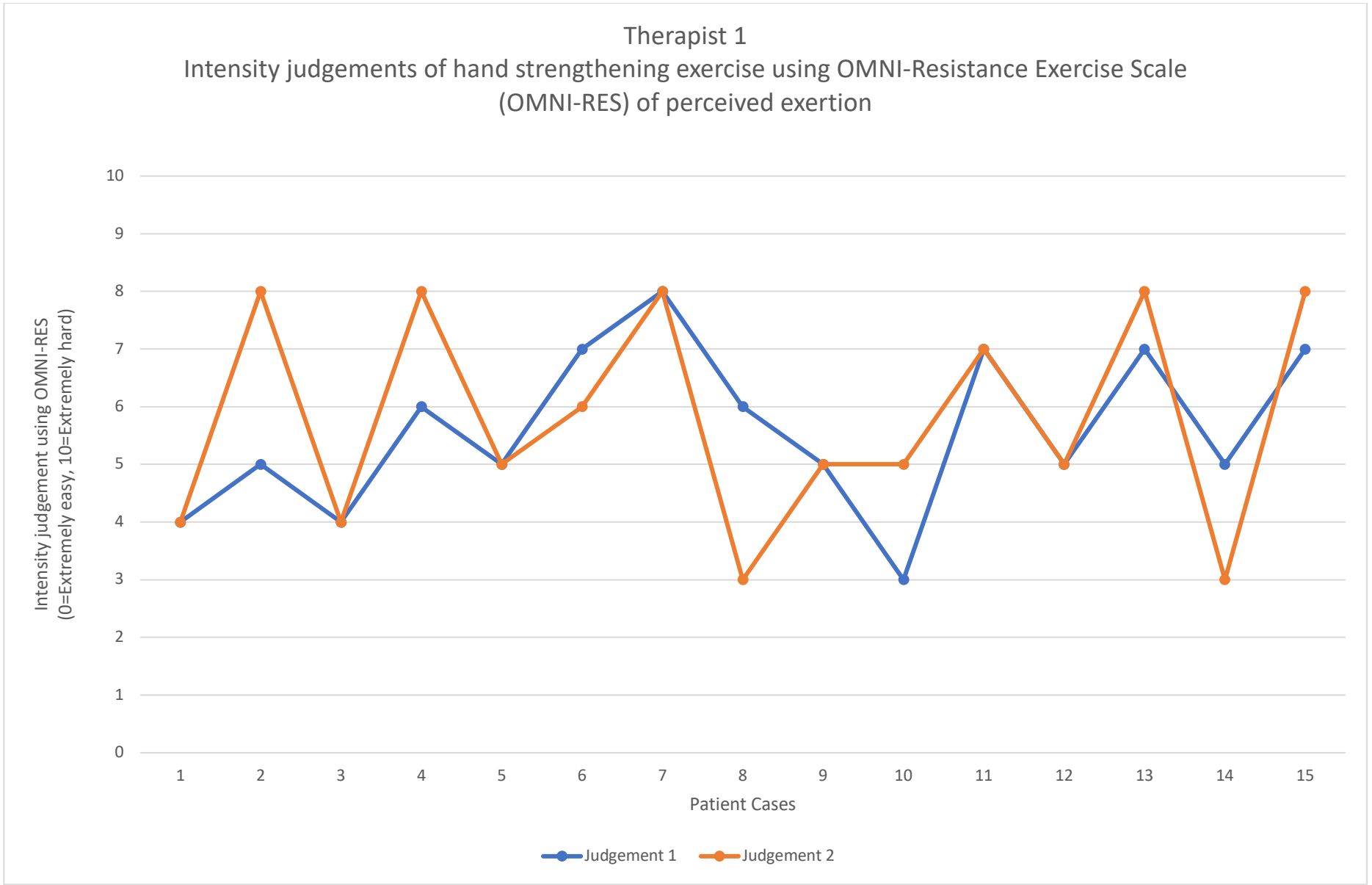
‡ OT = Occupational therapist/PT=Physiotherapist.

APPENDIX 15. STUDY THREE. PHASE I – CWS SCORES.



Graphical representation of judgements to the original and repeated patient case scenarios

(All completing therapists n=30)


Therapist 1
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
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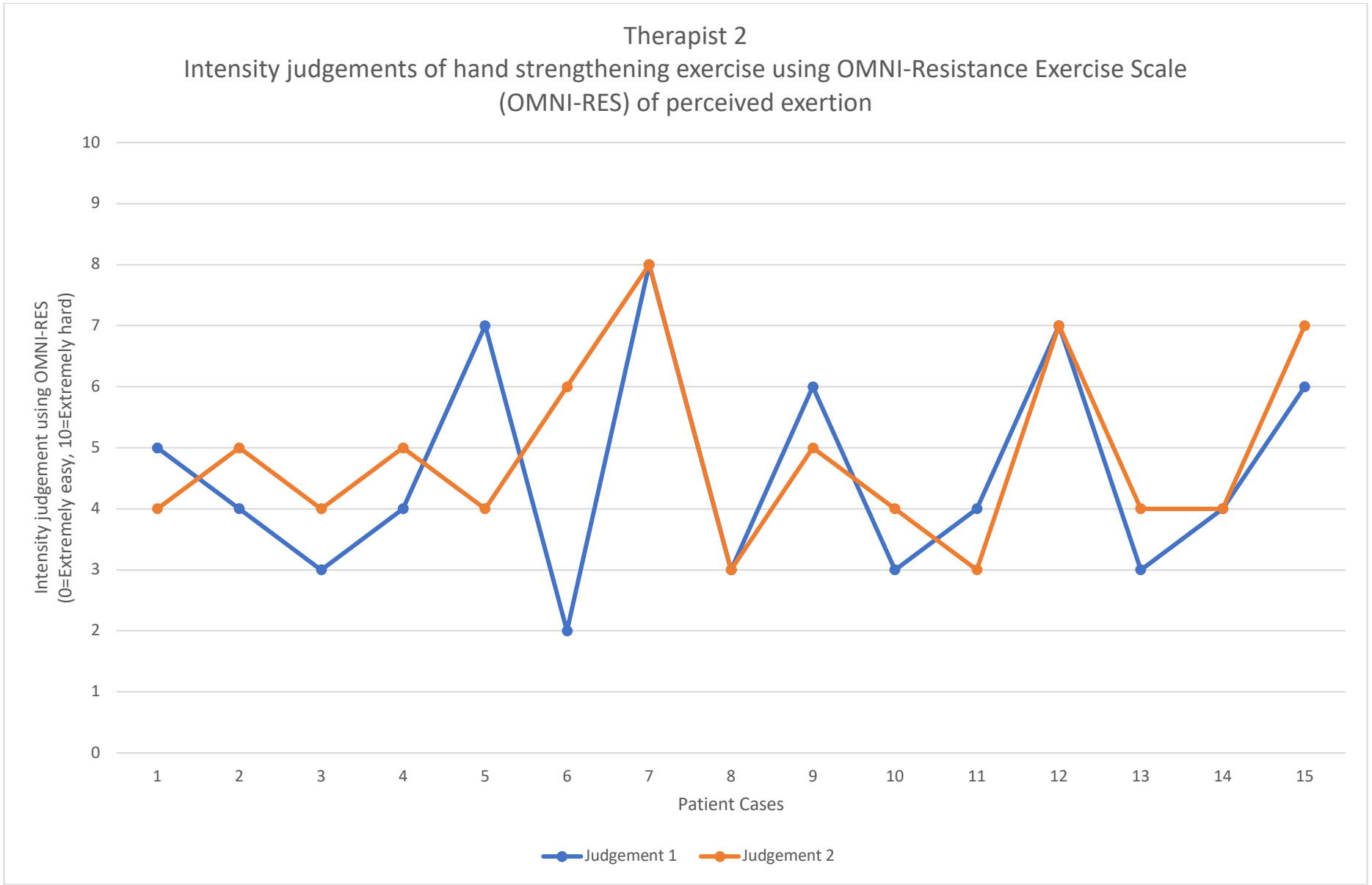
Patient Cases
Judgement 1
Judgement 2


Therapist 2
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
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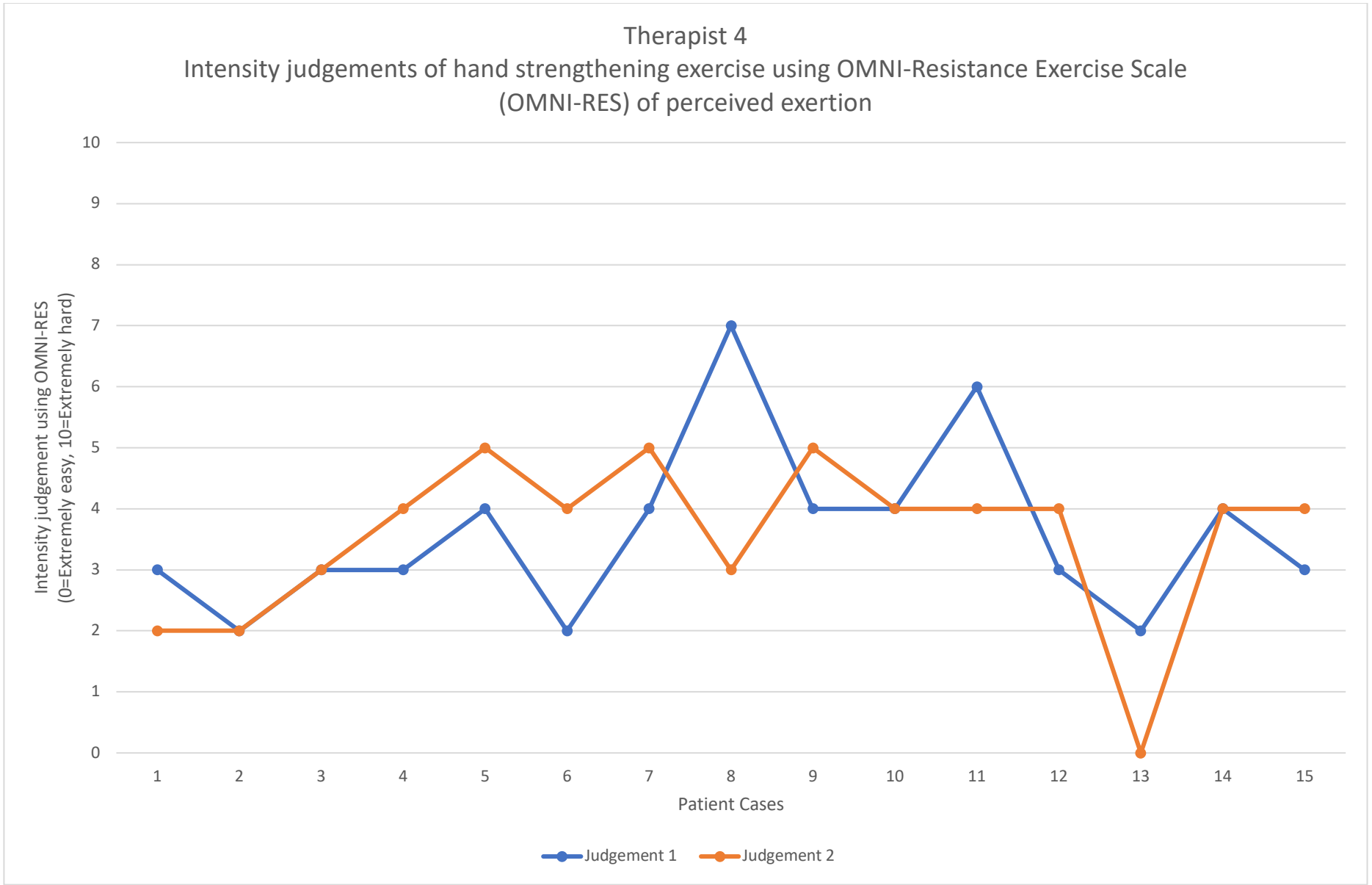
Patient Cases
Judgement 1
Judgement 2


Therapist 4
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
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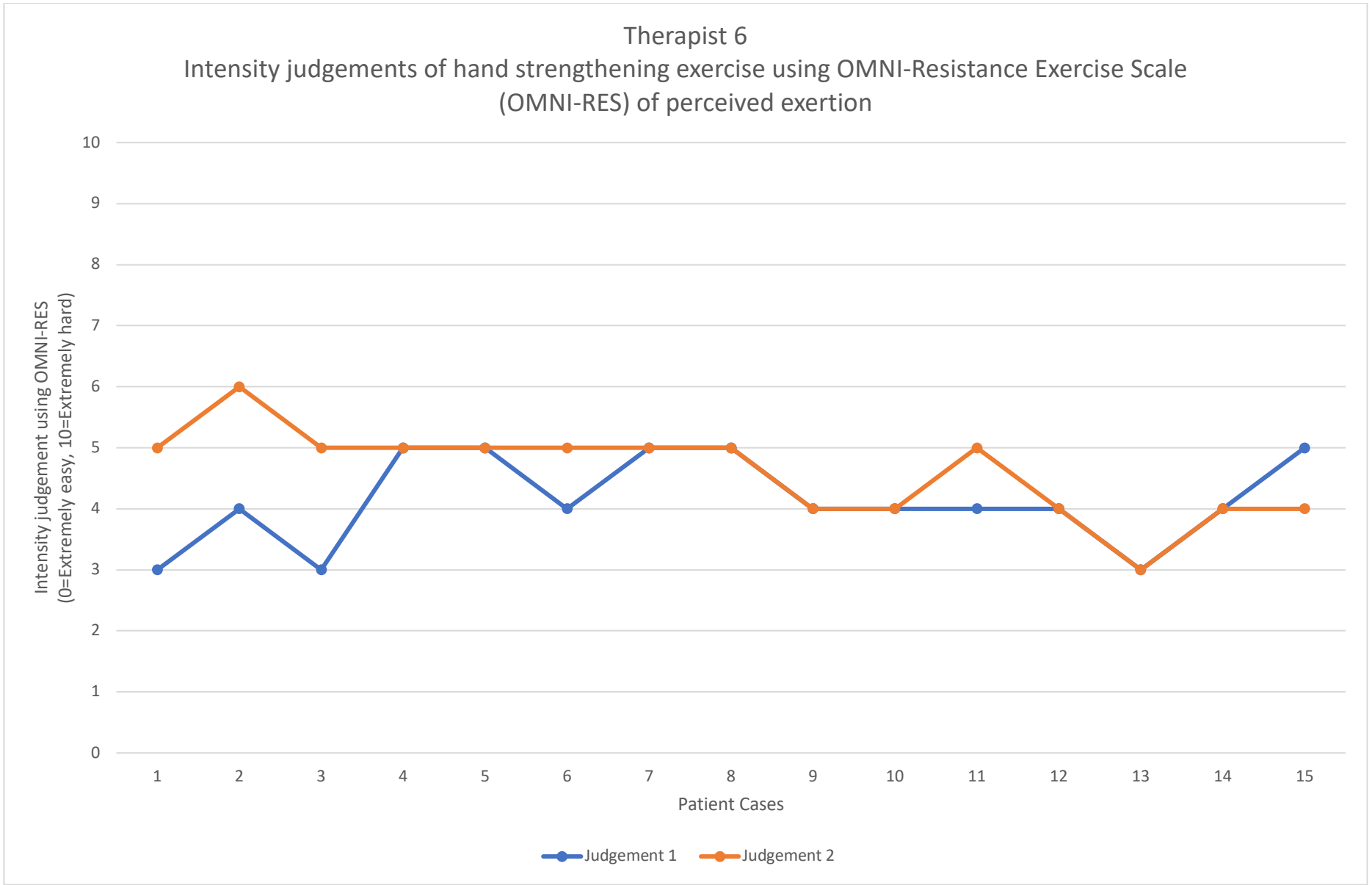
Patient Cases
Judgement 1
Judgement 2


