Reversing Frailty in Older Adults: A Scoping Review

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Thesis submitted to the University of Ottawa
in partial Fulfillment of the requirements for the
Master of Science in Nursing

School of Nursing

Faculty of Health Sciences

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Dissertation Abstract

Background: The exponential growth of the aging population makes research on reversing frailty increasingly important.

Objective: To explore the concept of reversing frailty in older adults and identify existing interventions that achieve frailty reversal as an outcome.

Methods: We used a five-stage scoping review methodology outlined by Arksey and O'Malley and enhanced by Joanna Briggs, Levac, and colleagues. We critically appraised all eligible studies and synthesized data using descriptive and narrative analyzes. We searched CINAHL, EMBASE, PubMed, and Web of Science.

Results: The concept of reversing frailty seems complex, and no standard intervention exists. That notwithstanding, a few types of single- or multi-component intervention characteristics showed effectiveness in reversing frailty.

Conclusion: Frailty can be reversed. However, concept analysis is needed to clarify and define reverse frailty. To ensure maximum effectiveness, the identified interventions, ranging from mostly physical activity to a combination of physical activity and nutrition, could be tailored to each individual's needs.

Keywords: Reverse frailty, scoping review, single-and multi-component

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Acknowledgments

My most sincere gratitude to Dr. Chantal Backman, my supervisor, for the guidance, understanding, and encouragement during this entire process. This incredible commitment to the project and belief in me gave me the encouragement I needed. It is an honour to have you as an instructor, mentor, and role model.

Thank you to my thesis advisory committee members, Dr. Krystina Lewis and Dr. Michelle Lalonde. I could not have asked for a better team to work with. You made it easy to seek guidance and clarifications due to your knowledge and personality. You also provided insightful feedback and guidance that was extremely valuable. I appreciate your patience and understanding.

To the librarians at the University of Ottawa, Valentina Ly (VL), Victoria Cole (VC), and Lindsey Sikora (LS) thank you for your time in helping design a search strategy and identify relevant studies.

To my secondary reviewers, Ojongetakah Baa (OB) and Mbi Ayuk Solange (MA), thank you for your time, responsiveness, and commitment to this project. Your support was indeed invaluable.

To my friend Dr. Nkoh Jackson Nkoh, thank you for your friendship, endless support, and encouragement. To Dr. Kenmoe Sebastien, thank you so much for your endless calls and advice. They were invaluable.

To my sister Lena Kessy, my brother Sean Larry, my dad Esemu Benedict and my mom Dr. Esemu Seraphine, thank you very much for your love and encouragement throughout this journey and other aspects of my life.

Last but not least, special thanks to my partner Dr. Joel M Kolle and our beautiful children Lahm, Rhema, and Reuel. Your immeasurable love, patience, pampering, and understanding through this period are humbling.

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Abbreviations

ADLs	Activities of daily living
BMC	BioMedCentral
BMI	Body Mass Index
CAN	Canadian Nurses Association
CR	Cardiac rehabilitation
CPR	Cardiopulmonary resuscitation
CES-D	Center for Epidemiologic Studies Depression Scale
COPD	Chronic obstructive pulmonary disease
CNO	College of Nurses of Ontario
CINAHL	Cumulative Index to Nursing and Allied Health Literature
Dur	Duration
FI	Frailty Index
FP	Frailty Phenotype
Freq	Frequency
GDS	Geriatric Depression Scale
HI	High intensity
iADL	Instrumental Activities of Daily Living
JBI	Joanna Briggs Institute
KCL	Kihon checklist
m	Months
MeSH	Medical Subject Headings
MEP	Multicomponent Exercise Program
NR	Not Reported
PRESS	Peer Review of Electronic Search Strategies
PIFU	Post intervention follow-up
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyzes
RCTs	Randomized control trials
RAI-HC	Resident Assessment Instrument-Home Care
RT	Resistance training
RMR	Resting metabolic rate
SPPB	Short Physical Performance Battery
TIDieR	Template for Intervention Description and Replication
Wks	Weeks
Yrs	Years

Chapter One: Introduction

1.1 Introduction

Frailty is a clinically recognized state of vulnerability that occurs when reserve and function across multiple physiological systems are compromised, impairing a person's ability to cope with daily stresses (Clegg, 2014). A rapidly ageing population of those 65 years and older are considered significantly susceptible and at a higher risk for developing frailty (Hoogendijk *et al.*, 2019). In Canada, for example, it is estimated that over two million older adults will live with frailty by 2030, an increase of 66.6 per cent from 2017 (Canadian Frailty Network, 2019). Several adverse outcomes are associated with frailty, including, but not limited to, dependency on social and health services, caregiver burden, mental disorders, and, most devastatingly, death.

1.1.1 Increased Dependency on Social and Health Care Services

An analysis of frail older adults and service utilization by Vaingankar and colleagues (2017) found that frail older adults have a significantly higher proportion of care needs than pre-frail and non-frail individuals. Additionally, they found that 58.8% of frail older adults had fewer social networks than 36.6% of pre-frail and 28.6% of robust individuals (Vaingankar *et al.*, 2017). Individuals with frailty are presumed to have more mobility issues, malnutrition, social isolation, and difficulties with various activities of daily living like eating, toileting, bathing, and performing household chores (Mehrabi & Béland, 2021). According to global evidence, frail older adults are more likely to access social care services, such as bathing, washing, and grooming (Canadian Frailty Network, 2019; Cristea et al., 2020; Kojima et al., 2019b; Nikolova et al., 2022).

1.1.2 Increased Caregiver Burden

Approximately four million Canadians are projected to become informal caregivers of frail older adults by 2025, an increase of 78% from 2017 (Canadian Frailty Network, 2019). A significant proportion of care provided to frail older adults is offered by friends, neighbours or family members (Chappell & Funk, 2011). Some caregivers have reported having heightened psychological stress, which in turn cause negative impacts on their health, loss of social life, and income due to the increased amount of time they spend taking care of the needs of their frail loved ones (Ding *et al.,* 2022; Keating *et al.,* 2014; Ringer *et al.,* 2017)

1.1.3 Predisposition to Mental Health Disorders

The decreased physiologic reserve of frail older adults and increased biological ageing make them more likely to experience mental illnesses, especially depression (Andrew & Rockwood, 2007), and more prone to anxiety (Frost *et al.,* 2020). Researchers are finding increasing evidence that markers of ageing, such as inflammation, oxidative stress, and shortened telomeres (protective caps at the end of chromosomes), are associated with schizophrenia and other severe mental disorders (Higgins-Chen *et al.,* 2020; Nguyen *et al.,* 2018). Frailty is also linked to delirium, a preventable neuropsychiatric disorder associated with underlying medical conditions (Persico *et al.,* 2018).

1.1.4 Death

There is often fatigue, weight loss, and poor strength in the frail elderly, resulting in their inability to recover from minor illnesses or injuries (Andrew & Rockwood, 2007; Hao et al., 2019; Kojima et al., 2019b; Rockwood & Mitnitski, 2007). As a result, their quality of life and life expectancy can be adversely affected. With increasing levels of frailty, mortality risk

increases substantially (Gilmour & Ramage-Morin, 2021; Wang *et al.*, 2019). Regardless of age, individuals with severe frailty who rely entirely on caregivers have an average life expectancy of 3.5 years less than those who are frail but do not rely on caregivers (Clegg *et al.*, 2016; Herr *et al.*, 2018).

These growing concerns lead to ongoing research to develop instruments that quantify frailty. Clinically, the value of these assessment instruments lie in their ability to identify frailty early and those at highest risk for adverse outcomes (Lee *et al.*, 2020). This allows for early intervention to prevent, slow or reverse frailty (Walston *et al.*, 2018).

1.2 Problem Statement

Studies on frailty in older adults have primarily focused on preventing or slowing its progression from a non-frail to a pre-and frail state (Gwyther *et al.*, 2018; Sacha *et al.*, 2020; Wilhelmson *et al.*, 2013). However, in recent studies, it has been alleged that frail individuals may regain their pre-or non-frail state (Kojima et al., 2019b; Marcucci et al., 2019; Ng et al., 2015). There seems to be an inconsistent approach concerning ideal interventions, their mode of implementation, duration, and frequency. For example, a randomized controlled trial (RCT) conducted by Kim *et al.*, (2015) examined the effects of combined exercise and nutrition therapy on 131 frail older adults. After an intervention period of 3 months and a follow-up of 4 months after completion, a reversal in exhaustion, low physical activity, and slow walking in the individuals were reported. Consistent with this approach, Tarazona-Santabalbina *et al.*, (2016) looked at a multi-component exercise program (MEP) to reverse frailty. It involved 100 participants, randomized into a control and intervention group. Those in the intervention group were engaged in physical exercises that consisted of 65 minutes of daily endurance, strength, coordination, balance, and flexibility, implemented by nurses and physiotherapists, five days a

week for 24 weeks. A reversal of frailty was reported in 31.4% of participants in the intervention group, without mention of the frail state of the remaining 68.6% within the same group (Tarazona-Santabalbina *et al.*, 2016). Using a completely different approach, Trendelenburg *et al.*, (2019) proposed pharmacological measures for reversing frailty. The study looked at geroprotectors i.e., compounds that slow down biological aging (Schubert *et al.*, 2018). The authors concluded that although this approach is promising in reversing frailty, there is not enough testing to validate its effectiveness (Trendelenburg *et al.*, 2019).

Based on these inconsistencies, a comprehensive and critical examination of the literature on interventions that reverse frailty is necessary. As Kojima and colleagues observe, frail older adults have chronic and complex health needs, which are not adequately addressed by current health care systems (Kojima et al., 2019a). This possibly explains why evidence from most studies on frailty is yet to be translated into health care policymaking and clinical practice (Buttery et al., 2015; Kojima et al., 2019a). However, identifying and integrating interventions that reverse frailty into policy can improve the quality of care provided, enhance healthy ageing, enable older adults to preserve their dignity, and reduce the impact of ageing on the health care system (Kojima et al., 2019b).

1.3 Personal Statement

My experience working in an acute care unit in a hospital inspired the development of this project. While I work with individuals of all ages, most patients I have encountered are over 50 years of age. Patients with difficulties thriving, mobility issues, or who need more personal care often need geriatric consultation, which I coordinate with the interprofessional team. I implement multiple interventions for older patients, such as walking in the hallways, ensuring they do lower and upper extremity exercises when bed-bound, and providing personal hygiene.

Sometimes patients refuse some interventions due to fatigue or a desire to be left alone. With the knowledge that we will all grow old and possibly be in a similar position, I have sought to understand the best methods of caring for this population to ensure that their quality of life is maintained as much as possible. Thus, with the opportunity to pursue a Master's degree with the thesis option, my first thought was on general care of older adults. During the winter session of the program's first year (January to April 2021), I had to complete a research proposal for my research course. As I researched the topics for my proposal, I decided to focus on 'The Nursing Interventions Used to Care for Older Adults Living with Frailty.' When reviewing the literature, I located articles about reversing frailty and interventions to slow the progression of frailty or improve coping skills. Reversing frailty would improve the quality of life for this population, restore functional dependence, and maintain dignity. Due to the unprecedented rise in the number of older people globally (United Nations, 2019), I became curious about how to achieve these benefits for my loved ones and patients. This thesis is the result of my interest in synthesising information on interventions that can reverse frailty and my commitment to enhancing the well-being of older adults.

1.4 Study Objectives

Through a scoping review, this study aims to provide an overview and synthesis of available interventions that achieve frailty reversal as an outcome. Further, key concepts, intervention components, and research gaps that can be used for clinical practice will be identified. This study will seek to answer the following research questions:

1. What is the available literature on interventions that achieve frailty reversal as an outcome?

2. What does it mean to reverse frailty?

1.5 Guiding Frailty Conceptual Framework

The complex nature of frailty (Hammami *et al.*, 2020) has been debated for decades (Buta *et al.*, 2016; Chen *et al.*, 2018; Fried *et al.*, 2021). However, two leading conceptual frameworks of frailty emerged in 2001, each offering specific definitions (Fried *et al.*, 2001; Mitnitski *et al.*, 2001). The *Frailty Phenotype (FP)*, developed by Fried and colleagues, can identify those at the highest risk for developing chronic illnesses and disabilities (Rodríguez-Mañasa & Walston, 2017), a possible reason for its dominant use in literature. The *Frailty Index (FI)*, developed by Rockwood and Mitnitski, is considered a manifestation of health deficits (Rockwood & Mitnitski, 2007). Though this index is quite common, it is not as widely used as the Fried's phenotype, possibly because it is more challenging to construct since it requires at least 30 health variables across several domains, such as functional, cognitive, psychosocial, and medical (Rockwood & Mitnitski, 2007). Nonetheless, it has a unique strength in considering frailty as more than just physical (Moreno-Ariño *et al.*, 2020).