Therapist 6
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
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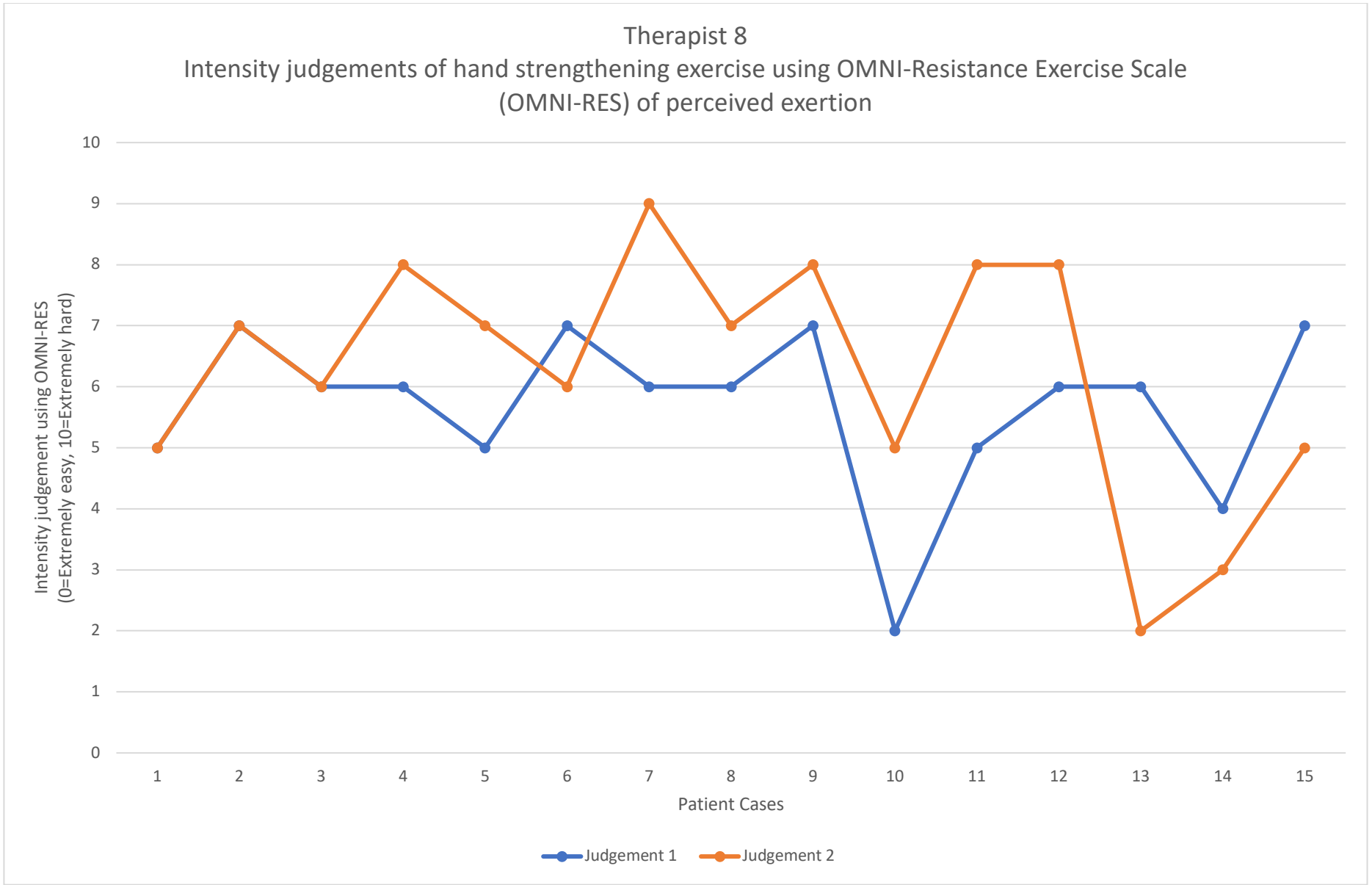
Patient Cases
Judgement 1
Judgement 2


Therapist 8
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
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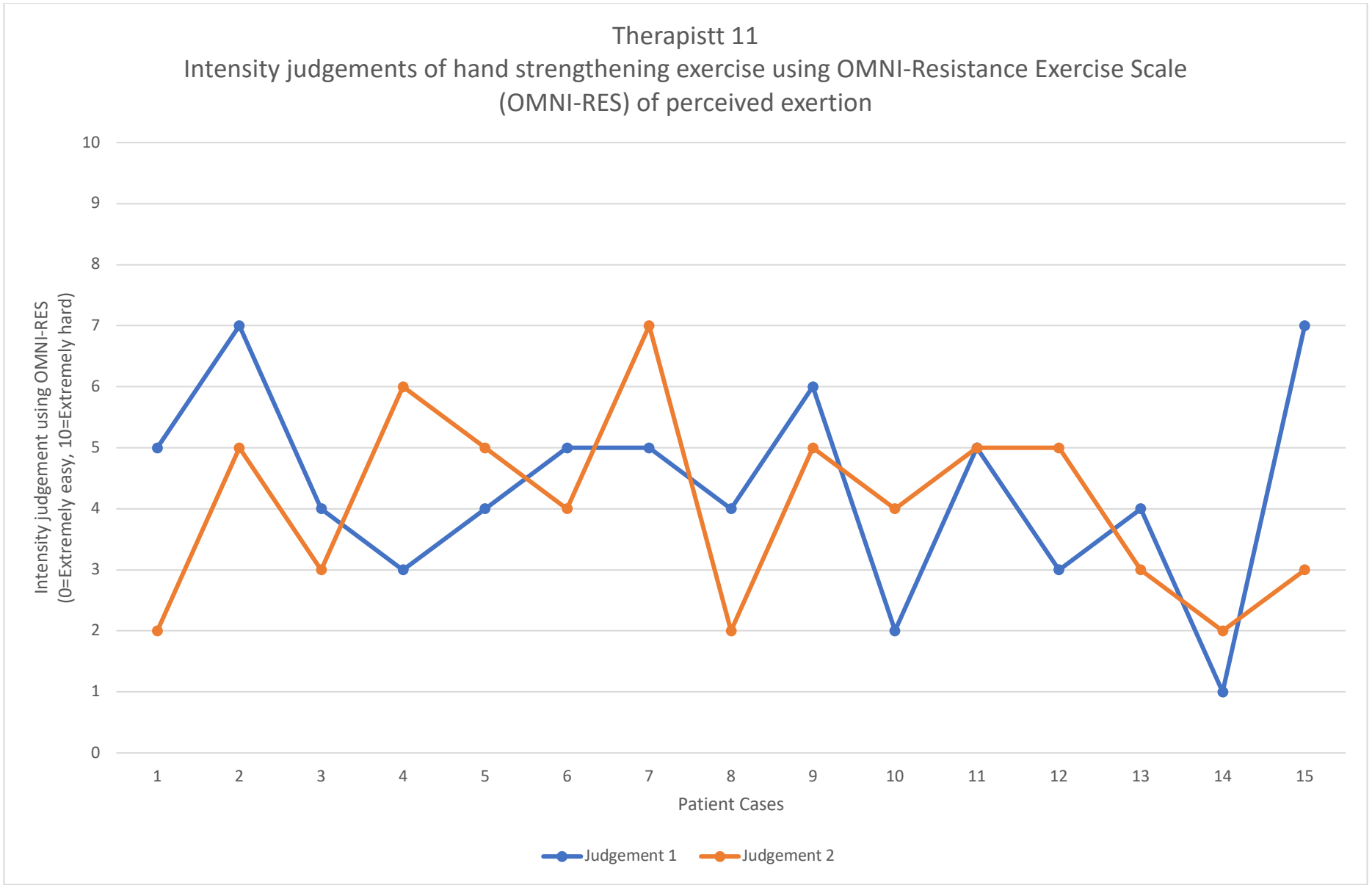
Patient Cases
Judgement 1
Judgement 2


Therapistt 11
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
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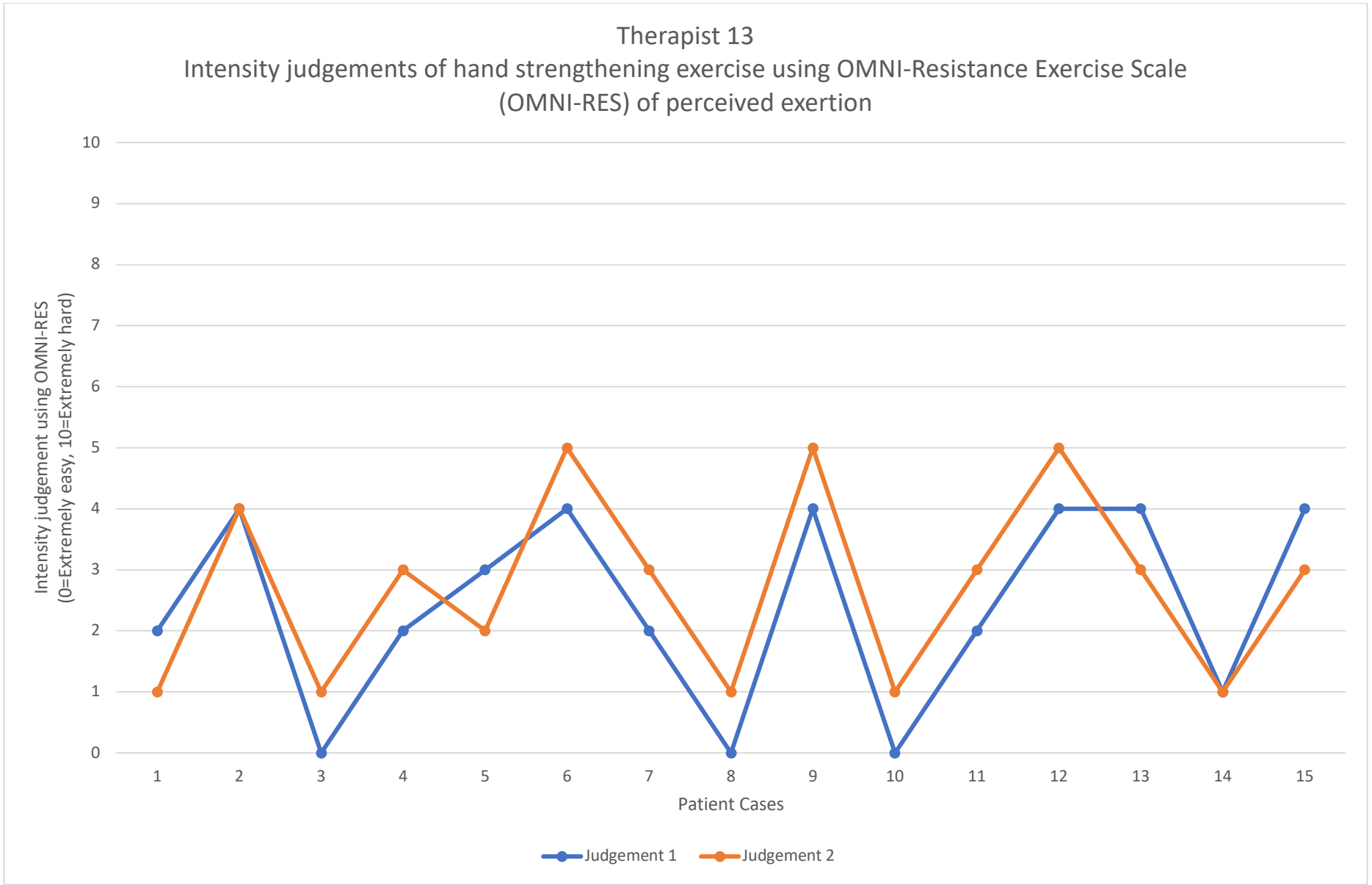
Patient Cases
Judgement 1
Judgement 2