1.5.1 Frailty Phenotype (FP)

In 2001, Fried and colleagues proposed that several components must be evident for frailty to be clinically present (Fried *et al.*, 2001). They defined frailty as an ontological state characterized by at least three of the following five phenotypes: weakness, low levels of physical activity, unintentional weight loss, slow walking speed, and exhaustion (Fried *et al.*, 2001). A non-frail state exists when none of the five phenotypes is evident, and a pre-frail condition occurs when one or two of the five phenotypes are present (Fried *et al.*, 2001). This operational

definition presumes that the frailty phenotype is an assessment model that revolves around the perception of frailty as primarily a physical manifestation (Vella Azzopardi *et al.*, 2018).

1.5.2 Frailty Index (FI)

Introduced in 2001, Rockwood and Mitnitski defined frailty in older adults as an accumulation of deficits which considers the proportion of health deficits an individual has across various domains rather than specific symptoms (Mitnitski *et al.*, 2001). To determine the frail state of an individual, they developed a 70-point scale (index) of different clinical deficits (variables) that measures several domains, such as functional, cognitive, psychosocial, and medical criteria (Mitnitski *et al.*, 2001; Rockwood, 2005) (Appendix A). Accordingly, this index projects frailty in older adults as a systemic rather than a specific dysfunction. Although the original FI counts 70 variables across multiple domains, no universal FI exists. When an individual, healthcare practitioner or researcher is constructing a FI, they can reference the original 70-point index scale (Mitnitski *et al.*, 2001; Rockwood, 2005) to identify the types or number of variables to measure. Nonetheless, to yield an accurate measure of determining the frail state of an individual, a FI needs a minimum of 30 variables (Searle *et al.*, 2008). In addition to adhering to the minimum number of variables per index, each variable should also meet the following criteria.

- The variables should be health-related deficits. For example, wrinkles, an age-related event (Zhang & Duan, 2018), should not be considered a variable. A deficit such as hearing, primarily health-related impairment, can be considered (Ciorba *et al.*, 2012).
- The prevalence of the variable should generally increase with age—for example, cognitive impairment (Kujawski *et al.*, 2018).

- The variable should not saturate too soon. For example, presbyopia, the loss of elasticity in the eye lens causing farsightedness, occurs in most people between 50 to 55 years (Lafosse *et al.,* 2020). It should not be considered a variable given its ability to appear frequently in individuals. A deficit such as unsteady gait that often does not occur too early in older adults can be considered (Jahn *et al.,* 2015).
- The variable should cover a range of different domains rather than a particular domain. For example, all the variables should not solely relate to frailty's physical, social, psychological, or cognitive domain. This is to ensure the multidimensionality of the index.

Once the variables have been established based on the criteria listed above, they can be coded as binary, using the convention '0' to indicate the absence of a deficit or '1' to reveal the presence of a deficit. Moreover, coding can take the form of ordinal and continuous variables with a grading between '0' and '1', whereby a lower self-rating of health is coded to represent a more significant deficit. For example, "Excellent = 0", "Very Good = 0.25", "Good = 0.5", "Fair = 0.75," and "Poor = 1". Based on these codes, an individual's state of frailty can be determined by calculating the ratio of variables present to those assessed, thereby generating a score between 0 and 1 for non-frail (0 to 0.10), vulnerable (0.10 to 0.21), frail (0.22 to 0.44), and $\geq$ 0.45 to 1.0 for most frail (Hoover *et al.,* 2013; Kulminski *et al.,* 2007; Martínez-Velilla *et al.,* 2017; Rockwood *et al.,* 2007; Theou *et al.,* 2016). Based on the different domains assessed by the two conceptual frameworks presented above, the guiding conceptual framework of this study will be the FI. This conceptual framework enables us to recognize frailty as more complex than a physical impairment, strengthening the case for interventions that address other health and personal deficits such as illnesses, environmental, social, cognitive, and psychosocial conditions.

Through the lens of this framework, we will explore the number of variables addressed in interventions that achieve frailty reversal as an outcome, and their relationship with one another if possible. We will also seek to understand the possible consequences of not addressing these variables on frailty status.

Thesis Outline

The following five chapters make up this thesis:

Chapter One: This chapter introduces the concept of frailty and presents a brief overview of some of its adverse outcomes, such as increased dependency on social and healthcare services, increased caregiver burden, predisposition to mental disorders, and death. The chapter further explains the problem statement and provides a personal statement on what motivated this research. The study objective and research questions are presented at the end of this section, including the conceptual framework that guides this study.

Chapter Two: This section presents the literature review, which provides a comprehensive understanding of frailty, and the various assessment methods. It concludes with how the research gaps for this project were initially identified.

Chapter Three: This section describes the scoping review methodology and provides a detailed overview of the steps and stages. In addition, it presents the challenges and considerations made during the implementation of the study design.

Chapter Four: This section is a structured manuscript prepared for submission to the BioMedCentral (BMC) Geriatrics Journal. The manuscript title is 'Reversing frailty in older adults: a scoping review'. It summarizes the key findings and relevant information from each included study in a descriptive and tabular manner and concludes with a discussion and conclusion.

Chapter Five: This chapter presents an integrated discussion of findings from the literature review (Chapter 2), methodology (Chapter 3) and findings of the review (Chapter 4). It also discusses the research implications for nursing practice, education, policy, and research.

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Chapter Two: Review of Literature

This review captures and critiques research and theories around reversing frailty in older adults to identify the research problem and provide a basis for the current research study. The Joanna Briggs Institute's "Population, Concept, and Context" approach guided the literature search content. The study population is "older adults 65 and above", the study concept is "reverse frailty," and the study context is "all contexts" (The Joanna Briggs Institute Reviewers, 2015).

2.1 Review Process

First, we developed a search strategy in collaboration with a librarian at the University of Ottawa to construct a search and identify relevant databases. Searches from electronic databases such as Medline, PubMed, the Cumulative Index to Nursing and Allied Health Literature *[CINAHL])* and grey literature, i.e., google scholar, dissertations, and scan of reference lists from selected articles were carried out to identify relevant studies for inclusion. We included studies on older adults 65 years and older given most studies focus on this age group (Apóstolo *et al.,* 2018; Chu *et al.,* 2019; García-García *et al.,* 2014; Taube *et al.,* 2018). The study dates were restricted to the last ten years to capture the two leading theoretical frameworks of frailty that have been published. The language was limited to English due to language restrictions. To ensure a comprehensive literature capture, no limits were applied to the study design, i.e., all knowledge syntheses, qualitative, quantitative, etc. Based on these inclusion/exclusion criteria, a literature search was conducted using Boolean operators "AND/ OR" and a few Medical Subject Headings (MeSH) terms such as "Frail Elderly /," "Aged/," "revers*." A total of 152 full-text articles were retrieved from all databases and grey literature. Twenty met the inclusion criteria

and were thoroughly screened among the articles considered. For a detailed breakdown of the search criteria and strategy, refer to Appendix B.

We were able to identify five themes in the literature using the Key Word in Context (KWIC) approach. In this approach, a pattern can be found by identifying common words or statements used in discussing a particular topic/subject (Ryan & Bernard, 2003). Some of the themes that emerged from the literature are: (1) *frailty affects more than one domain, (2) frailty is not the same as disability or comorbidity, (3) frailty can be assessed in different ways, (4) interventions for frailty may be single or multi-faceted,* and (5) *frailty can be reversed.*

2.1.1 The Domains of Frailty

Frailty occurs when an individual's vulnerability increases due to the inability to resolve homeostatic conditions due to stress (Kamaruzzaman S.B., 2018). As a result, severe outcomes such as disability, short-term memory loss, and sudden falls may occur (Clegg, 2014). To improve the predictive validity of the operational definition of frailty, researchers consider different domains of frailty, including physical, cognitive, psychological, and social impairments (De Roeck *et al.,* 2018; Van Oostrom *et al.,* 2017). Physical frailty is often associated with sarcopenia, i.e., having low muscle strength (Dent *et al.,* 2019), and other frailty phenotype traits, such as unintentional weight loss, exhaustion, a low level of physical activity, slow gait speed, and weak grip strength (Liu *et al.,* 2020). Cognitive frailty is a co-existence of physical deficits and mild cognitive impairment (Kwan *et al.*, 2019; Ma *et al.,* 2019). Psychological frailty looks at the consequences of age-altered brain function, affecting a person's mastery. Depleting this function may cause depression, anxiety, sadness, and decreased cognition, reducing the quality of life (Hoeyberghs *et al.,* 2020). Lastly, social frailty is when a person's overall social situation, such as limited social participation and the absence of social support and resources, makes them

susceptible to further insults, health-related or societal (Andrew *et al.,* 2012; Bunt *et al.,* 2017). It is well-known that frailty in older adults can adversely affect health, i.e., the experience of delirium, a higher risk of falling, and most often, increased hospitalization (Clegg, 2014). As a result of these consequences, the assumption is that as individuals advance in age, they may become physically, socially, psychologically, or economically dependent on others and society (Rely *et al.,* 2020). These dependencies are sometimes referred to as unstable disabilities (Kamaruzzaman S.B., 2018), often used interchangeably with frailty and comorbidity (Espinoza *et al.,* 2019).

2.1.2 Distinguishing Disability and Comorbidity

Disability is a state where an individual cannot function independently by not being able to perform self-care tasks, i.e., eating, bathing, dressing, toileting, mobility, and grooming. Furthermore, being unable to perform instrumental activities of daily living (IADLs) such as groceries, getting dressed independently, using cutlery, etc., is considered a state of disability (Espinoza *et al.,* 2019). Conversely, comorbidity is the occurrence of multiple chronic conditions, including but not limited to illnesses such as stroke, cancer, and diabetes mellitus (Nicholson *et al.,* 2019).

2.1.3 Assessing Frailty

Most older adults identified as frail are often referred to as geriatricians because they require extensive geriatric and multidisciplinary assessment and management (Alakare *et al.,* 2021). Multidisciplinary approaches often involve physiotherapists to help with rehabilitation, nutritionists to guide their diet, pharmacists to help manage aspects of polypharmacy, and social workers to help provide community and social support (Chen *et al.,* 2018). Added to this list are nurses who work with other professionals to assist patients' and families' understanding and

adaptation to treatment (Maxwell & Wang, 2017). Hundreds of frailty assessment instruments have been developed in the last two decades, looking at the correlation between frailty and adverse health outcomes (Buta *et al.,* 2016). Of these instruments, those frequently used are the frailty index, frailty phenotype and the frailty trait scale (Andrew *et al.,* 2018; Cesari *et al.,* 2014; Faller *et al.,* 2019). The purpose of these instruments is to aid in the early identification and detection of frailty in older adults and to assist in determining the appropriate measures of interventions to prevent, reduce, or reverse its progression.

The *frailty index (FI)* looks at the frequency in the number of clinical conditions, e.g., social factors, comorbidities, psychological factors, and functional and cognitive decline (Walston & Bandeen-Roche, 2015). Based on the FI scheme, individuals are classified as robust, pre-frail, or frail, depending on a count of accumulated deficits (Rockwood *et al.,* 2007). The *frailty phenotype* looks at five criteria to determine the presence or absence of signs of frailty, i.e., sedentary behaviour, slow gait speed, involuntary weight loss, exhaustion, and poor handgrip (Cesari *et al.,* 2014). Not being frail means having none of the criteria, being pre-frail means having one or two measures, and being frail means having three or more criteria (Cesari *et al.,* 2014). Lastly, the *Frailty Trait Scale* looks at factors such as environmental, genetic makeup and inheritance, lifestyle, and comorbidities to determine if an individual is frail or not (García-García *et al.,* 2014). Refer to Appendix C for a summary of the different domains, scale types used, ability to predict mortality, and psychometric properties, i.e., validity and reliability of these instruments.

Notwithstanding the disagreements in assessment norms, it is generally accepted that early screening for frailty facilitates decision-making on how to intervene best and manage its progression (H. Lee *et al.,* 2020; Morley *et al.,* 2013). In addition, despite the lack of standard

treatments or interventions that can be implemented (Aguayo *et al.,* 2017), a wide range of approaches such as exercise, nutritional modifications, cognitive therapy, and pharmacology are being explored as singular or multi-component factors to enhance the functionality of frail older adults (Bleijenberg *et al.,* 2016; Cameron *et al.,* 2013; Ng *et al.,* 2015).

2.1.4 Example of Interventions

Different types of interventions can be used to improve the health of frail individuals, i.e., single-component interventions, which consist of one nature of the intervention (i.e., either physical activity, nutritional interventions, or social interventions, amongst others), and multi-component interventions which involve a combination of two or more components (i.e., physical with nutritional, or cognitive, social, and physical, amongst others. Several studies report that exercise-based interventions are beneficial in mitigating the effects of frailty (Cesari *et al.,* 2015; Freiberger *et al.,* 2016; Strojnik & Gabrovec, 2019), with frequent and regular engagement in physical activities considered to be the best option to delay frailty for most older adults (L. Lee *et al.,* 2017). However, there is often no clarity on which physical activity is an ideal *single-component,* how often it should be performed, and how long (Freiberger *et al.,* 2016). For nutritional interventions, it has been reported that adhering to a Mediterranean-style diet entails a high intake of fruits, legumes, and vegetables, consumption of plant-based oils such as olive oil, and low to moderate intake of alcohol (Talegawkar *et al.,* 2012), is presumed beneficial in delaying and possibly avoiding frailty development in older adults (Hernández Morante *et al.,* 2019). Multi-component interventions often entail a combination of physical, nutritional, pharmacological, behavioural, or cognitive therapies (Cameron *et al.,* 2013; Jang *et al.,* 2018). This approach is deemed beneficial in enhancing the functional capacity of individuals, with the potential to completely reverse the occurrence of frailty (Ng *et al.,* 2015). Individual-tailored

care models are determined based on impairments identified after the individual has completed a comprehensive geriatric assessment (Walston & Xue, 2018).

Given that frailty is a complex syndrome with multidimensional characteristics (Uchmanowicz *et al.,* 2018), the multi-component approach is presumed to be the most effective, with the ability to reverse frailty in individuals already affected (Jang *et al.,* 2018; Kokai *et al.,* 2018; Tarazona-Santabalbina *et al.,* 2016; Uchmanowicz *et al.,* 2018).

2.1.5 Possible Interventions to Treat Frailty

Maintaining independence is essential in every individual's life, irrespective of age. Thus, identifying interventions that can reverse frailty, i.e., restoring a frail individual to either a pre-or non-frail state, is essential. According to the Cleveland Clinic (2020), although there are interventions with the capability to reverse frailty, it can be a daunting process because the frailty syndrome develops over several years, which makes its reversal challenging. Arc-Chagnaud et al., (2019) addressed the importance of physical exercise, nutrition, and pharmacological measures as interventions in reversing frailty. With exercise considered the most effective intervention in pre-clinical models of frailty, the authors asserted that to treat frailty with exercise, activities such as resistance, endurance, aerobic, and strength training need to be consolidated as mandatory procedures for frail and pre-frail individuals in the clinical practice.

Similarly, Macdonald et al. (2020) support a multi-component intervention that combines exercise such as muscle strength training and nutrition e.g., protein supplementation, as the easiest and most effective intervention in reversing frailty. In contrast, Hu et al., (2020) reported that even though increasing physical activity and improving dietary intakes can improve the frailty status, these interventions are most effective when carried out on pre-frail individuals as opposed to individuals who are already frail. With frailty being multidimensional, most studies

that address the concept of reversing frailty seem to focus on the physical and cognitive aspects, with only a few indicating if the studies' participants were non-frail, pre-frail, or frail. Accordingly, these studies focus on interventions with little or no effect on social and psychological deficits experienced by frail older adults (Sacha et al., 2020). According to Rezaei-Shahsavarloo et al., (2020), several studies that report multidimensional interventions that show frailty reversal as an outcome are of low quality, with few randomized controlled trials (RCTs) confirming their effectiveness. Thus, the efficacy or efficiency of these interventions seems questionable.

2.2 Summary

The multidimensional nature of frailty in older adults makes its definition, assessment, and ways to intervene a dynamic and evolving process. Emerging evidence showed that frailty is a complex syndrome requiring interventions with multiple components (Kojima *et al.,* 2019), also known as complex interventions (Craig *et al.,* 2008). Interestingly, both *single-component* and *multi-component* interventions have demonstrated potential to reverse frailty (Brown et al., 2000; Chin A Paw et al., 2001; Oh et al., 2019; Pek et al., 2020). However, existing interventions vary in their characteristics, content, and composition. A recent systematic review titled, '*delaying and reversing frailty'* compared the effectiveness of frailty interventions and their ease of implementation in primary care and found that muscle strength training and protein supplementation were the easiest and most effective interventions to delay or reverse frailty (Travers *et al.,* 2019). Our study will add to the body of literature as it sets out to map the evidence on interventions that achieve frailty reversal as an outcome. We will use the FI as a guide to identify the various frailty domains least and most targeted by these interventions and analyze how these targeted domains contribute to reversing frailty. Additionally, using a

descriptive approach, we will examine existing definitions of reverse frailty that the authors of these interventions used to gain conceptual clarity on this concept.

To the best of our knowledge, no literature organizes and summarizes existing research on the concept of reverse frailty or interventions to achieve this. Therefore, a knowledge synthesis is indicated to provide a comprehensive overview of these interventions, which may help identify gaps and areas that require deeper understanding to reach evidence-based conclusions about their effectiveness.

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Chapter Three: Methodology

This section describes the purpose, overview, and stages of the scoping review methodology. In addition, we present the challenges and mitigation strategies considered and taken throughout the study.

Frailty is a complex and broad concept that affects older adults. Even more complicated is the notion of possibly reversing frailty. A thorough understanding of these concepts can be gained by synthesizing research in these areas. Research synthesis analyzes data from two or more sources to determine similarities and differences while summarizing the results to establish generalizable and applicable recommendations (Cooper & Hedges, 2009). We conducted a review, which is a synthesis process of research. There are over forty-eight different types of reviews, including scoping, systematic, rapid, and umbrella reviews, among others (Sutton *et al.*, 2019). The choice of a review is influenced by the research questions (Grant & Booth, 2009). We have selected a scoping review approach, and the rationale is presented below.

3.1 What is a Scoping Review?

A scoping review is a study design suitable for areas or topics that are emerging, complex or heterogeneous (Pham *et al.,* 2014). This approach can also map, identify, and analyze all relevant literature relevant to a research question using rigorous, transparent methods (Arksey & O'Malley, 2005; Tricco *et al.*, 2016). Additionally, a scoping review can provide an overview of past and current research on broad topics while combining various research designs (Arksey & O'Malley, 2005; O'Brien *et al.,* 2016). Furthermore, this method can present results of reviewed material with or without a critical appraisal of the individual studies. These results can be presented in a narrative or descriptive format (Arksey & O'Malley, 2005). Researchers often

undertake this design method to summarize results, identify research gaps, and determine the value and feasibility of conducting a comprehensive systematic review of the literature (Arksey & O'Malley, 2005; Grant & Booth, 2009; Levac *et al.,* 2010). Systematic reviews are distinct in that they summarize the best available research on a particular question, collect evidence from several studies, determine the effectiveness of interventions, and synthesize evidence from studies assessed for bias, emphasizing the importance of detailed *a priori* methods (Arksey & O'Malley, 2005; Grant & Booth, 2009; Uman, 2011).

3.2 Why is a Scoping Review Appropriate?

The multifaceted nature of frailty in older adults requires ongoing interventions to improve the quality of life of these individuals. Moreover, there is emerging evidence of interventions that can potentially reverse frailty in older adults. Given the nature of our research questions (chapter one), a scoping review is considered ideal because it will assess the scope and nature of research activity in emerging fields of reversing frailty and clarify key concepts and definitions of reverse frailty within the literature. It will also analyze how relevant research has been conducted on this topic and advise on the need for further research (Arksey & O'Malley, 2005).

3.3 Study Design

In this method, we followed the scoping review approach proposed by Arksey and O'Malley's (2005) methodological framework, which has been updated by Levac and colleagues (2010) and the approach proposed by Joanna Briggs Institute (The Joanna Briggs Institute Reviewers, 2015). Furthermore, we used the Preferred Reporting Items for Systematic Review extension for Scoping Reviews (PRISMA-ScR) checklist to guide the reporting of the study

(Tricco *et al.*, 2018). Arksey and O'Malley's (2005) methodological framework consists of six stages.

3.3.1 Stage One: Identifying the Research Question

Identifying the research question is a fundamental step that drives the study. It is recommended to broaden the research questions to capture a wide range of data (Levac *et al.*, 2010). In addition, it is also essential to align the research questions with the purpose of the study (Arksey & O'Malley, 2005). Here is a breakdown of how our two research questions align with these recommendations. Since the concept of reversing frailty in older adults is relatively new, studies may have outcomes of frailty reversal without using the term. As a result, our first research question *(What is the available literature on interventions that achieve frailty reversal as an outcome?)* is quite broad to allow for the identification of a wide range of interventions that achieve frailty reversal as an outcome. This study also strives to gain conceptual clarity on reversing frailty through our second research question (*What does it mean to reverse frailty?).*

3.3.2 Stage Two: Identifying Relevant Studies

In this stage, we determined keywords to search for, sources such as electronic databases, language criteria, timeframe, and type of study to be searched for (Levac *et al.*, 2010). We initially identified five databases, of which we ultimately used four. We did not use the Nursing and Allied Health ProQuest, even though this database is used for nursing and allied health literature searches. A preliminary search of articles in collaboration with a health science librarian revealed very few relevant articles, all of which were duplicates from other included databases. Consequently, this database was excluded. No language restrictions were applied to the initial search for articles. Unfortunately, we decided to limit the language to French and English due to time and resource constraints such as the translation of articles. Study designs

were restricted to primary studies. However, during our initial search of articles, we identified a few relevant secondary studies (scoping and systematic reviews) that we used to inform the study background, review of literature, and compare and contrast with the findings from the primary studies. Additionally, the search returned videos, websites, and PowerPoint presentations, none of which were relevant to the study. No thesis or dissertations met our eligibility criteria.

3.3.3 Stage Three: Study Selection

The process of selecting and extracting data was iterative. After the selected studies were imported into Covidence, I enlisted the assistance of a second independent reviewer (OB) for screening, as recommended (Levac *et al.,* 2010). We met at least three times to discuss the eligibility criteria and clarify any concerns before beginning the process. However, a significant life event prevented this reviewer from finishing the process after the title and abstract screening phase, so I enlisted another reviewer (MA). We also clarified the eligibility criteria once again. We encountered a few hiccups during the full-text screening, one of which was the increasing number of articles that needed to be resolved due to conflicting answers. The conflicts were caused by the two reviewers not choosing the exact reasons for exclusion. We agreed that if an article is to be excluded, the chronological order of exclusion should be followed based on the eligibility criteria, which included P-Population (65 and older), C-concept (frail), C-context (all settings), design (all studies), Language (English or French), and year (all years). As the screening progressed, this approach significantly reduced the number of conflicts. Another hiccup was the back-and-forth movement of some articles between the exclusion list and those needing screening. This was primarily because many studies listed the frailty components of participants without explicitly stating whether they were frail. For instance, frailty can be defined

as having at least three out of five components, using the Fried criteria (chapter one). In some articles, the participants met three of the Fried criteria. Therefore, the other reviewer needed to understand the Fried criteria to determine if the participants were frail or not. As a result, most articles required to be re-screened for inclusion.