Therapist 13
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
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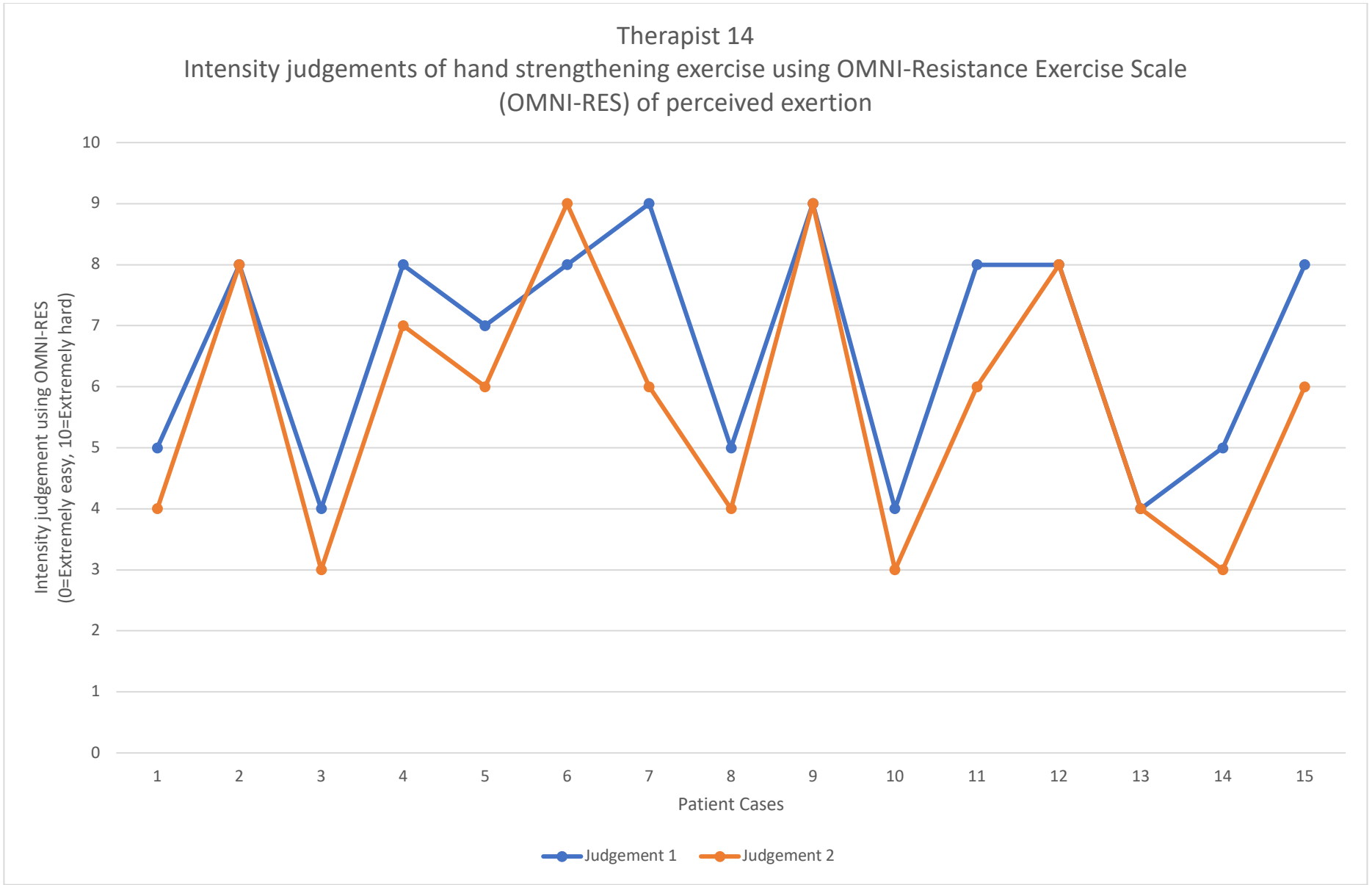
Patient Cases
Judgement 1
Judgement 2


Therapist 14
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
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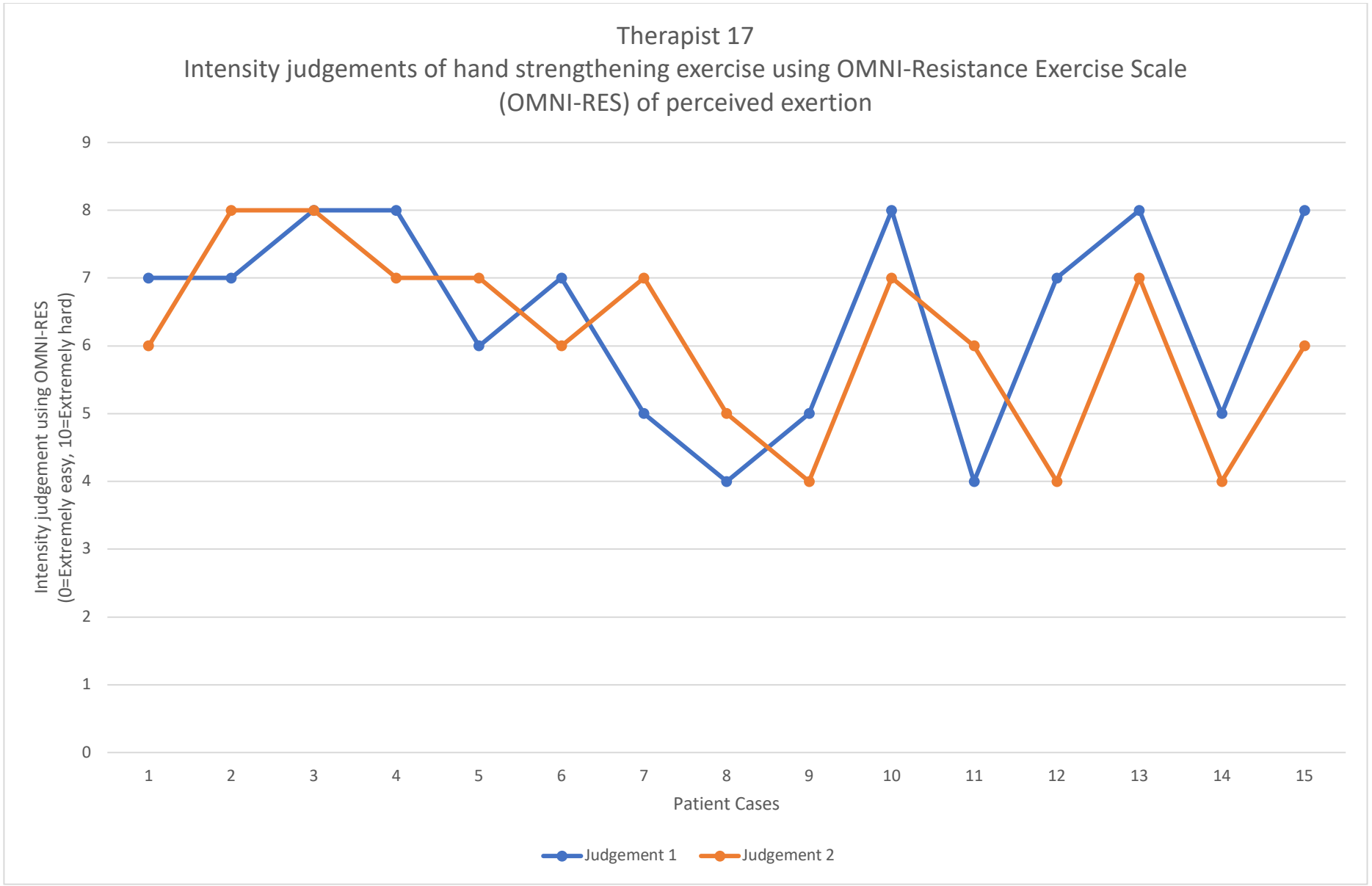
Patient Cases
Judgement 1
Judgement 2


Therapist 17
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
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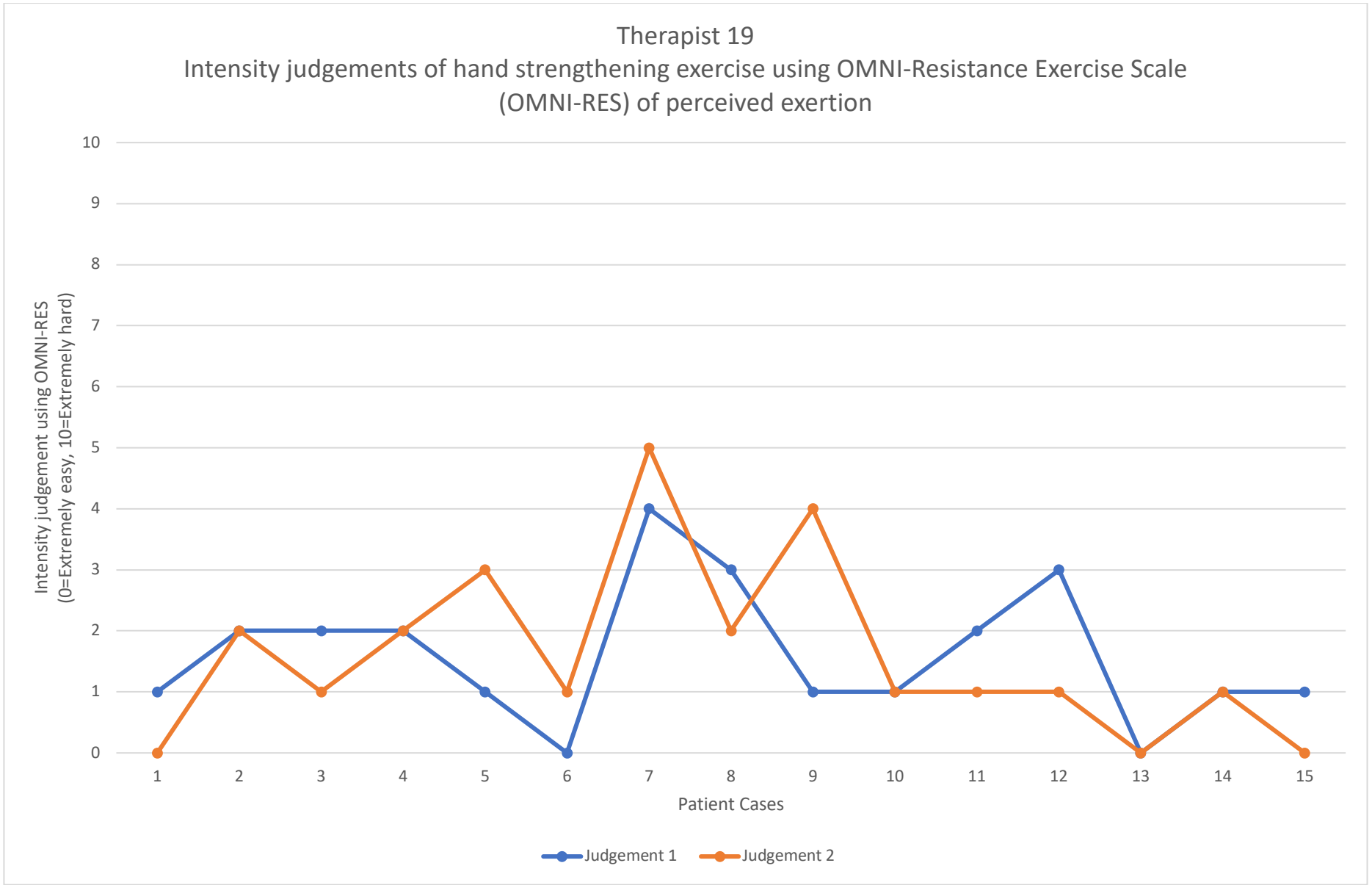
Patient Cases
Judgement 1
Judgement 2


Therapist 19
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
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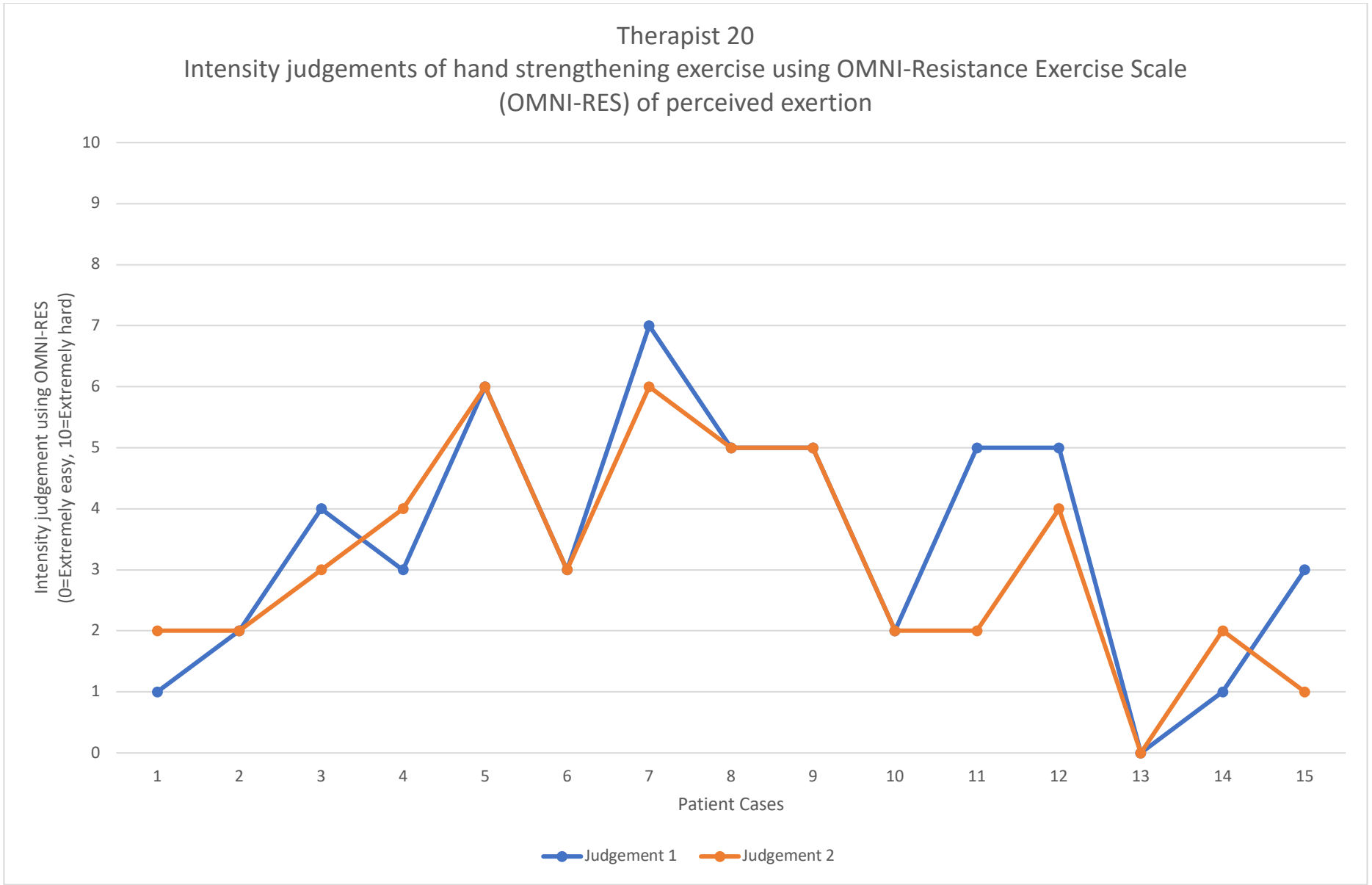
Patient Cases
Judgement 1
Judgement 2