3.3.4 Stage Four: Charting the Data

This stage was an iterative process. In the beginning, I created a draft table with a list of items to be extracted in Microsoft Excel. With ongoing consultation with the research team and continued reading of the included articles, I was able to identify more relevant information to be extracted, which required constant revisions to the extraction sheet. A template for the Intervention Description and Replication (TIDieR) checklist was used to extract data about interventions reported in the included studies. This checklist guides authors by outlining interventions in ways that can be used by clinicians and replicated by researchers (Hoffmann *et al.*, 2014). Some recommendations extracted from this checklist are the study's theoretical framework, materials used during the intervention, who conducted the interventions, and delivery methods, among others.

3.3.5 Stage Five: Collating, Summarizing, and Reporting the Results

The study objective and research questions were used to guide concepts to look for in the various studies and categorize the findings. We examined the data extraction table multiple times to identify common patterns during this iterative process. As the results were organized, back-and-forth discussions with the research team were conducted to ensure adequate data relating to the research questions were recorded. The outcome of this stage is discussed in the next chapter.

3.3.6 Stage Six: Stakeholder Consultation

Engaging stakeholders in systematic and scoping reviews aim to establish credibility, provide transparency and accountability, and improve the study's relevance (Motu'apuaka *et al.,* 2015). Stakeholders can be health professionals, researchers, policymakers, patients, or public members (Pollock *et al.,* 2018). While this stage is optional in a scoping review (The Joanna Briggs Institute Reviewers, 2015), it can be beneficial by way of integrating various perspectives from individuals who are interested in and could use the review's findings (Erika Cottrell, Evelyn Whitlock *et al.,* 2014). Considering the time constraints of this Master's thesis, expert consultation was excluded due to its time-consuming nature.

3.4 Ethics Approval

This scoping review is based on scholarly literature that has already been published or publicly reported and does not involve personal patient information. According to the Tri-Council Policy Statement (TCPS), a research study does not need to be reviewed by a research ethics board (REB) if it *"relies exclusively on information in the public domain, and the individuals to whom the information refers have no reasonable expectation of privacy"* (Tri-Council Policy Statement, 2018, p.15). As a result, ethics approval was not required.

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Chapter Four: Reversing Frailty in Older Adults: A Scoping Review

The following unpublished manuscript is formatted for submission to BioMed Central Geriatrics Journal

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Abstract

Background: Individuals 65 years or older are presumably more susceptible to becoming frail, which increases their risk of multiple adverse health outcomes. Reversing frailty has received recent attention; however, little is understood about what it means and how to achieve it. Thus, this scoping review aims to provide an overview and synthesis of evidence on available interventions that achieve frailty reversal as an outcome.

Methods: We followed Arksey and O'Malley's five-stage scoping review approach and conducted searches in CINAHL, EMBASE, PubMed, and Web of Science. We hand-searched the reference list of included studies and conducted a grey literature search. Two independent reviewers completed the title, abstract screenings, and full-text review using the eligibility criteria, and independently extracted approximately 10% of the studies. We critically appraised studies using Joanna Briggs critical appraisal checklist/tool, and we used a descriptive and narrative method to synthesize and analyze data.

Results: Of 7499 articles, thirty met the criteria and three studies were identified in the references of included studies. Seventeen studies (56.7%) framed frailty as a reversible condition, with 11 studies (36.7%) selecting it as their primary outcome. Reversing frailty varied from either frail to pre-frail, frail to non-frail, and severe to mild frailty. We identified different types of single and multi-component interventions each targeting various domains of frailty. The physical domain was most frequently targeted (n=32, 97%). Interventions also varied in their frequencies of delivery, intensities, and durations, and targeted participants from different settings, most commonly from community dwellings (n=23; 69.7%).

Conclusion: Some studies indicated that it is possible to reverse frailty. However, this depended on how the researchers assessed or measured frailty. The current understanding of reverse frailty is a shift from a frail or severely frail state to at least a pre-frail or mildly frail state. To gain further insight into reversing frailty, we recommend a concept analysis. Furthermore, we recommend more primary studies considering the participant's lived experiences to guide intervention design and delivery.

Keywords: Multicomponent, reverse frailty, frailty domains, frailty phenotype, frailty index

4.1 Background

Within the next few decades, the population of people aged 65 and over will continue to rise more than all other age groups, with roughly one in six people over 65 by 2050, compared to one in eleven in 2019 [1]. Individuals over 65 years are presumably at greater risk of becoming frail [2–4]. Theoretically, frailty is considered a clinically recognized state of vulnerability that results from an age-related decline in reserve and function, compromising an individual's ability to cope with the daily challenges of life [5, 6]. The Frailty Phenotype (FP), which is the most dominant conceptual model in literature [3, 7–10], considers an individual frail by the presence of at least three of five phenotypes: weakness, low levels of physical activity, unintentional weight loss, slow walking speed, and exhaustion. Physical, cognitive, psychological, and social impairments often characterize the different domains of frailty [11]. The physical domain is devoted to FP-related conditions [12], the cognitive domain is the co-existence of physical deficits and mild cognitive impairments [13], the psychological domain focuses on an individual's coping mechanisms based on their own experiences [14], and the social domain looks at a person's limited participation in social activities and limitations in social support [15]. Frail older adults are prone to adverse outcomes such as frequent falls, hospitalizations, disabilities, loneliness, cognitive decline, depression, poor quality of life, and even death [16–18]. In response, researchers propose different interventions to prevent or slow frailty progression by targeting a single domain (e.g., physical, social, cognitive, etc.) or targeting two or more domains using single or multi-component interventions. Hergott and colleagues investigated the effects of a single-component intervention, functional exercise, on acromegaly-induced frailty [19]. Abizanda and colleagues examined the effects of a multi-

component intervention, targeting nutrition and physical activity, on frail older people's physical function and quality of life [20]. Besides using varying types of interventions to prevent or slow the progression of frailty, many studies indicate that frailty can be reversed [3, 21, 22]. However, the current understanding of reverse frailty is unclear, and the characteristics of interventions needed to reverse frailty seem to vary.

Authors have measured the reversal of frailty using various methods. For instance, Kim and colleagues' study [23] on exercise and nutritional supplementation in frail elderly community-dwellers demonstrated reversals in FP components. Components included fatigue, low physical activity, and slow walking, an improvement from the presence of 5 components of frailty (according to the FP) to 2 indicating a pre-frail state [23]. Conversely, other studies indicated frailty reversal based on changes in frailty index (FI) scores. FI considers frailty to be a measure of accumulation of deficits [24]. A FI score of 0.22 or greater indicates frailty, score less than or equal to 0.10 indicates a non-frail state. De Souto and colleagues used this approach to show frailty reversal [25]. Hergott et al. (2020) used frailty severity to indicate frailty reversal. Participants in their study reversed frailty from a severe state to a mild state [19]. These studies demonstrate the variability in how reversing frailty is measured and understood. There is further variability in characteristics of interventions that can reverse frailty. For example, some interventions have a single component (e.g., pharmaceuticals [26]) and others have two or more (e.g., nutrition and physical activity) [20, 27, 28]. For a more comprehensive understanding of reverse frailty and the characteristics of interventions, a comprehensive review of the literature on this topic is needed. Therefore, through a scoping review, this study aims to present an overview and synthesis of available interventions that

result in frailty reversal. This methodology is ideal because it encompasses a broad scope and can comprehensively analyze and synthesize data on a subject [29]. Findings from this review will clarify the concept of reverse frailty, provide a synthesis of reported interventions that reversed frailty, and identify knowledge gaps for future research.

Guiding Conceptual framework

The FI, unlike the FP, considers frailty as more than a physical deficit but rather an accumulation of health-related deficits across multiple domains [24]. For this reason, the FI serves as our guiding conceptual framework. Through this framework, we recognize frailty as a complex phenomenon, strengthening the case for interventions addressing other health and personal concerns, such as illness, environmental disturbance, social dysfunction, cognitive decline, and psychosocial distress. This framework provides a helpful lens through which we can examine the number of variables addressed in interventions designed to reverse frailty and their relationship to one another. Additionally, we will explore the implications of not addressing a range of factors (social, physical, cognitive, psychological, etc.) on frailty.

4.2 Methods

We followed Arksey and O'Malley's [29] five-stage approach, elaborated by Levac et al., [30] and Joanna Briggs Institute (JBI) for scoping review [31]. They propose six stages: (1) identifying the research question, (2) locating relevant studies, (3) selecting the study, (4) charting data, (5) summarizing results, and (6) consulting with stakeholders. We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyzes Extension for Scoping Reviews (PRISMA-ScR) checklist [32] to guide study reporting (Appendix D).

4.2.1 Stage One : Identifying the Research Question

According to Levac and colleagues, fundamental research questions should be broad enough to enable comprehensive analysis and appropriate mapping of relevant literature [30]. Following this, our two research questions are as follows:

1. What is the available literature on interventions that achieve frailty reversal as an outcome?
2. What does it mean to reverse frailty?

4.2.2 Stage Two: Identifying Relevant Studies

We performed literature searches, search strategy refinement, and screening of articles iteratively.

Eligibility Criteria

JBI's PCC mnemonic guided eligibility criteria, where P (population): frail older people over 65yrs of age, C (concept): reversing frailty, and C (context): all contexts. We included French and English studies of frail older adults over 65 years because most studies focus on this age group [33–36]. We also included studies that evaluated the association of interventions with frailty severity, assessed the effectiveness or feasibility of interventions to either reduce, improve, manage, enhance, treat, or reverse frailty. We did not apply any limitations to study dates and settings. However, we excluded secondary studies (knowledge syntheses, conference abstracts, etc.) and any study about interventions to prevent frailty. Lastly, we performed a grey literature scan to identify relevant primary studies to ensure a comprehensive literature search.

Search Terms

An a priori concept analysis [37] of frailty and frailty interventions revealed relevant search terms regarding the population of interest and aim of the intervention. Identified keywords for the former included 'frail elderly, frail, aged hospital patient, institutionalized elderly, very elderly, geriatrics, senior, and aged'. Those for the latter were 'reverse, improve, change, intervene, modify, and reduce frailty'. These keywords were presented to and approved by an academic librarian (VL). Since reversing frailty is an emerging concept, we recognized the need to have a broad range of search terms to capture a comprehensive list of studies that may be relevant. Therefore, we considered interventions aimed at reducing, treating, enhancing, and improving frailty since the outcomes of these studies could reverse frailty without necessarily using the word "reverse". Medical Subject Headings (MeSH) and boolean operators of these terms were used in different databases to identify relevant studies.

Search Strategy

Two academic librarians (VL & VC) guided the development of the search strategy and selected databases. We conducted the searches between August 6th and August 9th, 2021, using MEDLINE (OVID interface), Embase (OVID interface), Cumulative Index to Nursing and Allied Health Literature (CINAHL), and Web of Science. We first implemented the search in MEDLINE (Appendix E), which we later adapted for the other three databases. We manually searched for relevant studies from the reference lists of included/eligible articles and reviewed conference abstracts and secondary analyzes to identify primary studies. A third academic librarian (LS) peer-reviewed the search strategy using the Peer Review of Electronic Search Strategies (PRESS) guidelines [38] on August 19th, 2021, without modification. On August 23rd,

2021, we imported the results in RIS format into Covidence, a web-based system for systematic reviews provided by Cochrane [39, 40], which also removed duplicates. We did not import the articles identified via hand-searching the reference list into Covidence for screening. However, two reviewers independently assessed the articles' eligibility according to our eligibility criteria.

4.2.3 Stage Three: Study Selection

There were two reviewers (AF, OB) involved in this stage, which involved a first and second screening level. The first level included an independent screening of the titles and abstracts, and we decided by selecting 'yes', 'no', or 'maybe'. To qualify for full-text screening, a study must receive two "yes" or two "maybe" votes. Two 'no' votes moved the study to exclude, and one 'no' vote along with one 'yes' or 'maybe' vote moved it to conflicts, pending resolution. After consultation with the second reviewer, the first author (AF) resolved conflicts. Following this initial screen, the second level involved a full-text review of all studies included at the title-abstract level. Using the same principles as the first level screening, the first author (AF) and another reviewer (MA) completed this stage. In cases where full-text articles could not be located or had to be purchased, the corresponding authors were contacted once by email to request copies. We excluded the articles if we did not receive a response after two weeks. We also searched Google Scholar for conference abstracts to see if the full text of the papers had been cited and accessible. For most searches, this process was ineffective, leading to the exclusion of all conference abstracts. Appendix H contains articles excluded with reasons.

4.2.4 Stage Four: Charting the Data

To extract essential information from the articles, we developed a standard Microsoft Excel form a priori. Additionally, we used the Template for Intervention Description and

Replication (TIDieR) checklist [41] to guide the extraction of the interventions. The form was pilot tested with five articles and revised following recommendations from the research team. After establishing the information to be extracted, we imported the data into Google Forms to facilitate the extracting process for the reviewers. To ensure consistency and reliability in data extraction, two reviewers (AF and MA) independently extracted data from at least 10% of the included studies and compared the results, as recommended by Levac and colleagues [30]. Once we established consistency, the first author (AF) extracted data from the remaining studies.

Data Extracted

We list the data extraction items in Appendix F. They include a bibliography (authors, the journal-title and year of publication), setting, study population (frail, number and age of participants), aims of the study, the conceptual framework of frailty used, domains of frailty considered, details on interventions that reduce, enhance, treat or reverse frailty, the framework used to develop interventions, assessment tools or instruments to assess frailty outcome before and/or after the intervention, outcomes (frailty completely, partially, or not reversed).

Quality Appraisal (QA)

We critically appraised included studies strengths and limitations of the studies (e.g., randomized controlled trials, quasi-experimental studies, case reports, case series, and cohort studies) using the corresponding JBI checklist for quality appraisal. Checklists, ranged from eight to 13 items [35]. Answers to the questions in each scale ranged from 'yes', 'no', and 'unclear'. Three reviewers (YA, MA, and AF) independently appraised the included studies. After

completing the assessment, the first author (AF) sorted the answers to determine any discrepancies. When two reviewers reported the same answer, agreement was achieved. When answers differed, the first author extensively reviewed the study and discussed the differences with the other two to reach a consensus. After completion, we converted all the answers into descriptive variables, with yes representing '1' and no and unclear meaning '0'. Following recommendations from some studies [42, 43], we used these variables to generate a total score, which we further used to classify a study into "low", "moderate", and "high" risk of bias using our interpretation scale (Appendix G).

4.2.5 Stage Five: Summarizing and Reporting the Results

Data Analysis

To summarize and elaborate on the first research question, we used a narrative synthesis. Initially, we developed a preliminary synthesis by grouping studies that focused on similar concepts into a tabular format. Next, we explored relationships between and within studies using graphs. Through the use of conceptual mapping, we linked multiple pieces of evidence from individual studies to highlight key concepts and ideas [44, 45].

Our approach to answering the second research question, comparing study demographics and participant characteristics, was descriptive in nature. Using Excel, we calculated the number and percentage of variables in each category and compared their percentages across studies [46]. To report on the results of my analysis, we used the PRISMA Extension for Scoping Review checklist as a guide [32].

Study Selection

We identified 7499 potential records, of which thirty met eligibility criteria. In addition, our hand search of references of included studies revealed three eligible studies, reaching a total of thirty-three. We illustrate the screening and selection process for the included studies using the PRISMA 2020 flow diagram for systematic reviews (Figure 4.1).

Study Characteristics

Sample sizes ranged from one to 250,428 participants across the studies. The most common study designs were randomized controlled trials - RCTs (n=23) [22, 23, 52–61, 25, 62–64, 27, 28, 47–51], quasi-experimental (n=4) [65–68], Cohort Studies (n=3) [20, 69, 70], case series (n=2) [71, 72] and case report (n=1) [19]. Geographically, the studies took place in fifteen different countries, namely Japan (n=6) [23, 52, 56, 61, 68, 70], Spain (n =6) [20, 47, 62, 63, 66, 71], United States of America (n=4) [19, 28, 48, 49], China (n=3) [54, 55, 65], Sweden (n=2) [53, 58], South Korea (n=2) [67, 72], Singapore (n=2) [22, 57], Australia (n=1) [50], Netherlands (n=1) [27], Canada (n=1)[69], France (n=1) [25], Brazil (n=1) [51], Thailand (n=1) [59], Turkey (n=1) [60], Denmark (n=1) [64]. Publication dates ranged from June 23rd, 1994, to January 2nd, 2021, with most articles (n=24) published after 2015.

Critical Appraisal Results

The quality assessment scores of the studies ranged from seven to twelve, and study bias was low to moderate for all included studies (Appendix G). Given that scoping reviews do not mandate the inclusion of studies based on critical appraisal results [73], we did not exclude studies based on their QA scores.

Participant Characteristics

Twelve studies (36.4%) included participants over 65 years of age, 11 studies (33.3%) over 70 years of age, and 10 studies (30.3%) over 75 years of age. Most authors referred to participants' gender solely as male or female, making it difficult to distinguish between gender and sex. Consequently, we present the results as reported in the studies. All but one study reported the gender of participants [60], with one study having only male participants [19] and two studies having only female participants as per their eligibility criteria [23, 64]. In many studies, the presence of certain comorbidities was not a requirement for participation (n=27). Some studies, however, required comorbid conditions for inclusion, such as acromegaly (n=1) [19], cardiovascular disease (n=1) [68], chronic obstructive pulmonary disease/lung disease (n=1) [63], fatigue (n=1) [65], and risk of mobility disability and sedentary lifestyle (n=1) [49]. Table 4. 1 presents a summary of participant characteristics.

Most and least common domains targeted

Twenty-six studies involved intervention and control groups. Additionally, each study's intervention targeted at least one domain of frailty. For example, some interventions targeted one single domain (n=23) [19, 20, 53, 55, 56, 58–60, 62–64, 66, 23, 68–70, 27, 28, 47–49, 51, 52], two domains (n=6) [4, 22, 57, 59, 60, 74], three domains (n=2) [50, 61], and four domains of frailty (n=2) [54, 67]. Counts per domain are presented in Figure 4. 2. The most targeted domains were the physical and the cognitive domains. The social domain was the least targeted.

Single and multi-component interventions

Thirteen studies (39.4%) focused on single-component interventions; twelve were physical activity interventions [47, 48, 72, 49, 51, 55, 56, 59, 63, 66, 69], and one was a social intervention [70]. These activities were either individually tailored or performed in a group. Over 50% of the studies focused on multicomponent interventions [19, 20, 54, 57, 58, 61, 62, 65, 67, 68, 71, 22, 23, 25, 27, 28, 50, 52, 53]. The number of components varied across interventions; from two components to the interventions (n=10) [20, 23, 27, 28, 52, 53, 58, 62, 65, 71], three components to the interventions (n=8) [19, 22, 25, 50, 57, 61, 67, 68], or four components to the interventions (n=2) [54, 67]. Characteristics of the interventions are included in Table 4. 2.

Typical use of Fried's phenotype

Frailty was defined in all but three studies (n=30) [28, 52, 64]. Two different definitions of frailty were used: Fried's (n=20) [20, 22, 57, 59, 60, 62, 65–68, 71, 72, 23, 47, 49–51, 54–56], and the Frailty Index (n=4) [25, 63, 67, 69].

Definition/clarity about the concept of reverse frailty

Authors of 17 studies referred to frailty as a reversible condition. However, the concept of reversing frailty was not clarified or explained in six studies [22, 48, 49, 57, 60, 61]. When defined, definitions varied. Some authors defined it as a shift from a frail to pre-frail state (n=1) [59], frail to non-frail (n=2) [25, 62], frail to pre- and non-frail (7) [23, 51, 55, 66, 68–70], and severe frailty to mild frailty (n=1) [19]. What was common across all definitions is that the direction of reversal was from a more severe state of frailty to a less severe state of frailty or pre-frail state. What is different is the degree of frailty, given that some definitions indicated a

participant should be frail while others indicated participants being severely frail. This suggests the use of different definitions, assessments methods, and measures of frailty. For example, seven of the studies that showed reversal used the definition of Fried et al., [23, 51, 55, 59, 62, 66, 68], one study used the frailty index [69], and another study used the clinical frailty scale [19]. Finally, one study used the Kihon checklist, consisting of 25 yes or no questions on daily-life-related activities, motor functions, nutritional status, oral functions, homebound, cognitive functions, and depressed mood [70].

Composition of Interventions that achieve frailty reversal as an outcome

Out of the 17 studies that mentioned it was possible to reverse frailty [19, 22, 75, 51, 55, 59, 62, 66, 68–70], 11 of them had frailty reversal as an outcome. Like the definitions, the interventions that were the subject of these studies differed, and different domains could be indicated based on them. The physical domain was targeted in over 80% of the studies (n = 9) [19, 23, 51, 55, 59, 62, 66, 68, 69], while the social [70] and cognitive domains [22] were each targeted in one study. In single interventions such as physical activities (n=5) [51, 55, 59, 66, 69], resistance exercises appeared to be the most common [22, 23, 65–68, 71, 28, 51, 52, 55–57, 59, 61], done on its own or in combination with other physical exercises. Meanwhile, the social intervention enhanced the patient's social capital, a social network that facilitates access to benefits and helps individuals solve problems through association [70].

The multi-component intervention consisted of physical activity combined with either nutritional counselling/advice or supplements. Some of the interventions included physical activity, nutrition, plus pharmaceutical intervention in one study [68], physical activity, nutritional plus cognitive intervention in another study[22], and physical activity combined with

occupational and speech therapy [19]. Each of these studies used different intervention frequencies, ranging from 12 hours per week to monthly, varying durations from six to 24 weeks.

4.3 Discussion

The objective of this study was to present a comprehensive review of the evidence on existing interventions that achieved frailty reversal as an outcome in adults over 65, so that we have a better understanding of what these interventions are and what it means to reverse frailty. From 33 included studies, which revealed that despite frailty being a complex syndrome requiring a holistic approach encompassing multiple domains, there is important variations in the different domains targeted by the interventions. The physical domain, for example, seems to receive the most attention and the social domain the least. Further, our results showed that interventions that achieved frailty reversal as an outcome, and the definition of the concept depend primarily on how frailty is defined, addressed, or assessed. Our findings lead us to the following discussion points.

4.3.1 Frailty Reversal may Depend on Targeted Domains

To the best of our knowledge, the present study is the first to systematically map interventions that achieve frailty reversal as an outcome and relates these interventions to the targeted frailty domains. We used our frailty conceptual framework (frailty index) as a lens to identify potential areas of frailty to target. Through this lens, we anticipated interventions would target multiple domains of frailty, such as psychological, physical, social, cognitive, etc., to achieve a holistic outcome. However, this was not the case per the findings in this review. We identified that the physical domain of frailty is the most frequently targeted compared to

the cognitive, social, and psychological domains. This is supported by the findings of other reviews where authors perceived frailty as primarily a physical impairment, measured by the Fried criteria [76–81]. Therefore, this suggests that reversing frailty depends on the domain that is targeted by the intervention, or the conceptual framework used to identify and measure its outcome.

4.3.2 Definition of Reverse Frailty Remains Unclear

There is no standard definition of reverse frailty, yet the concept appears in several research studies. We used a descriptive approach to examine the differences and similarities between the various definitions. A fundamental similarity is that the individual must be deemed frail at baseline. However, the process of determining an individual's frailty score or status differed among the studies because of the different assessment instruments used. Another similarity was that to reverse frailty, frailty scores or status must not progress to a more severe state but rather improve to a pre-frail or mild frailty state. Further research is required to clarify this concept, preferably through concept analysis.

4.3.3 Absence of a Universal Method to Reverse Frailty

This review included a heterogeneous group of studies with a diverse range of participant characteristics, intervention types, and duration of intervention. Single-component and multi-component interventions have shown efficacy in reversing frailty, with more studies of single-component interventions (i.e., physical activity or social interventions) than the latter.