Therapist 20
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
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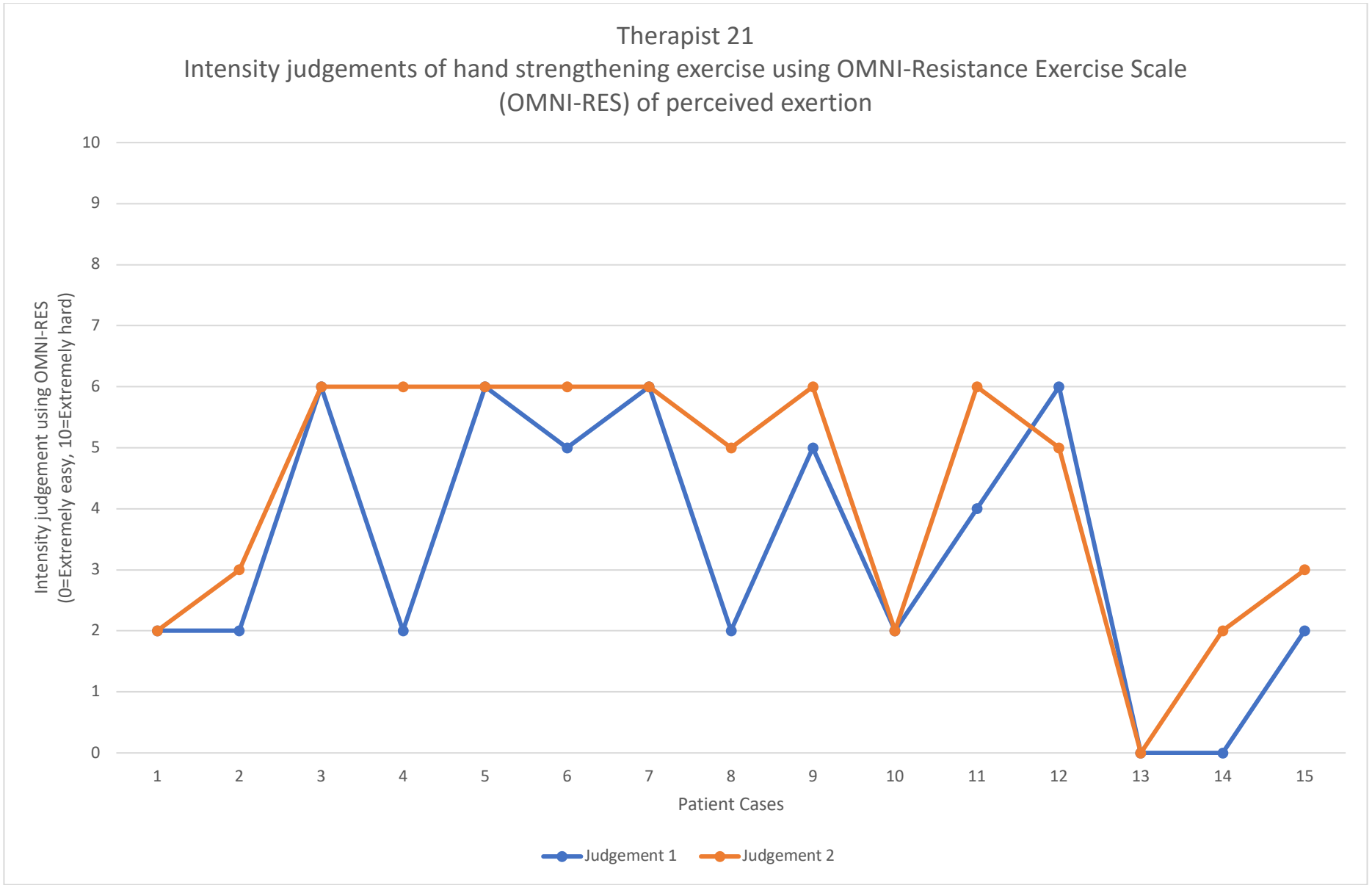
Patient Cases
Judgement 1
Judgement 2


Therapist 21
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
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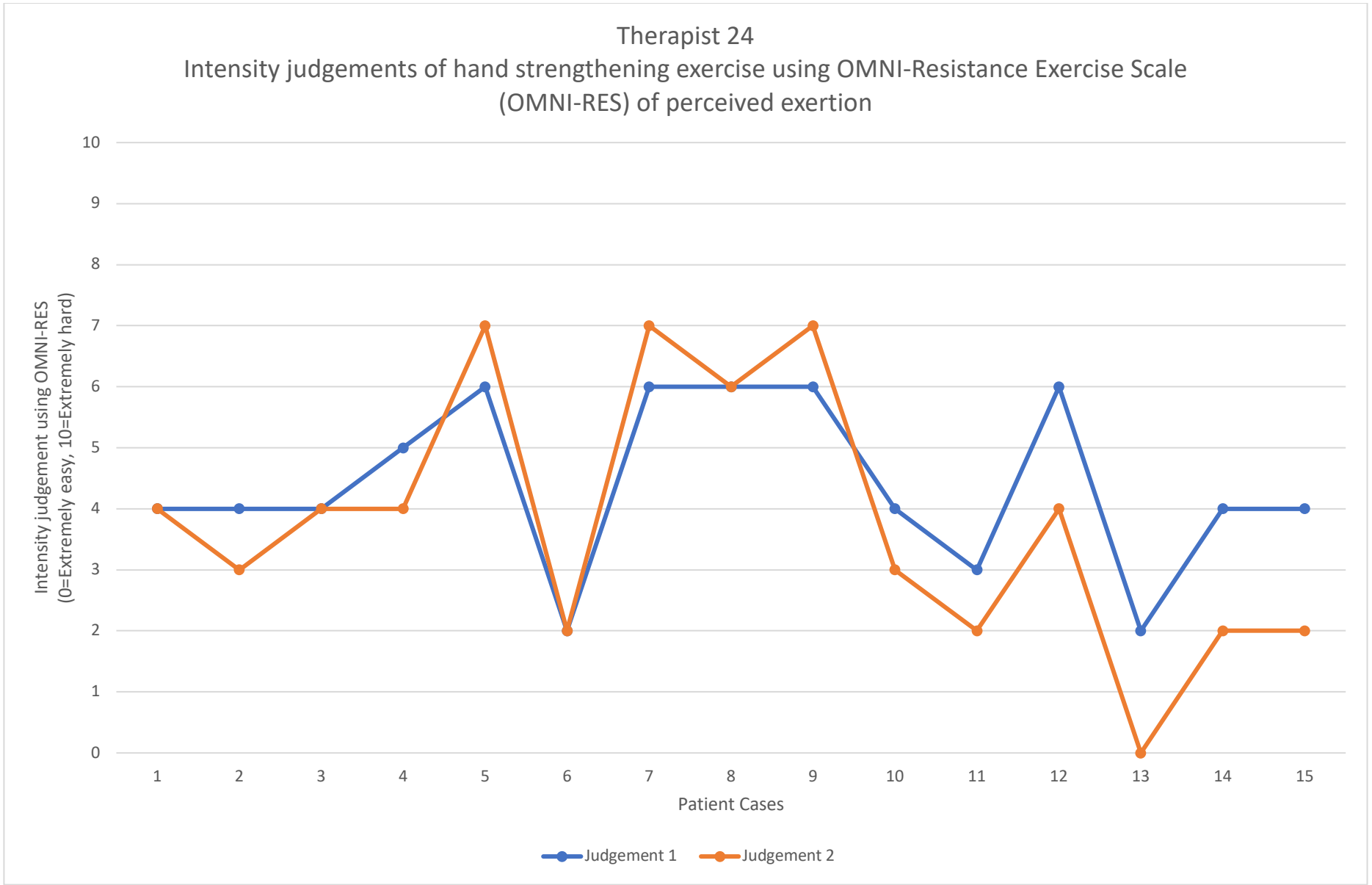
Patient Cases
Judgement 1
Judgement 2


Therapist 24
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
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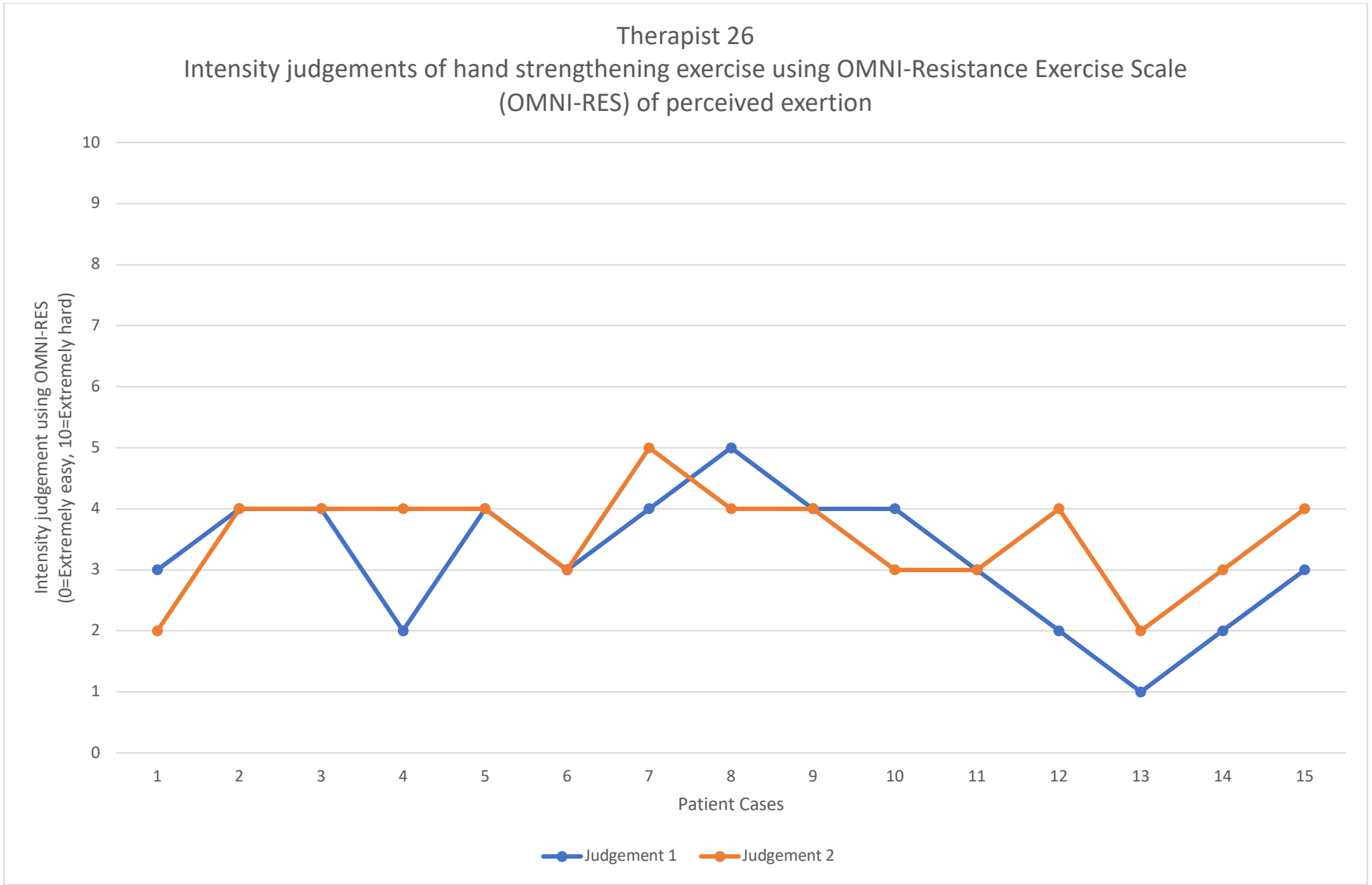
Patient Cases
Judgement 1
Judgement 2


Therapist 26
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
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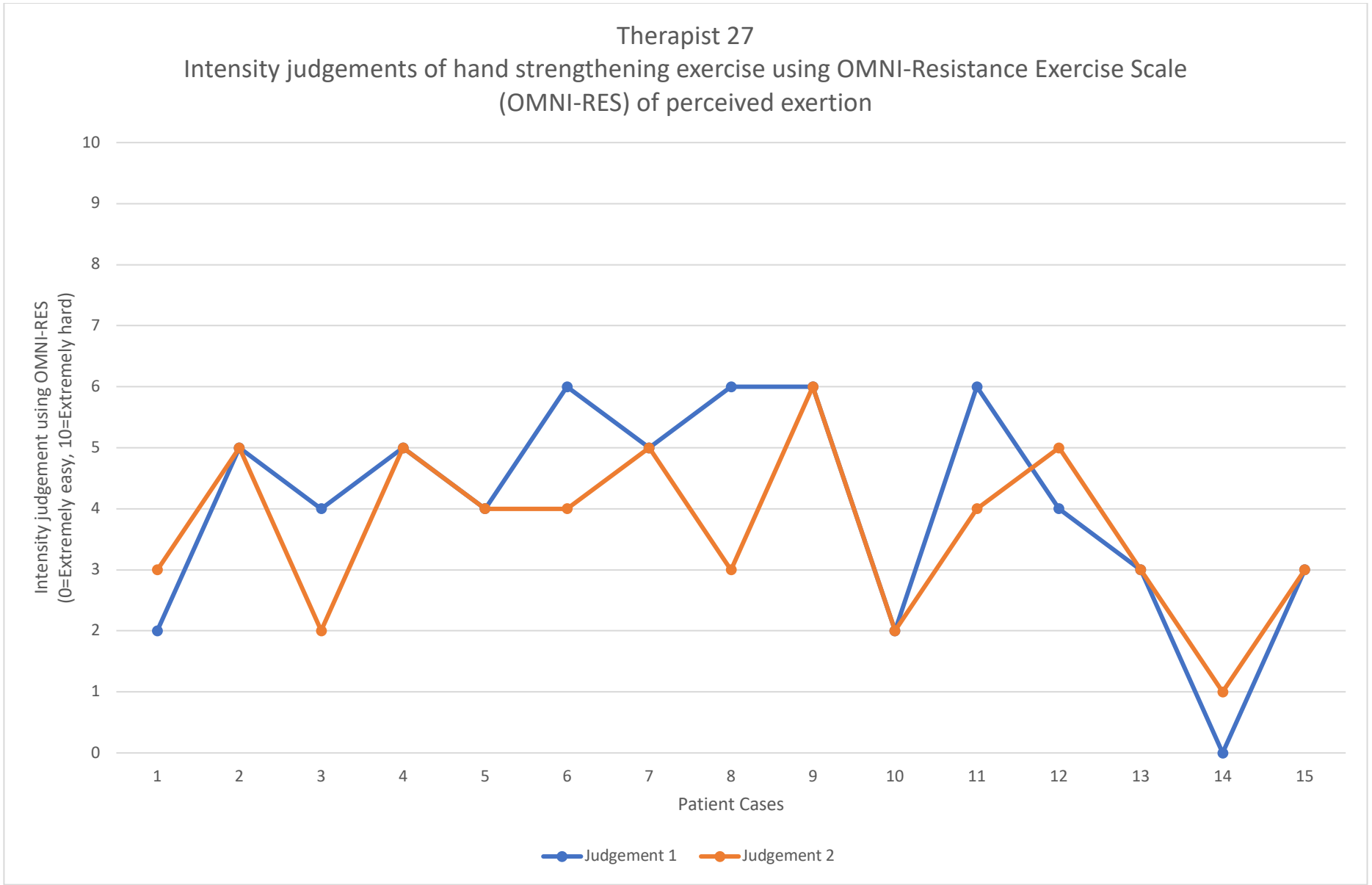
Patient Cases
Judgement 1
Judgement 2