Use of single-component interventions to reverse frailty

Our study identified physical activity as the most used intervention across studies that reversed frailty. This fits with previous findings that physical activity is essential in interventions

for frail older adults [79–82]. The activities were performed together (combination exercises) or separately (resistance only). Exercise frequency varied from daily to three times per week, with varying intensities (moderate to high) and durations ranging from 6 weeks to 6 months. As stated in some studies, resistance exercise performed at high intensity over a minimum of 12 weeks had the most desirable effect on physical frailty [28, 83], and when done regularly over six months, has the potential to improve both physical and physiological dimensions of frailty [84]. In one study, we identified a desirable (frailty reversed) effect as early as six weeks [66], likely because of the combination of resistance, strength training and aerobic exercises. Therefore, when combined with other types of exercise, resistance exercise could promote the rapid improvement of physical frailty.

According to a recent scoping review, social frailty has not received adequate attention [15]. The same notion applies to this review, which identified only one study [70] that explored frailty reversal through social interventions. Using a checklist of items, the study monitored the effects of enhanced social capital (increased interaction with neighbours, increased trust in the community, increased social participation in activities) on frailty reversal over two years. The results showed that 31.8% of the participants changed their frailty status to pre-frail or robust. Another study [61] showed that increasing participants' social capital improved their adherence to activities and encouraged them to continue interventions even after the study had ended. Thus, interventions that consider this approach may have better outcomes when it comes to frailty reversal.

Use of multi-component interventions to reverse frailty

Some studies that showed frailty reversal employed a combination of two or more intervention components tailored to participant needs or conducted in small groups. Physical activity, particularly resistance exercise, is recommended in conjunction with nutritional interventions as a preventative measure of muscle atrophy in older adults [61], which may explain why this combination was the most common among the multi-component interventions. We also noted other activities such as strength, balance gait and aerobic exercise performed in combination with others at varying frequencies and durations. Nutritional interventions utilized various strategies, including dietary supplements and nutritional education (advice and counselling) on making healthy food choices, with the latter being the most used. Participants who feel empowered by interventions that incorporate their input (e.g., choosing meals) are more likely to feel in control and autonomous over their life choices [85, 86]. This likely explains how nutritional education may provide older adults with more food variety and improved food intake compared with dietary supplements [61]. In addition to nutritional education and physical activity, Ushijima et al. [68] also provided medication guidance, to address polypharmacy, which is known to negate the effects of the physical and nutritional interventions [87, 88].

4.4 Recommendations

The results and discussion points above guide our research, practice, and policy recommendations.

Research

Some studies failed to report whether interventions were modified, personalization of interventions were planned, fidelity and adherence were measured, or how intervention fidelity was maintained or improved. Therefore, we recommend that studies use the template for intervention description and replication (TIDIER) checklist whenever possible to improve intervention reporting. This checklist facilitates clinician use of interventions and researchers' synthesis and replication [41]. Additionally, we recommend that authors of future studies provide details on the definition and components of frailty since this information was lacking in some studies. Clinically, this may help identify groups of individuals in need of care and facilitate understanding among researchers.

Despite having no study design restrictions, we could not identify any qualitative or mixed method studies exploring the lived experiences of frail older adults. None of the included studies reported engaging participants in decision-making or incorporating participant experiences into intervention delivery. A recent scoping review [89] echoes this concern, as older adults worry that they are not involved in health and well-being decisions. It is known that engaging older adults in decision-making improve health outcomes [90]. Therefore, we recommend qualitative and mixed methods studies considering participants' lived experiences when delivering and possibly designing future interventions.

Similarly, we found one study that reported on behavioural enhancements such as goal setting, action plans, and goal execution [65]. The benefits of this approach included fostering self-management skills and sustaining changes over time [65]. Thus, our recommendation is for

more studies to adopt the above behavioural enhancement approach to facilitate adherence to interventions and maintain the long-term benefits of interventions.

Practice

Further to considering the lived experiences of older adults with frailty while delivering interventions, we recommend tailoring interventions to fit the needs and capabilities of each individual rather than generalizing it across an entire population. For example, Latham and colleagues [91] conducted a resistance training program with Vitamin D supplements over ten weeks for participants with certain functional limitations, such as dependence on activity of daily living (ADL), prolonged bed rest, or impaired mobility. Contrary to other studies reporting positive effects of resistance exercise, such as improved functional outcomes and decreased frailty scores during this period [28, 51, 56, 61], Latham and colleagues reported increased fatigue and musculoskeletal injury risks, which may be related to the participants' functional limitations. We, therefore, recommend tailoring interventions to match participants' needs and abilities rather than having set durations, frequencies, or intensities of interventions. Another reason is that some older adults may have functional limitations affecting their ability to adhere to prescribed interventions, including the potential adverse effects of polypharmacy, such as a possible decrease in the effectiveness of an intervention [88]. Lastly, we have highlighted how frailty has no standard method for assessment or measurement, suggesting the need for more work to be done in this area to standardize definitions and measures of frailty. Even with a standardized definition and measurement of frailty in place, we recommend tailoring interventions to the participant's needs for the reasons presented above.

Policy

Research results influence guidelines and expectations for delivering care, services, and programs [92]. For all the studies included in this review, we observed a representation from most continents, except for Antarctica, Africa, and South America. Frailty is becoming a potential global concern. Therefore, we encourage that studies be represented from all continents, if possible, for a better understanding on the global challenges of expectations, implementation, or care delivery for frail older adults. Such information can facilitate the transfer of healthcare professionals between continents by bridging the knowledge gap concerning frailty, its interventions, and potential methods for reversing the condition.

4.5 Strengths and limitations

Our study has many strengths. We established a reproducible, systematic approach, from the literature search to screening and data extraction. Furthermore, the search strategy was guided and peer-reviewed by academic librarians with extensive knowledge of scoping and systematic reviews. We quality appraised included articles permitting us to have a better sense of the quality of the evidence on this topic. Although not formally published or registered, an a priori protocol approved by the research team guided this study.

We advise considering the following limitations when interpreting the results of this review. First, the included studies were heterogeneous in their study objectives, frailty definition, frailty domain targeted, and intervention characteristics. Some studies used self-administered questionnaires as outcome measures to assess frailty, potentially increasing the risk of bias and making replication difficult because there is no guarantee of having the same responses among different participants. In addition, some studies did not report the

characteristics of the intervention [19, 69], and others indicated that participants were frail but did not specify how frailty was determined [28]. Lastly, we acknowledge that using only a few databases may have limited the number of studies we were able to find.

4.6 Conclusions

we used a narrative and descriptive approach to summarize the studies on reverse frailty, giving us the ability to have a better understanding of the concept. Despite the lack of a standard definition of frailty, our study found that it is possible to reverse frailty. However, that largely depends on how frailty is defined or measured. Though there is increasing use of the concept of reverse frailty, we acknowledge the need for concept analysis to achieve a true definition. Based on our findings, we identified that to consider the notion of reversing frailty, an individual must first and foremost be considered frail, irrespective of the assessment methods used. We also identified the need for future research, such as RCTs with larger sample sizes, to investigate frailty's social, psychological, and cognitive aspects, which have received less attention so far. In addition, more qualitative analysis that explores the lived experiences of frail older is crucial to guide the choice of interventions. These recommendations will enhance our understanding of frailty interventions and possibly increase our chances of reversing frailty in more individuals. Lastly, a holistic approach that considers multiple domains at once and participants' lived experiences remains essential.

Abbreviations
ADLs: Activities of daily living; BMI: Body Mass Index; CES-D: Center for Epidemiologic Studies Depression Scale; MEDLINE: Medical Literature Analysis and Retrieval System Online; COPD: Chronic obstructive pulmonary disease; CPR: Cardiopulmonary resuscitation; Dur: Duration; FI: Frailty Index; FP: Frailty Phenotype; Freq: Frequency; GDS: Geriatric Depression Scale; HI: High intensity; iADL: Instrumental Activities of Daily Living; JBI: Joanna Briggs Institute; KCL: Kihon checklist; MEP: Multi-component Exercise Program; MeSH: Medical Subject Headings; PIFU: Post-intervention follow-up; PRESS: Peer Review of Electronic Search Strategies; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyzes; RAI-HC: Resident Assessment Instrument-Home Care; RCTs: Randomized control trials; RMR: Resting metabolic rate; RT: Resistance training; SPPB: Short Physical Performance Battery; TIDieR: Template for Intervention Description and Replication;wks: Weeks; yrs:years; m:months

Acknowledgements
We would like to thank the University of Ottawa Health Science Librarians: Valentina Ly (VL), Victoria Cole (VC), and Lindsey Sikora (LS), for their guidance in ensuring searching for relevant studies. Special thanks also go to Ojongetakah Enokenwa Baa and Mbi Ayuk Solange, who acted as secondary screeners for selecting relevant studies.

Authors' contributions
AF, the principal investigator, initiated the project, designed the search strategy, carried out data extracted, and performed an analysis of the findings. KL critiqued and guided the project's direction, such as the research questions, methodology, and results. ML offered suggestions about the thesis design results, critiqued and provided feedback as needed. CB guided the development of the research topic, provided regular feedback, and edited and approved every stage of the project. All authors read and approved the final manuscripts.

Funding
Not applicable

Availability of data and materials
Data supporting the findings of this study are available in the article [and its supplementary information files].

Declarations

Ethics approval and consent to participate
Not applicable

Consent for publication
Not applicable

Competing interests
The authors declare that they have no competing interests

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Table 4. 1 Study and Participant Characteristics

Author/year	Research design	Country of study	Age (years)	Comorbidity	Number of participants		Female (%)	Setting	Critical Appraisal Rating
					Control group	Intervention group			
Abizanda, 2015 [20]	Cohort Studies	Spain	≥70	NR	0	69	70	Nursing/ Retirement	Moderate
Arrieta, 2019 [47]	RCT	Spain	≥70	NR	45	43	70.5	Nursing/ Retirement	Low
Brown, 2000 [48]	RCT	USA	≥75	NR	36	48	56	Nursing/ Retirement	Moderate
Cadore , 2014 [71]	Case Series	Spain	≥75	Dementia	NR	11	55	Nursing/ Retirement	Low
Cameron, 2013 [50]	RCT	Australia	≥70	NR	109	107	68	Community-Dwelling	Moderate
Cesari, 2015 [49]	RCT	USA	≥70	Risk of mobility disability, Sedentary lifestyle.	211	213	68.9	Community-Dwelling	Moderate
Chin A Paw, 2001 [27]	RCT	Netherlands	≥70	NR	37	120	70	Community-Dwelling	Moderate
Coelho-Júnior, 2021 [51]	RCT	Brazil	≥65	NR	13	26	64.3	Community-Dwelling	Moderate
de Souto Barreto, 2018 [25]	RCT	France	≥70	NR	163	185	64.7	Community-Dwelling	Low
Fiatarone, 1994 [28]	RCT	USA	≥70	NR	26	74	63	Nursing/ Retirement	Moderate
Hergott , 2020 [19]	Case report	USA	≥70	Acromegaly	NR	NR	0	Nursing/ Retirement	Moderate
Imaoka, 2016 [52]	RCT	Japan	≥75	NR	17	58	75.8	Nursing/ Retirement	Moderate
Kim, 2015 [23]	RCT	Japan	≥75	NR	33	98	100	Community-Dwelling	Moderate
Kim, 2020 [72]	Case Series	South Korea	≥70	NR	NR	10	100	Community-Dwelling	Low
Lammes, 2012 [53]	RCT	Sweden	≥75	NR	21	72	60	Community-Dwelling	Moderate

Larsen, 2020 [69]	Cohort Studies	Canada	≥65	NR	NR	110297	57.6	Community-Dwelling	Low
Li ,2010 [54]	RCT	China	≥65	NR	31	26	47.7	Community-Dwelling	Low
Liao, 2019 [55]	RCT	China	≥70	NR	16	16	69.2	Community-Dwelling	Low
Liu, 2017 [65]	Quasi-Experimental	China	≥65	Fatigue	21	58	92	Community-Dwelling	Low
Losa-Reyna, 2019 [66]	Quasi-Experimental	Spain	≥75	NR	5	8	75	Community-Dwelling	Low
Nagai, 2018 [56]	RCT	Japan	≥65	NR	9	7	90	Community-Dwelling	Moderate
Ng, 2015 [22]	RCT	Singapore	≥65	NR	7	61	61.4	Community-Dwelling	Low
Ng, 2017 [57]	RCT	Singapore	≥65	NR	7	61	61.4	Community-Dwelling	Low
Oh, 2021 [67]	Quasi-Experimental	South Korea	≥65	NR	196	187	72.3	Community-Dwelling	Low
Rydwik, 2010 [58]	RCT	Sweden	≥75	NR	14	50	60	Community-Dwelling	Moderate
Sadjapong, 2020 [59]	RCT	Thailand	≥75	NR	32	32	61	Community-Dwelling	Low
Sahin, 2018 [60]	RCT	Turkey	≥65	NR	16	32	NR	Nursing/ Retirement	Low
Seino, 2017 [61]	RCT	Japan	≥65	NR	0	21	31	Community-Dwelling	Low
Takatori, 2021 [70]	Cohort Studies	Japan	≥75	NR	NR	942	50.3	Community-Dwelling	Low
Tarazona-Santabalbina, 2016 [62]	RCT	Spain	≥70	NR	49	51	54	Community-Dwelling	Low
Torres-Sánchez, 2017 [63]	RCT	Spain	≥65	COPD/Lung disease	29	29	27.6	Hospital-Based	Low
Ushijima, 2021 [68]	Quasi-Experimental	Japan	≥65	Cardiovascular disease	66 (non-frail group)	23 (frail group)	23.6	Hospital-Based	Low
Vestergaard, 2008 [64]	RCT	Denmark	≥75	NR	28	25	100	Community-Dwelling	Moderate

NR= Not reported

Table 4. 2 Study Intervention Characteristics

Author (year) Study country	Study objective	Frailty Framework	Frailty Domains Targeted	Characteristics of interventions	-Frequency -Duration -PIFU	Frailty Reversed?	Outcome of intervention
SINGLE-COMPONENT INTERVENTIONS							
Arrieta, 2019 [47] **Spain**	To determine the general effect of the intervention on frailty outcome.	Fried	Physical	Physical activity Balance, strength, and walking exercises at progressive to moderate intensity.	**Freq=** 2x/wk **Dur=** 26wks **PIFU =** 6m	No	Lower prevalence of frailty
Brown, 2000 [48] **USA**	To determine the general effect of the intervention on physical frailty.	PPT ≤ 32	Physical	Physical activity Strength, Balance, Sensation, Coordination and range of motion	**Freq=** 3x/wk **Dur=** 12wks **PIFU =** NR	No	Decreased prevalence of frailty, increased physical performance test scores.
Cesari, 2015 [49] **USA**	To determine the effect of physical activity in reducing frailty prevalence.	Fried	Physical	Physical activity Walking, Aerobic, Strength, Flexibility, and balance are all done at progressive intensities.	**Freq=** Weekly 1-2x/wk 3x/wk **Dur=** 52wks **PIFU =** NR	No	Frailty prevalence reduced.
Coelho-Júnior, 2021 [51] **Brazil**	To determine the effects of the intervention on frailty status	Fried	Physical	Physical activity Resistance exercise at progressive to moderate intensity.	**Freq=** Daily **Dur=** 16wks **PIFU =** NR	Yes	
Kim, 2020 [72] **South Korea**	To determine the effectiveness of interventions on cognitive and depressive functions.	Fried	Physical, Cognitive	Physical activity Aerobic, Strength, Flexibility. Exercise intensity not reported.	**Freq=** Monthly **Dur=** 12wks **PIFU =** NR	No	Improved mental state and cognitive function.
Larsen, 2020 [69] **Canada**	To determine the effects of the	Frailty index	Physical	Physical activity	NR	Yes	

	intervention on frailty status			Activity characteristics not reported			
Liao, 2019 [55] **China**	To determine the effectiveness of interventions on frailty status.	Fried	Physical	Physical activity Resistance, aerobic, balance, exergaming at progressive intensities.	**Freq=** 3x/wk **Dur=** 12wks **PIFU =** NR	Yes	
Losa-Reyna, 2019 [66] **Spain**	To determine the effect of the intervention on physical and frailty outcomes.	Fried	Physical	Physical activity Resistance, Strength, Aerobic performed at high intensity.	**Freq=** 2x/wk **Dur=** 6wks **PIFU =** NR	Yes	
Nagai, 2018 [56] **Japan**	To determine the effect of the intervention on the physical and mental outcomes of frail individuals	Fried	Physical	Physical activity Resistance at progressive intensity	**Freq=** 2x/wk **Dur=** 24wks **PIFU =** NR	No	Increased physical strength, decreased frailty score, no significance in frailty status.
Sadjapong, 2020 [59] **Thailand**	To determine the effect of intervention in reversing frailty and functional outcome	Fried	Physical	Physical activity Aerobic, balance, resistance at progressive moderate to high intensity.	**Freq=** 3x/wk **Dur=** 24wks **PIFU =** NR	Yes	
Sahin, 2018 [60] **Turkey**	To determine the effectiveness of the intervention on functional outcome	Fried	Physical	Physical activity Balance exercise at low and high intensities.	**Freq=** 3x/wk **Dur=** 8wks **PIFU =** NR	No	Increased SPPB score (better in HI group), Increased Barthel index score, decreased fatigue severity, increased muscle strength.
Takatori, 2021 [70] **Japan**	To determine the effect of the	Kihon checklist	Social	Social activity	NR	Yes	

	intervention on frailty reversal.			Enhance social capital, such as interaction with neighbours, trust in the community, etc			
Torres-Sánchez, 2017 [63] **Spain**	To determine the effect of the intervention on disability	Frailty index	physical	Physical activity Pedal exercise	**Freq=** NR **Dur**= Based on length of stay at the institution **PIFU=** NR	No	Increased exercise capacity, increased muscle strength, increased balance
Vestergaard, 2008 [64] **Denmark**	To determine the effect of the intervention on functional outcome	NR	Physical	Physical activity Aerobic, Flexibility, Balance, Strength done at progressive intensities	**Freq=** 3x/wk **Dur=** 20wks **PIFU =** NR	No	Improved functional outcomes such as walking speed, biceps & handgrip strength, balance, and mobility.
MULTICOMPONENT INTERVENTIONS							
Abizanda, 2015 [20] **Spain**	To determine the effect of intervention in improving functionality	Fried	Physical	Physical activity + Nutrition **Exercise=** Flexibility, balance, strength. Intensity not reported. **Nutrition=** Supplements	**Freq=** 5x/wk **Dur=** 3yrs **PIFU =** NR	No	Increased nutritional and functional status
Cadore , 2014 [71] **Spain**	To determine the effect of the intervention on falls and functional outcome	Fried	Physical Cognitive	Physical activity + Cognitive **Exercise=** Walking, Balance, Resistance. Intensity not reported **Cognitive=** cognitive exercise	**Freq=** 2x/wk **Dur=** 24wks **PIFU =** 6m	No	No significance on any of the physical outcomes assessed.

Cameron, 2013 [50] **Australia**	To determine the effectiveness of intervention in reducing frailty and improving mobility	Fried	Physical Psychological Social	Physical activity + nutrition + social intervention **Exercise=** Balance exercise at moderate intensity **Nutrition=** Home delivered meals, supplements **Social =** increased access to social interactions	**Freq=** 3-5x/wk **Dur=** NR **PIFU =** NR	No	Decreased frailty score by 0.80, Increased SPPB
Chin A Paw, 2001 [27] **Netherlands**	To determine the effect of the intervention on functional outcome	Chin a Paw	Physical	Physical activity + Nutrition **Exercise=** Strength, Flexibility, and Endurance done progressively. **Nutrition=** supplements	**Freq=** 2x/wk **Dur=** 26wks **PIFU =** NR	No	Slight increase in ADL score, increased fitness and balance, no effect on disability score
de Souto Barreto, 2018 [25] **France**	To determine the association of intervention with frailty severity.	Frailty index	Physical Cognitive	Physical activity + Nutrition + Cognitive **Exercise=** Advice on varying exercises **Nutrition=** counseling **Cognitive=** Memory and reasoning training	**Freq=** Monthly **Dur=** 24wks **PIFU =** NR	No	Though no significant effect on frailty severity, it has a higher chance of reducing frailty development.
Fiatarone, 1994 [28] **USA**	To determine the effect of intervention in reducing frailty	NR	Physical	Physical activity + Nutrition	**Freq=** 3x/wk **Dur=** 10wks	No	Increased physical activity, increased

				Exercise= Resistance exercise done progressively at high intensity. **Nutrition=** supplements	**PIFU =** NR		muscle strength, increased gait velocity.
Hergott, 2020 [19] **USA**	To determine the effect of intervention in reversing frailty	CFS	Physical	Physical activity + occupational therapy + speech therapy **Physical activity =** Types of activities not identified. Exercises done at progressive intensities. **occupational therapy =** No further details presented **Speech therapy =** No further details presented	**Freq=** 12hrs/week **Dur=** 17 wks **PIFU =** NR	Yes	
Imaoka, 2016 [52] **Japan**	To determine the effect of the intervention on falls	NR	Physical	Physical activity + Nutrition **Exercise=** Resistance, Balance, Strength at low frequencies. Intensities not reported. **Nutrition=** supplements	**Freq=** 2x & 3x weekly **Dur=** 24wks **PIFU =** 6m	No	Rate of falls decreased by 72.4%
Kim , 2015 [23] **Japan**	To determine the effect of the	Fried	Physical	Physical activity + Nutrition	**Freq=** 2x/wk **Dur=** 8wks	Yes	

	intervention on frailty status			**Exercise=** Resistance, Balance, Strength, and Gait training at progressive intensities **Nutrition=** Supplements	(4+ 4 wks) **PIFU =** 1m		
Lammes, 2012 [53] **Sweden**	To determine the effect of the intervention on body composition.	Chin a Paw	Physical	Physical activity + Nutrition **Exercise=** Aerobic, Strength, Balance progressively at low-intensity. **Nutrition=** Counseling	**Freq=** 2x/ wk **Dur=** 52wks **PIFU =** 6m	No	No effect on body composition, no effect on energy intake, Increased RMR.
Li ,2010 [54] **China**	To determine the effect of the intervention on frailty status	Fried	Physical Social Psychological Cognitive	Activities designed per participant's need.	Specific to participant's needs	No	No significant outcome on frailty status and Barthel index.
Liu, 2017 [65] **China**	To determine the general effect of the intervention	Fried	Physical Psychological	Physical activity + Behavioral intervention **Exercise=** Aerobic, Balance, Resistance at progressive intensities **Behavioral=** Motivational enhancement	**Freq=** weekly **Dur=** NR **PIFU =** NR	No	Increased physical endurance, increased rate of participation in activities.
Ng, 2015 [22] **Singapore**	To determine the effect of intervention in reversing frailty	Fried	Physical Cognitive	Physical activity + Nutrition+ cognitive **Exercise=** Resistance, Balance at increasing progressive intensities	**Freq=** 2x/wk **Dur=** 12wks **PIFU =** 6m	Yes	

				Nutrition= supplements **Cognitive=** Stimulate short-term memory, enhance attention, information processing, reasoning, and problem-solving skills			
Ng, 2017 [57] **Singapore**	To determine the effect of the intervention on depressive symptoms	Fried	Physical Cognitive	Physical activity + Nutrition+ cognitive **Exercise=** Resistance, Balance at increasing progressive intensities **Nutrition=** supplements **Cognitive=** Stimulate short-term memory, enhance attention, information processing, reasoning, and problem-solving skills	**Freq=** 2x/wk **Dur=** 12wks **PIFU =** 6m	No	No significance on GDS
Oh, 2021 [67] **South Korea**	To determine the general effect of the intervention	Fried + Frailty index	Physical Social Cognitive Psychological	Physical activity + Nutrition + Social + Pharmaceutical+ Psychological **Exercise=** Resistance, Balance, Aerobic at progressive intensities **Nutrition=** supplements	**Freq=** 2x/wk **Dur=** 12 wks **PIFU =** 18m & 30m	No	Lower frailty phenotype & frailty index scores. No statistically significant difference in CES-D score. No statistically significant prevalence of polypharmacy.