Therapist 27
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
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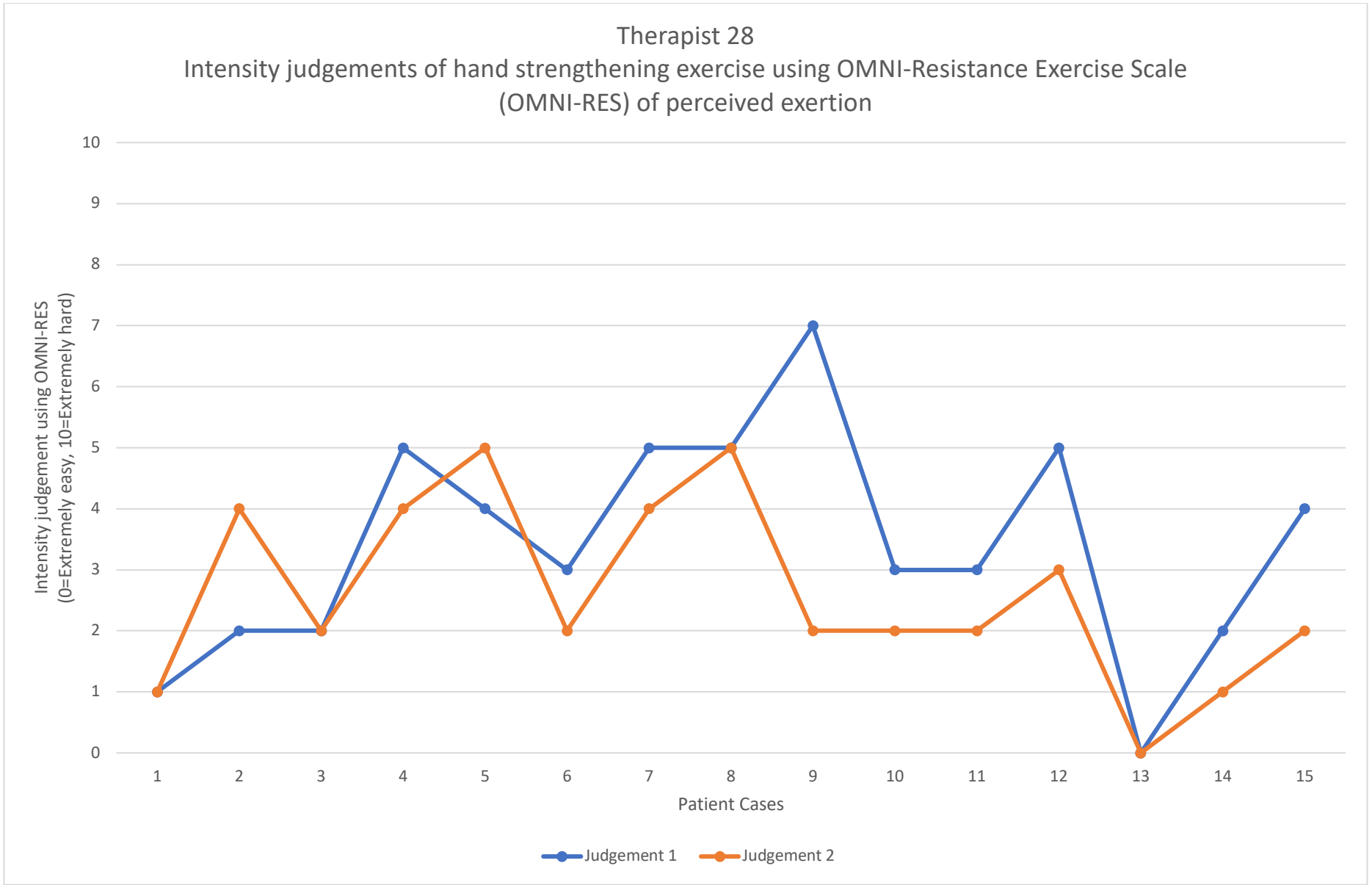
Patient Cases
Judgement 1
Judgement 2


Therapist 28
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
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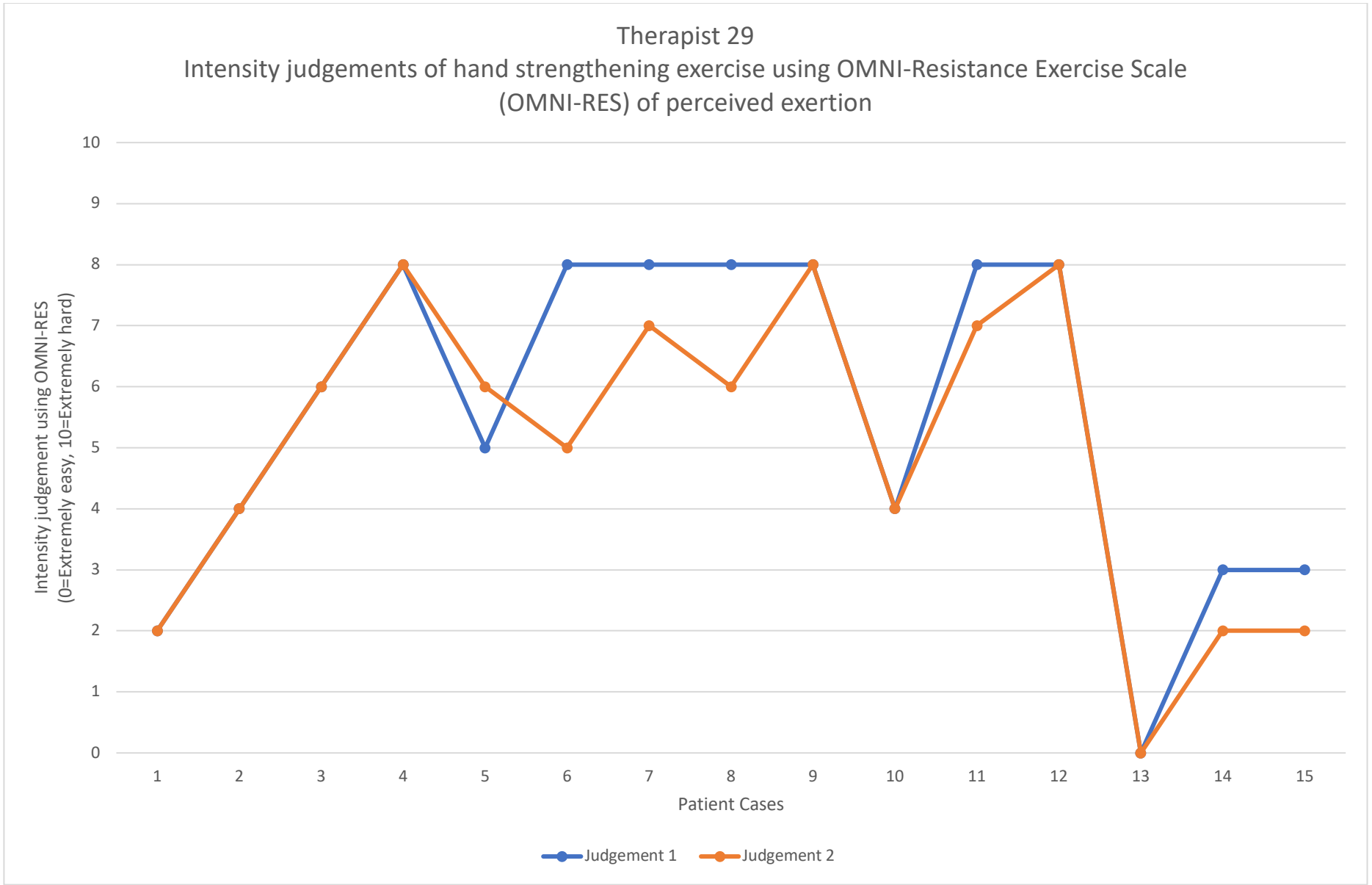
Patient Cases
Judgement 1
Judgement 2


Therapist 29
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
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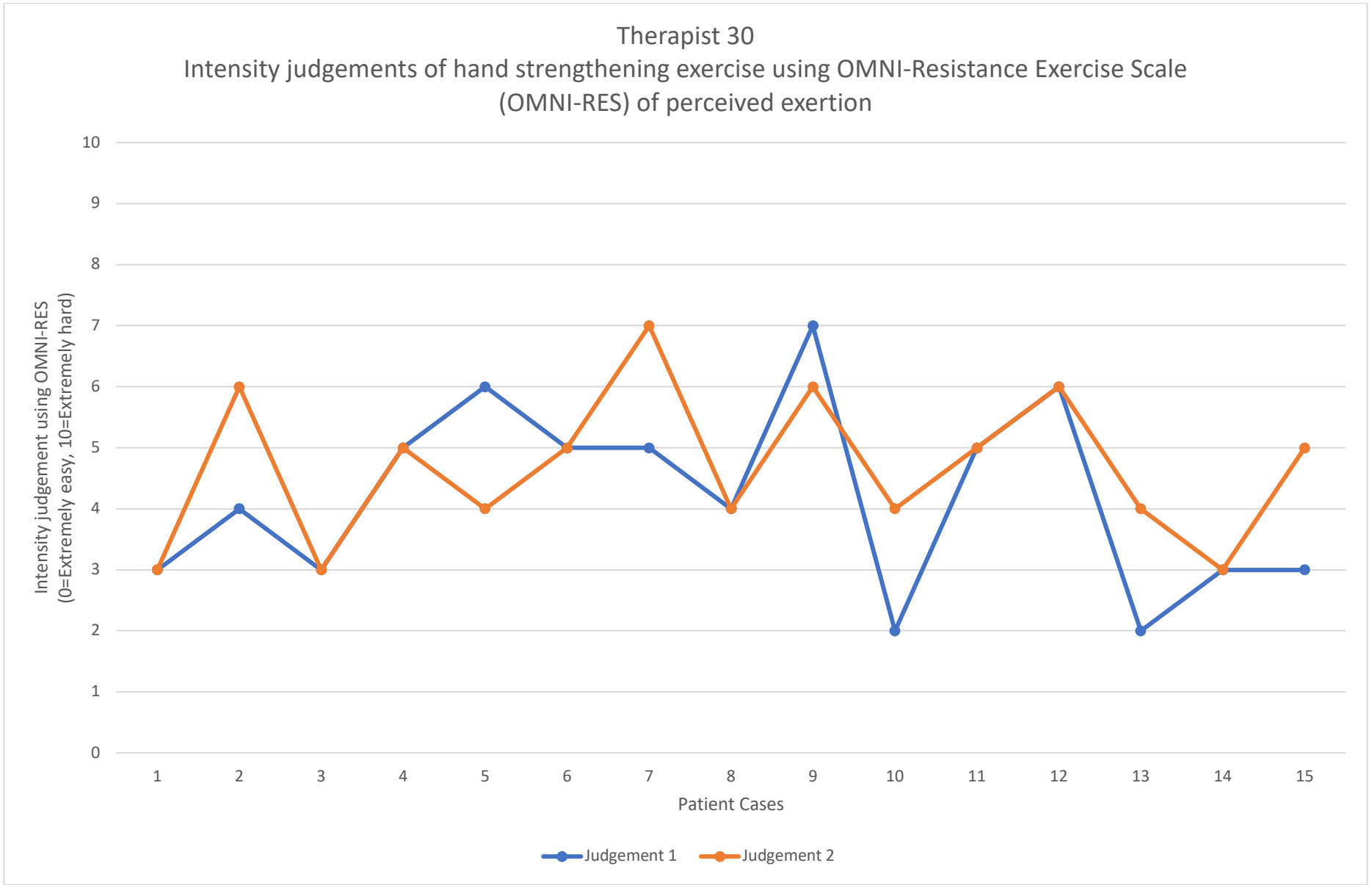
Patient Cases
Judgement 1
Judgement 2


Therapist 30
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
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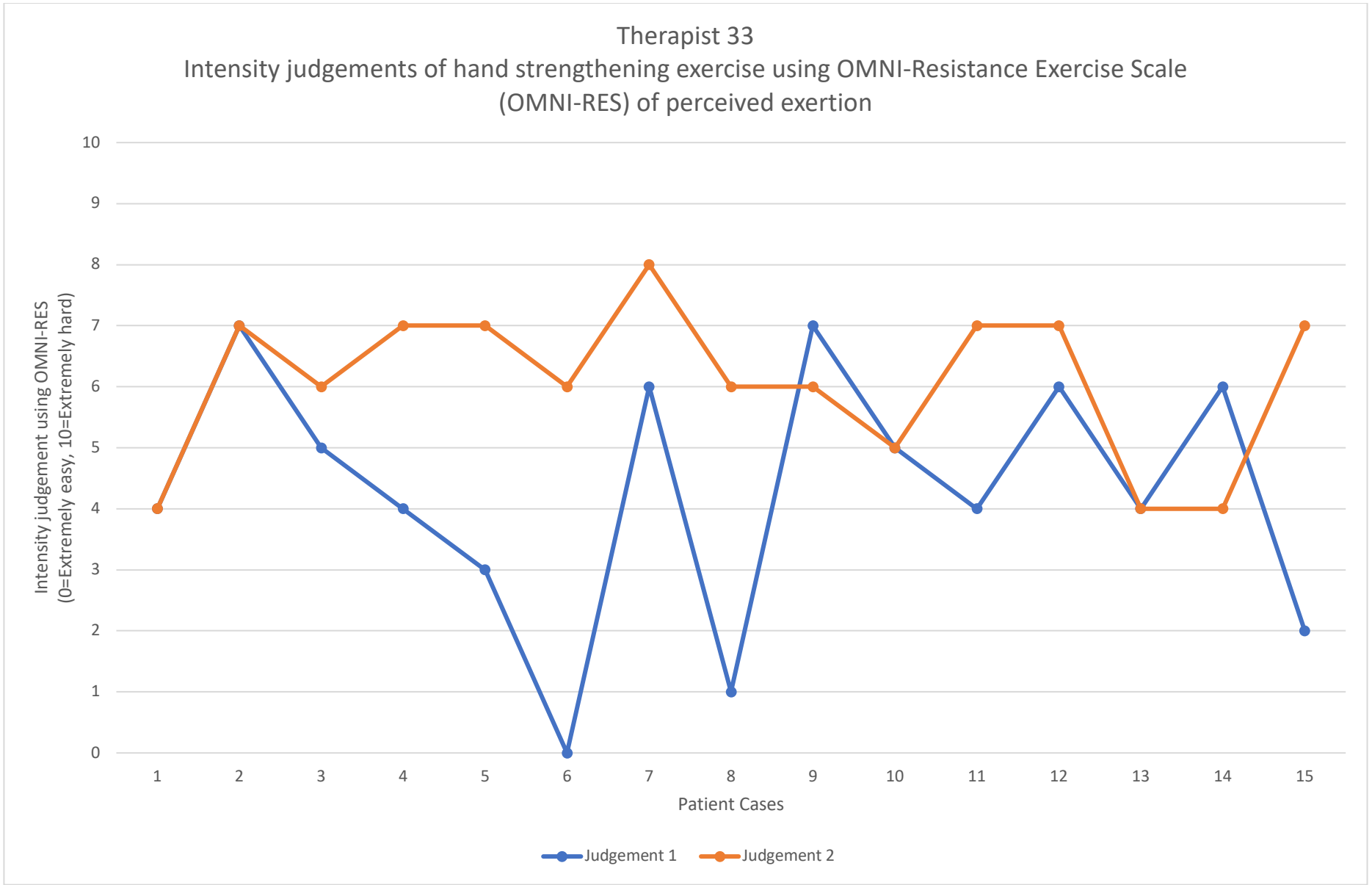
Patient Cases
Judgement 1
Judgement 2


Therapist 33
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
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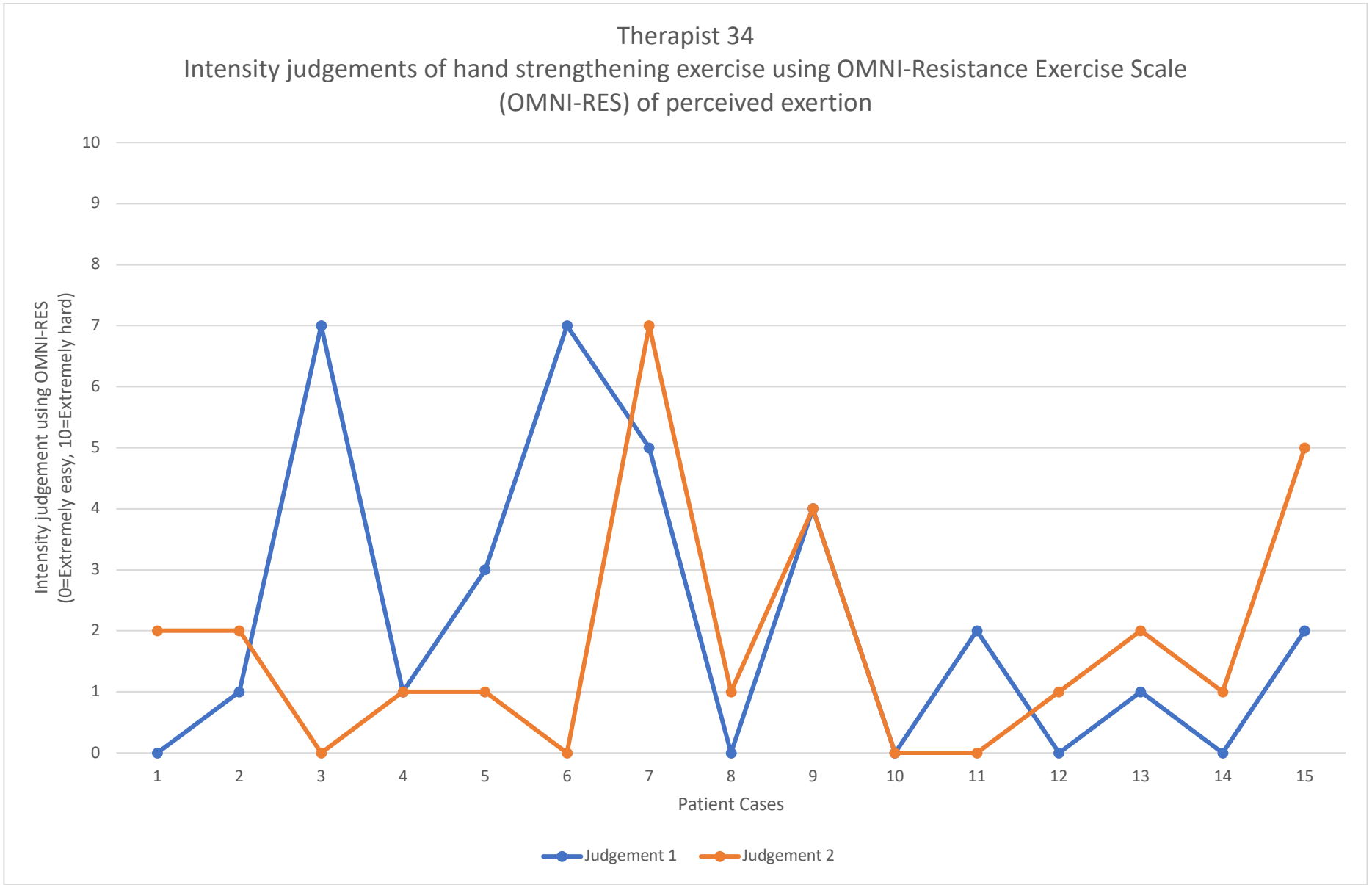
Patient Cases
Judgement 1
Judgement 2


Therapist 34
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
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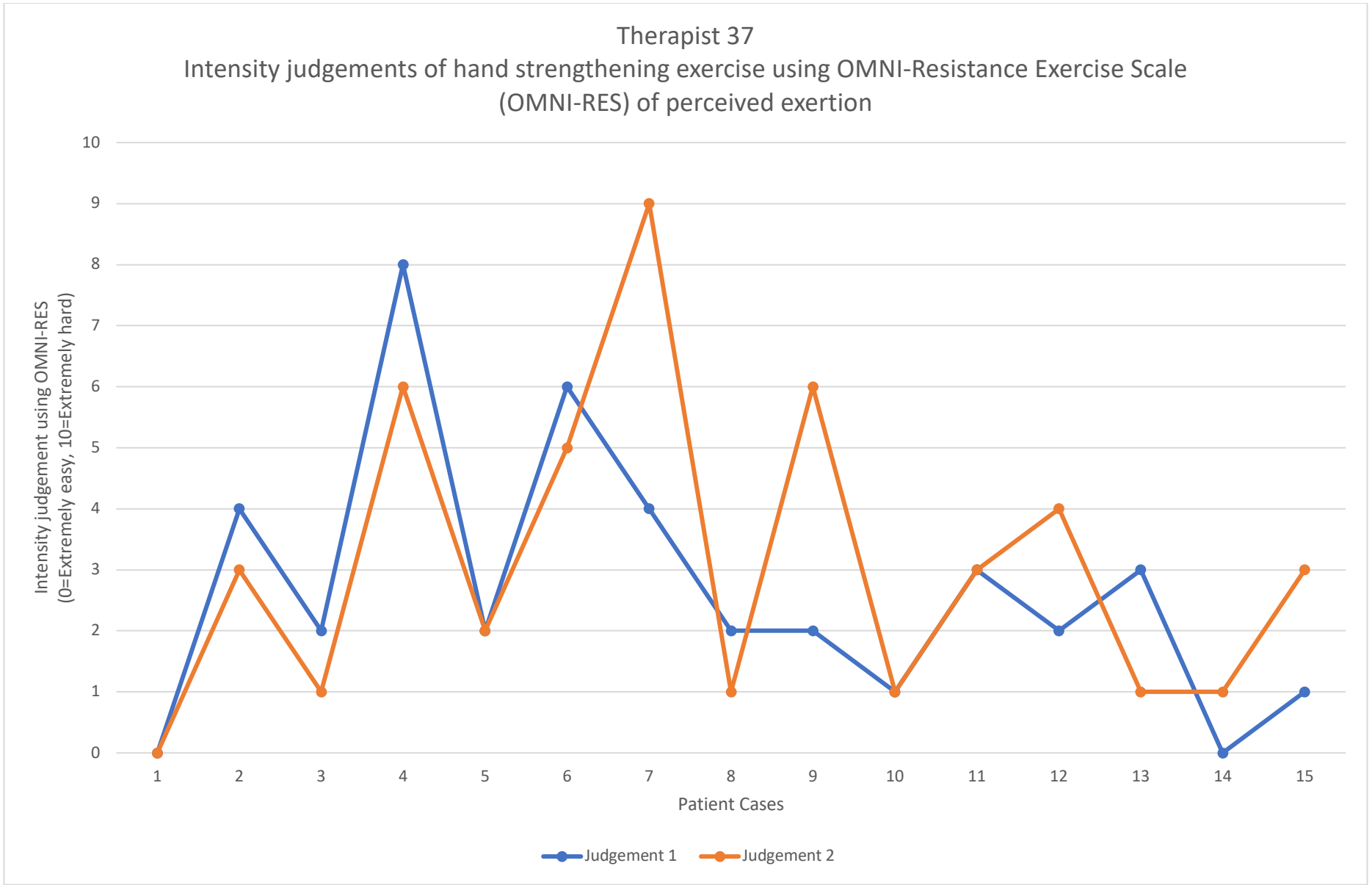
Patient Cases
Judgement 1
Judgement 2


Therapist 37
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
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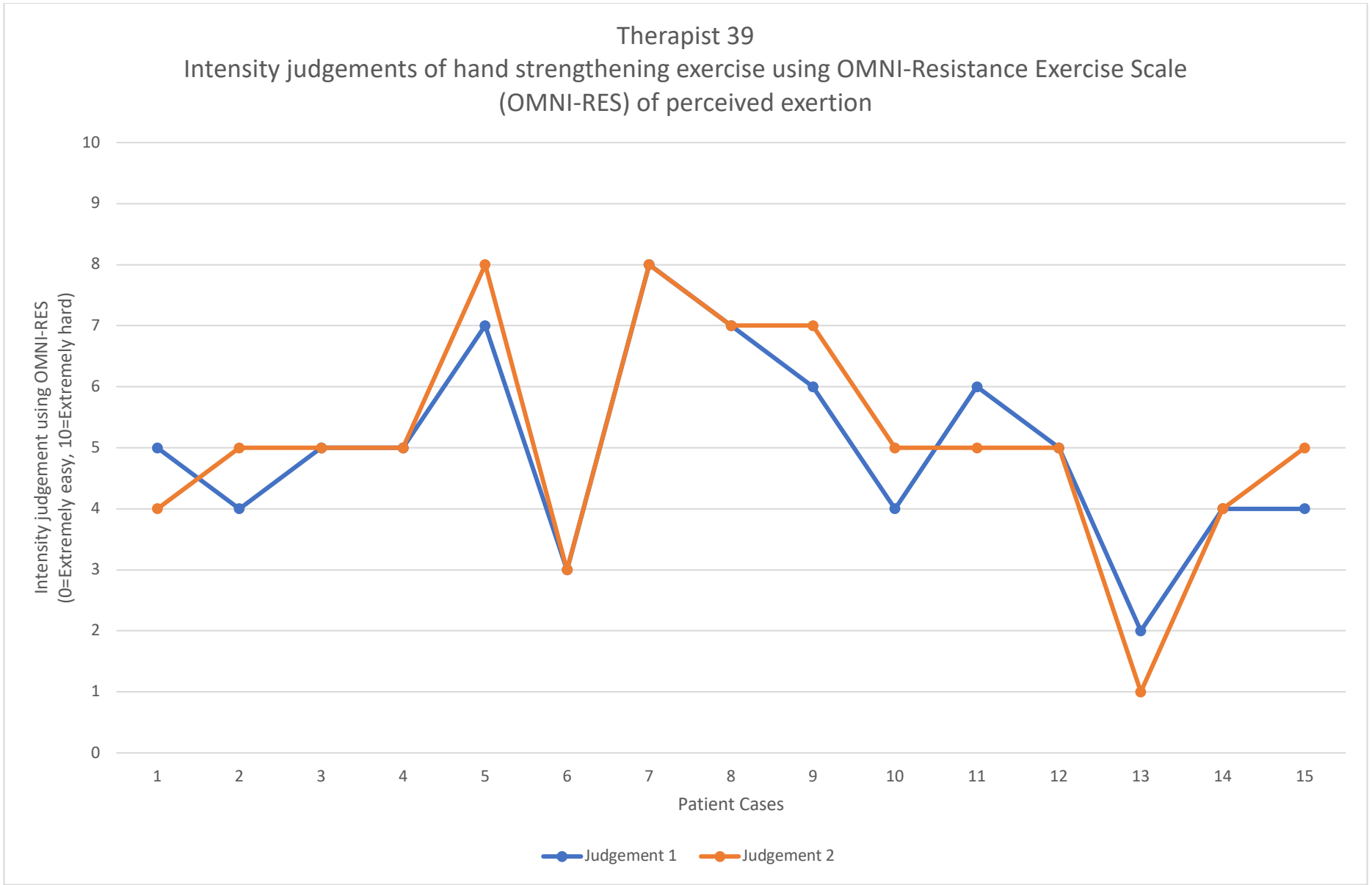
Patient Cases
Judgement 1
Judgement 2


Therapist 39
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
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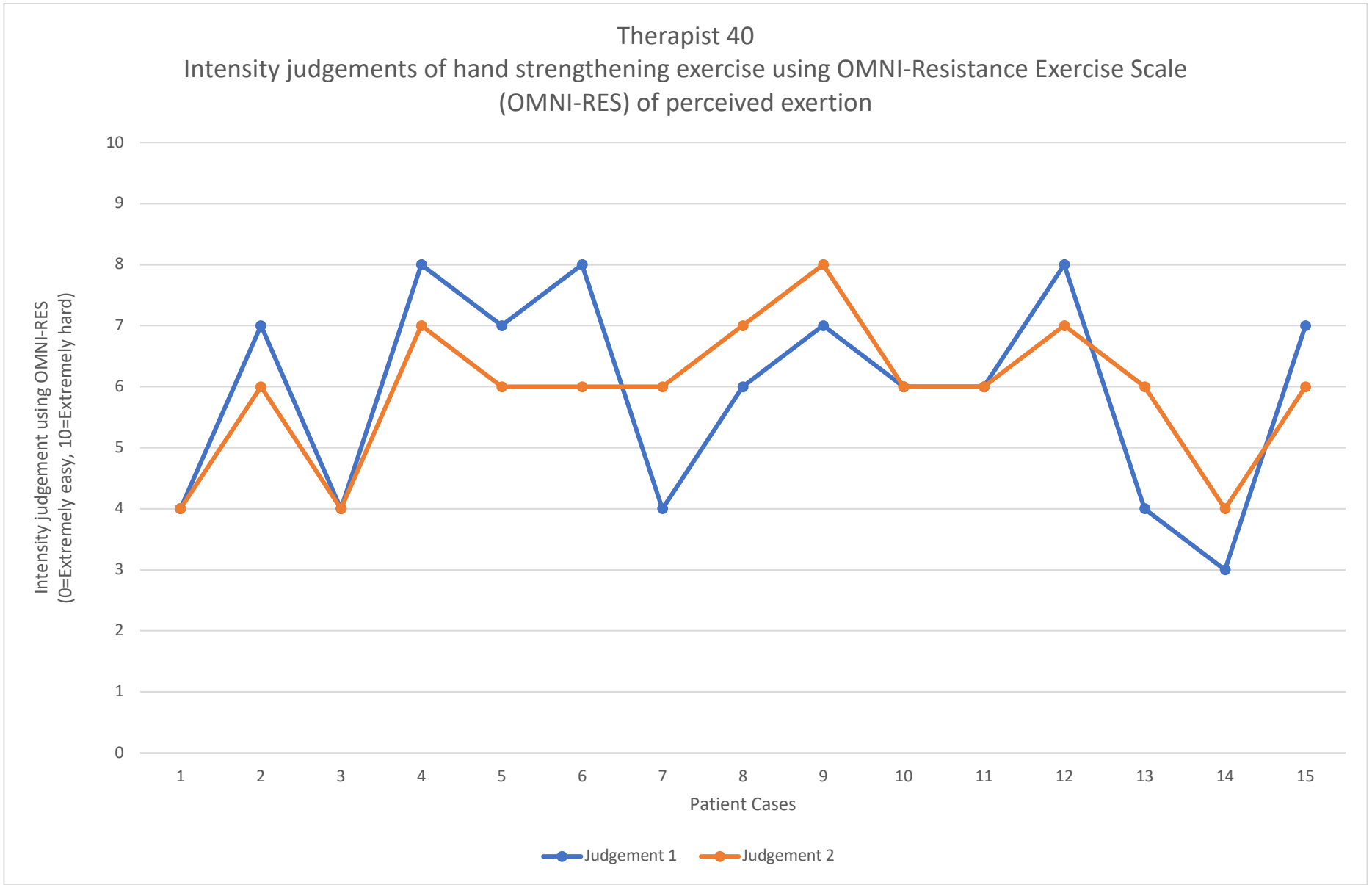
Patient Cases
Judgement 1
Judgement 2


Therapist 40
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
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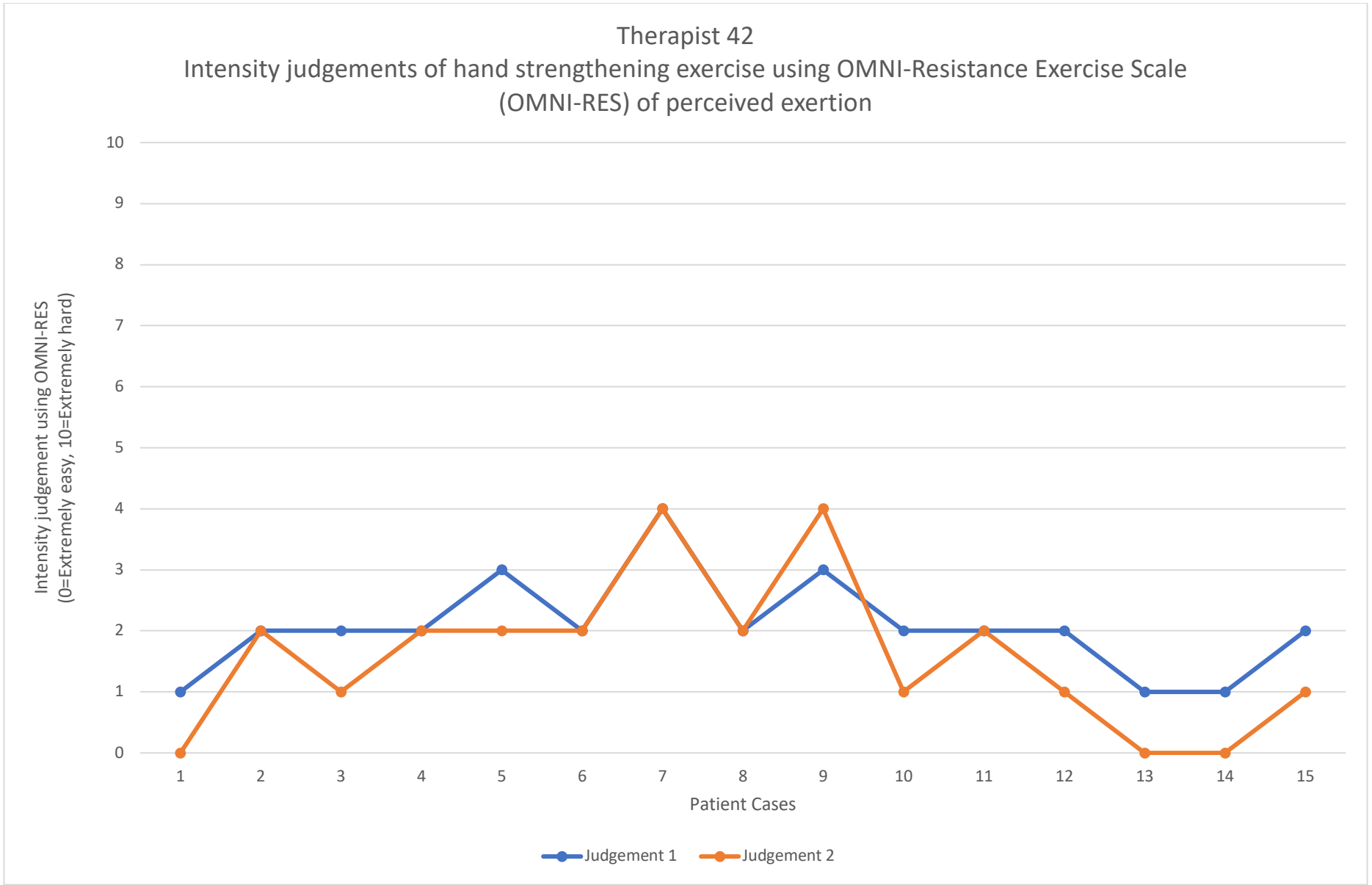
Patient Cases
Judgement 1
Judgement 2


Therapist 42
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
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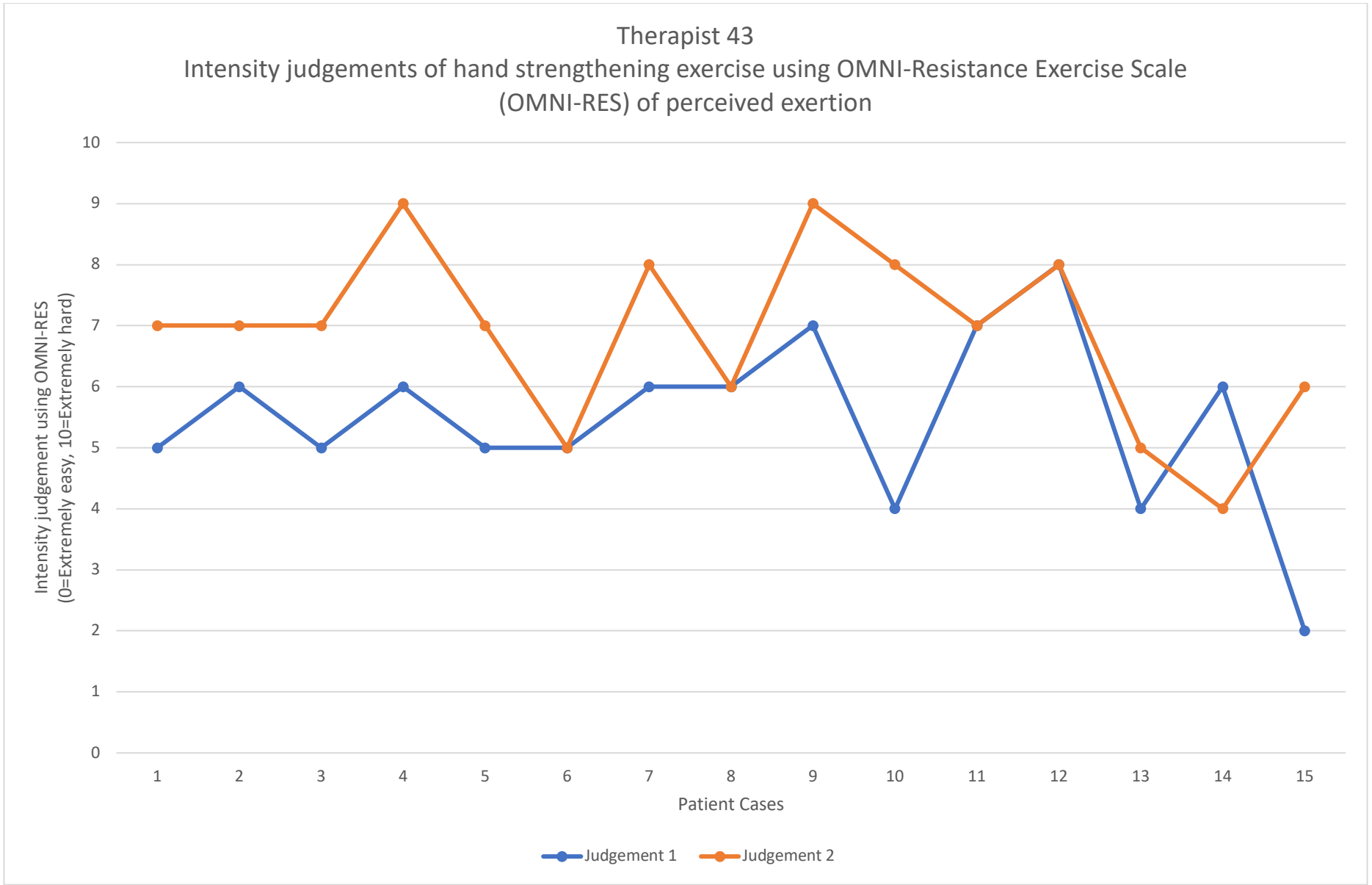
Patient Cases
Judgement 1
Judgement 2


Therapist 43
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
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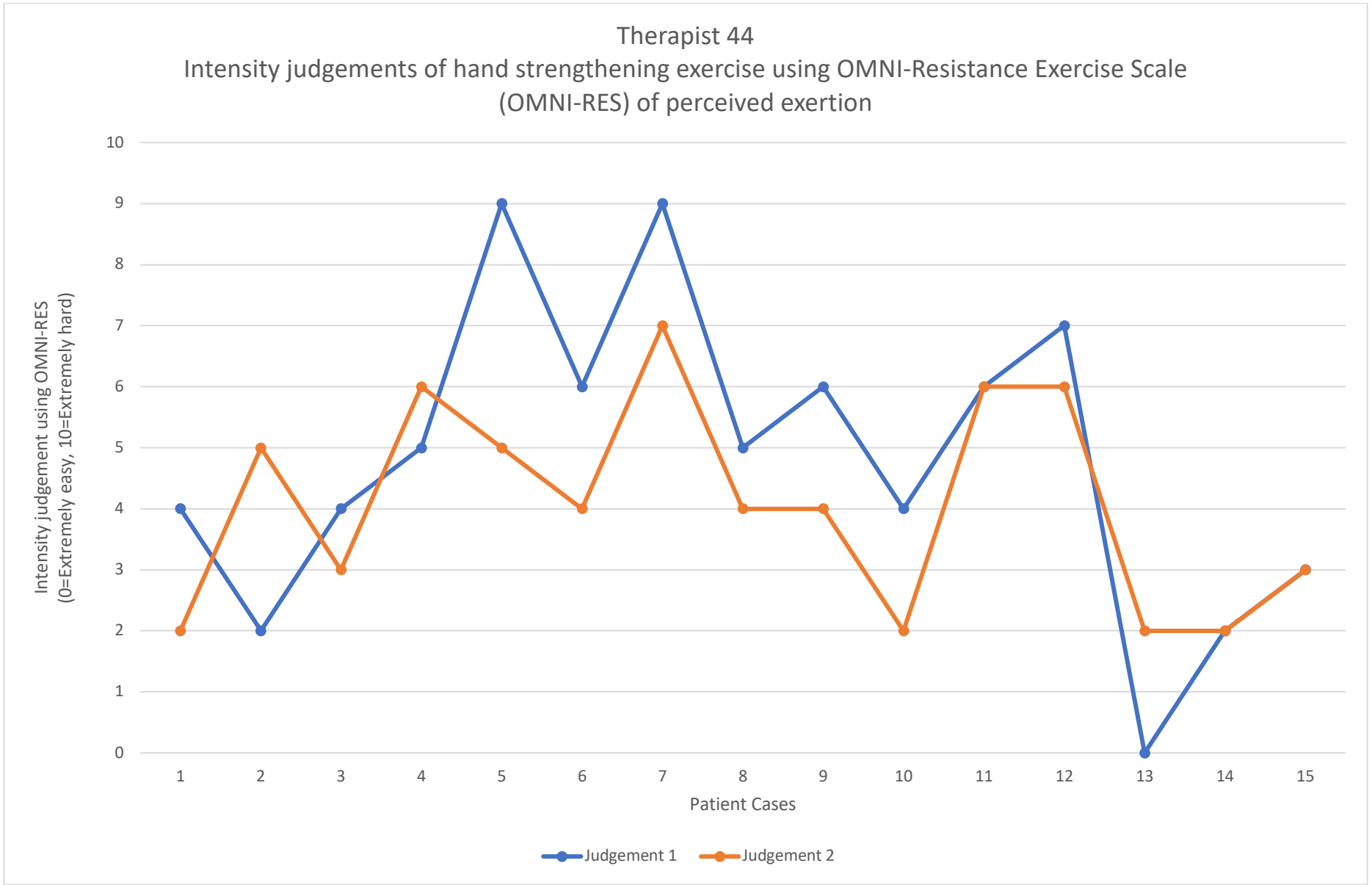
Patient Cases
Judgement 1
Judgement 2


Therapist 44
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
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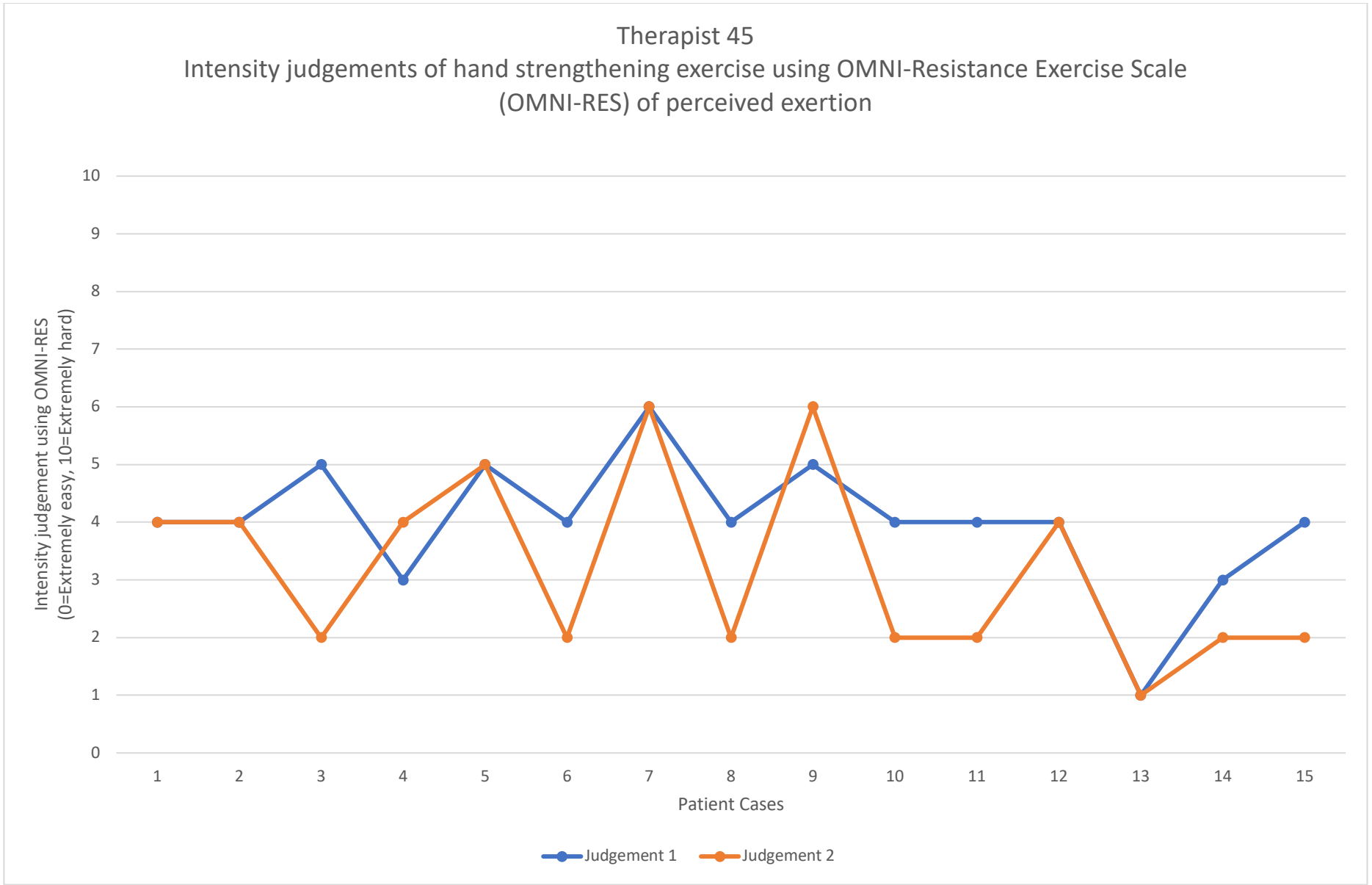
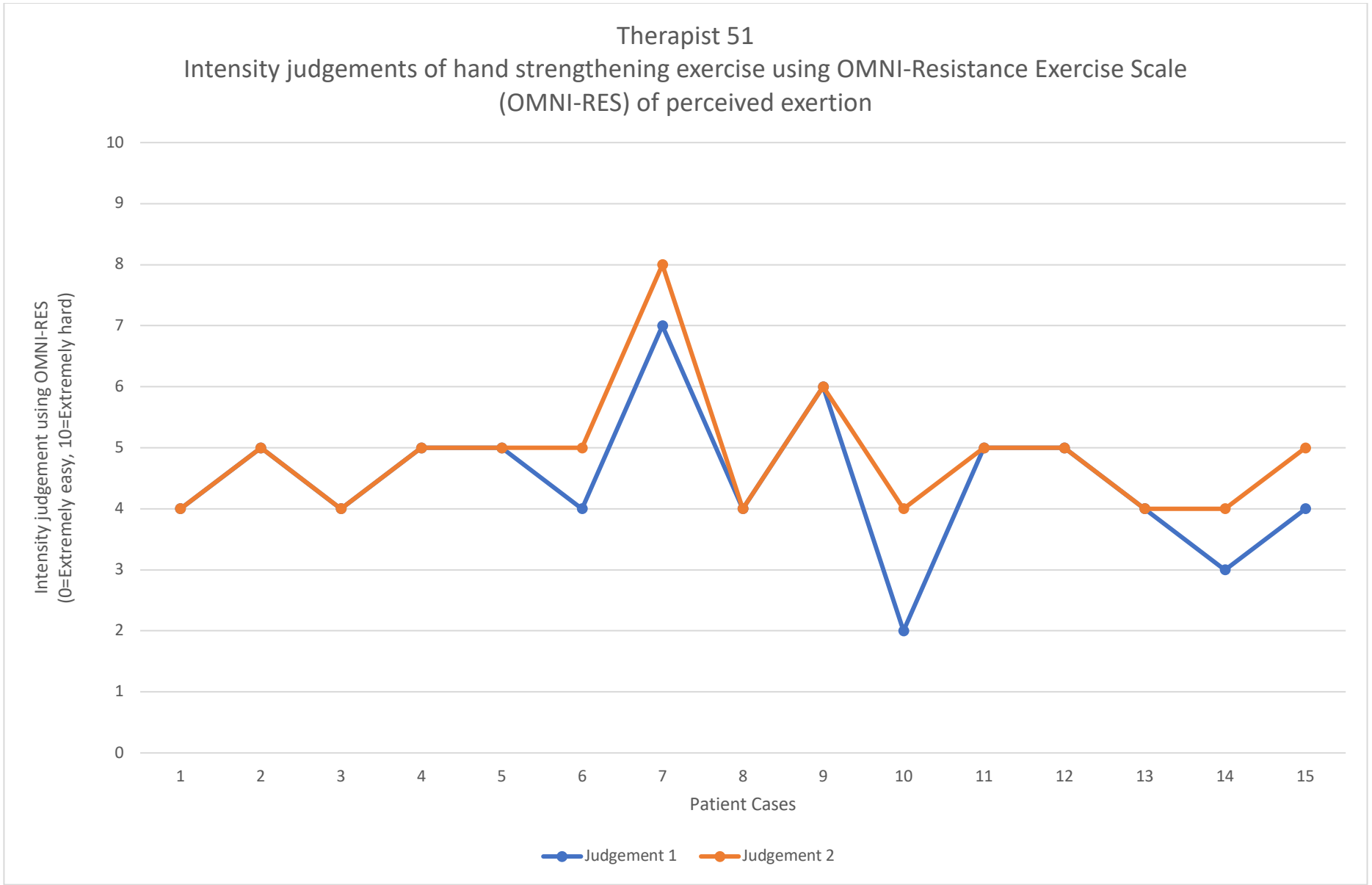
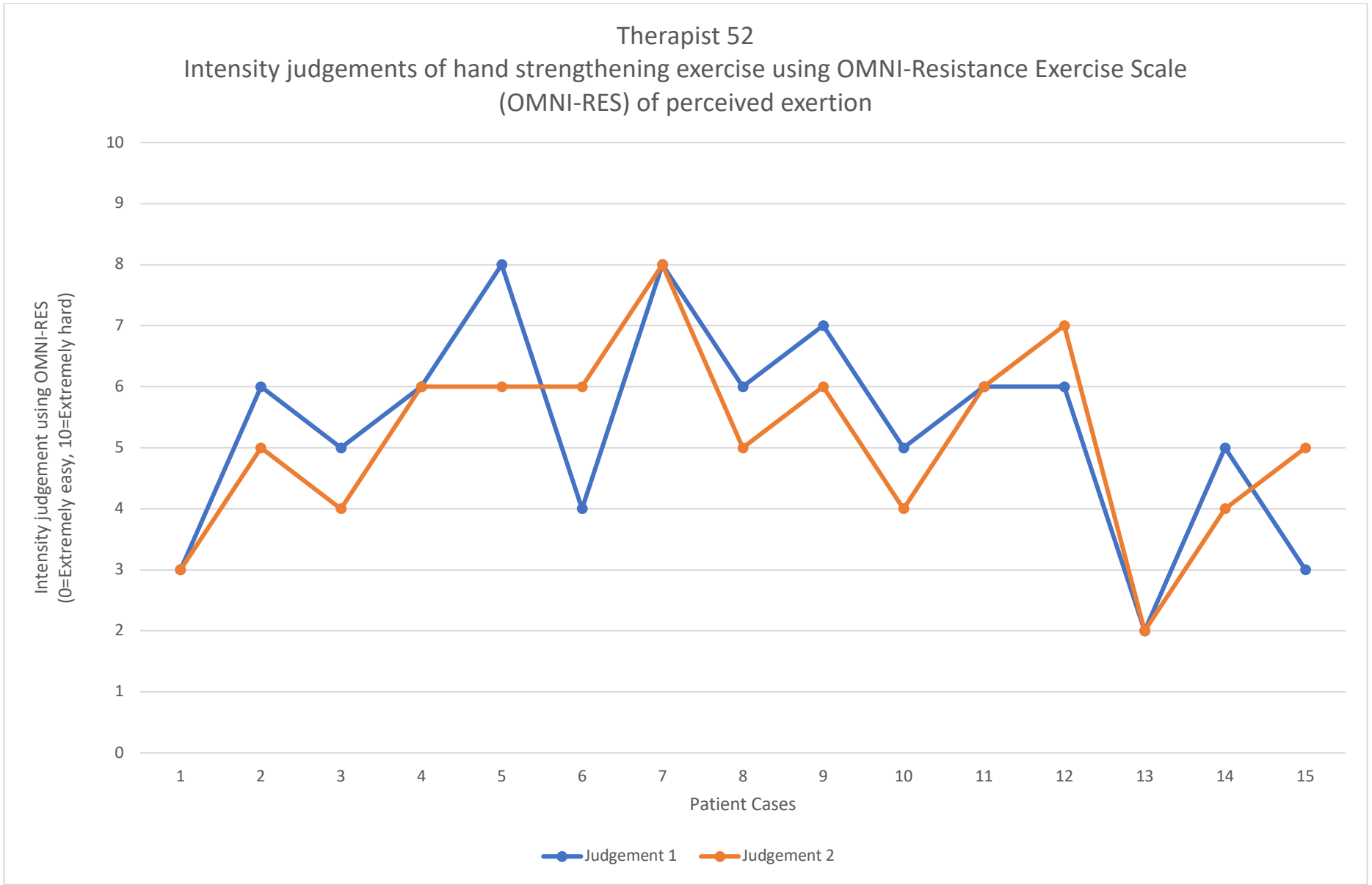
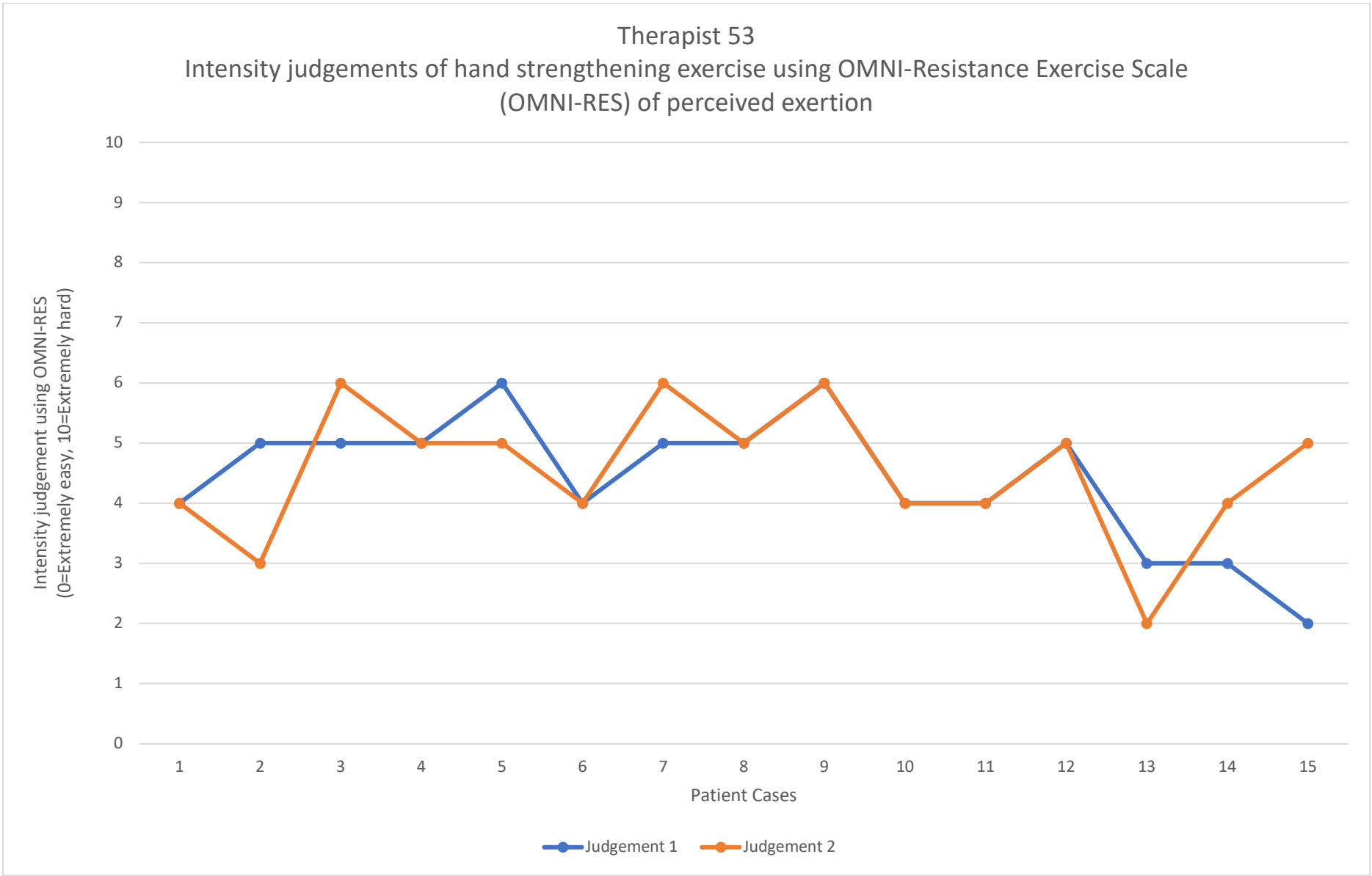
Patient Cases
Judgement 1
Judgement 2


Therapist 45
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
10
9
8
7
6
5
4
3
2
1
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
Patient Cases
Judgement 1
Judgement 2


Therapist 51
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
10
9
8
7
6
5
4
3
2
1
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
Patient Cases
Judgement 1
Judgement 2


Therapist 52
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
10
9
8
7
6
5
4
3
2
1
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
Patient Cases
Judgement 1
Judgement 2


Therapist 53
Intensity judgements of hand strengthening exercise using OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion
Intensity judgement using OMNI-RES (0=Extremely easy, 10=Extremely hard)
10
9
8
7
6
5
4
3
2
1
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
Patient Cases
Judgement 1
Judgement 2