				Social= Increase access to social interactions **Psychological=** psychotherapy **Pharmaceutical =** deprescription and depression management			Lower rates of mortality. Lower rates of long-term care institutionalization.
Rydwik, 2010 [58] **Sweden**	To determine the effect of the intervention on functional outcome	Chin a Paw	Physical	Physical activity + Nutrition **Exercise=** Aerobic, Strength, Balance progressively at moderate intensity. **Nutrition=** Counseling + supplements	**Freq=** 2x/wk **Dur=** 52wks **PIFU =** 2yrs	No	No significant changes in physical activity. No effects on ADLs
Seino, 2017 [61] **Japan**	To determine the effect of the intervention on frailty status	Check-List 15	Physical, Psychological, Social	Physical + Nutrition + Social intervention **Exercise=**Resistance exercise at progressive intensity. **Nutrition=** counseling **Social=** Improve social skills, increase social support, and increase access to social interactions & community gatherings. Structured counselling, relapse prevention.	**Freq=** 1x q 2 wks **Dur=** 12wks **PIFU =** NR	No	Decreased prevalence of frailty, increased social participation

Tarazona-Santabalbina, 2016 [62] **Spain**	To determine the effect of intervention in reversing frailty and improving functional outcome	Fried	Physical	Physical activity + Nutrition. **Exercise=** Proprioception, Aerobic, Strength, Stretching **Nutrition=** Counseling	**Freq=** 5x/wk **Dur=** 24wks **PIFU =** NR	Yes	
Ushijima, 2021 [68] **Japan**	To determine the effect of the intervention on functional outcome	Fried	Physical	Physical activity + Nutrition + Pharmaceutical **Exercise=** Resistance, aerobic at individually tailored intensities **Nutrition=** counseling **Pharmaceutical =** Medication guidance, CPR resuscitation practice	**Freq=** 3-5x/wk **Dur=** 12 wks **PIFU =** 30m	Yes	

Notes: PIFU (Post-intervention follow-up); **Freq** (Frequency); **Dur** (Duration); **NR** (Not reported); **RMR** (Resting metabolic rate); **ADLs** (Activities of daily living); **iADL** (Instrumental Activities of Daily Living); **CES-D** (Center for Epidemiologic Studies Depression Scale); **RCTs** (Randomized control trials); **COPD** (Chronic obstructive pulmonary disease); **BMI** (Body Mass Index); **RT** (Resistance training); **CPR** (Cardiopulmonary resuscitation); **CFS** (Clinical Frailty Scale); **wks** (weeks); **yrs** (years); **m** (months); **≤** (Less than or equal to); **PPT** (Physical Performance Test; **q** (every)

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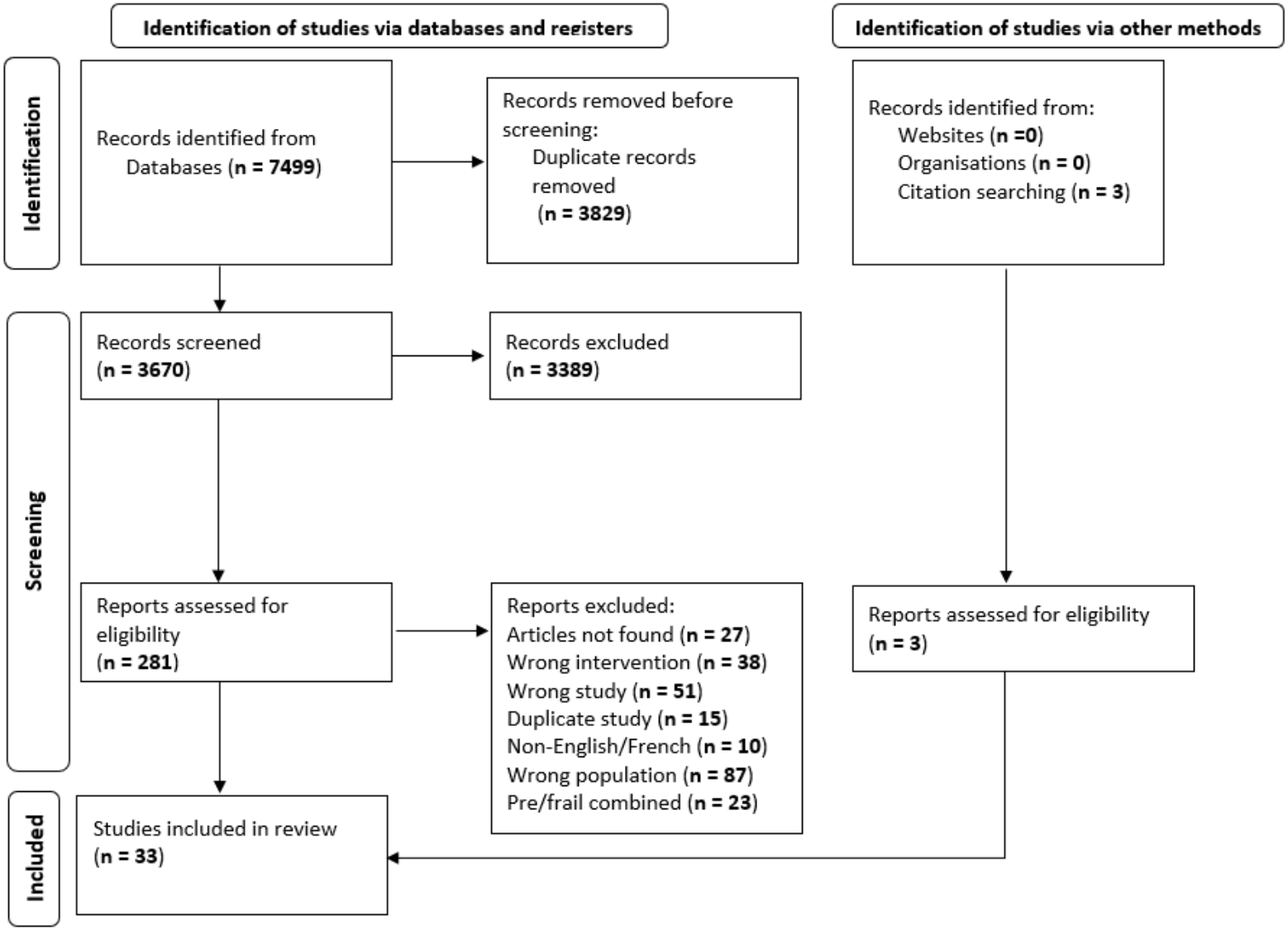

Figure 4. 1 Screening results of included studies

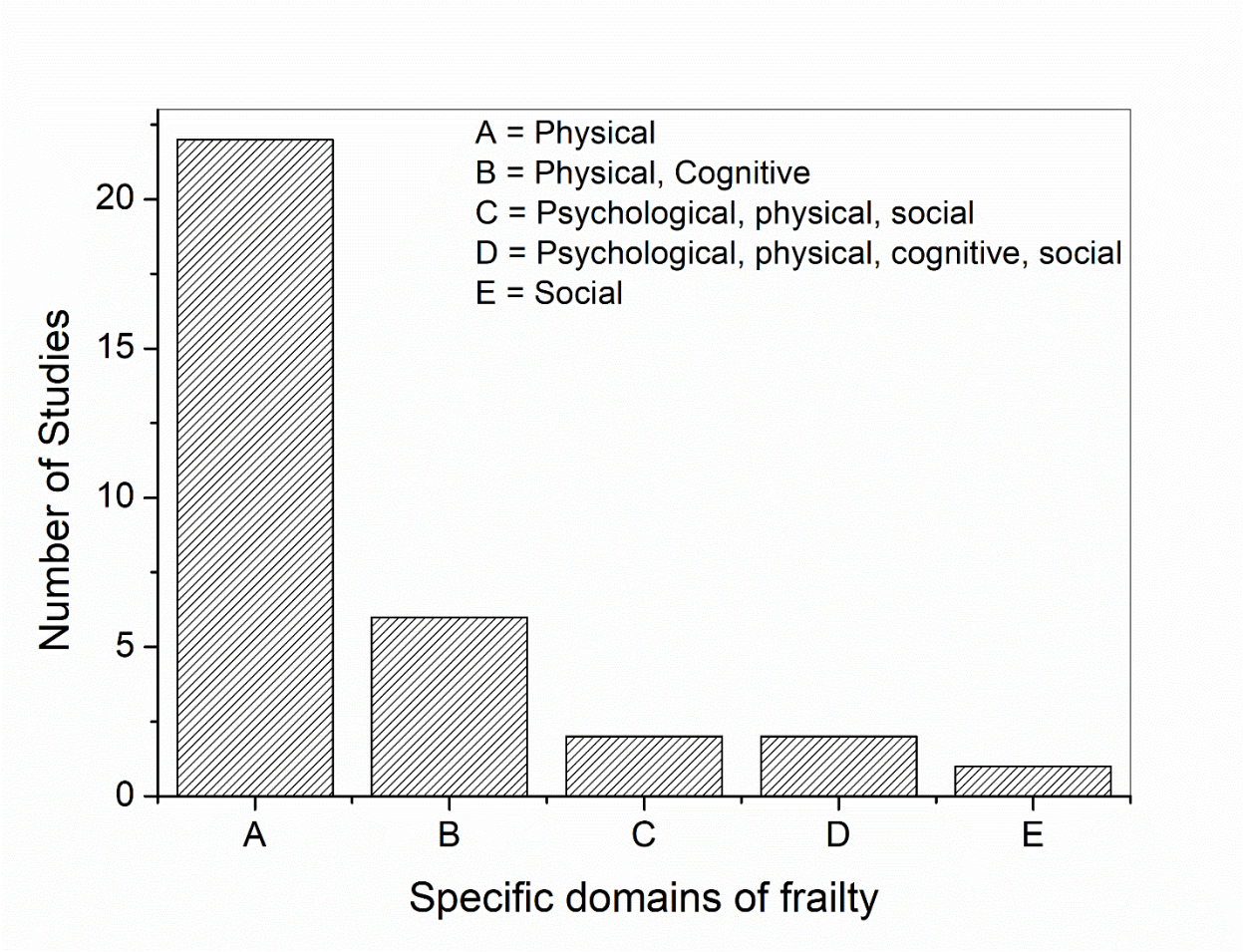

Figure 4. 2 Breakdown of The Domains Identified in Studies

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Chapter Five: Integrated Discussion

This chapter summarizes the main findings of our review of the literature and the research questions that guided our study. Additionally, we compare our findings with existing literature and discuss the implications for nursing practice, education, leadership, research, and policy.

5.1 Thesis Results Summary

In Chapter 1, I presented an overview of frailty and its adverse outcomes. Through a review of the literature (Chapter 2), I identified inconsistencies in the characteristics of interventions recommended to reverse frailty and explained the need to address these. To fill this research gap, we conducted a scoping review of interventions that can reverse frailty to enhance our understanding of this concept and the elements needed to achieve it (Chapters 3 and 4). Two research questions guided this study, and the following are highlights and key findings:

5.1.1 What is the available literature on interventions that achieve frailty reversal as an outcome?

We began this thesis by outlining the paucity of literature on interventions that achieve frailty reversal. We identified and evaluated relevant studies based on the methodological approach proposed by Arksey and O'Malley (Arksey & O'Malley, 2005) and reinforced by Joanna Briggs (Joanna Briggs Institute, 2020) and Levac (Levac et al., 2010). We searched four databases for articles written in French or English without regard to publication date. Among the 33 eligible articles, 17 mentioned it was possible to reverse frailty, and 11 studies had frailty reversal as an outcome (Chapter 4). Due to the differences in the frailty assessment methods used

by the authors, frailty did not appear to be identified consistently in participants across studies. These studies also included a range of single-component or multi-component interventions, such as physical activity, the most common, and social interventions, the least common. Physical activity and nutrition were the most combined to create multi-component interventions. Having established that it is possible to reverse frailty from the results of the first research question, we then sought to answer the second research question on what reverse frailty means.

5.1.2 What does it mean to reverse frailty?

Studies (n=11) reporting frailty reversal as an outcome explained what this meant. The different definitions were; frail to pre-frail (Sadjapong et al., 2020); frail to non-frail (Tarazona-Santabalbina et al., 2016); frail to pre- and non-frail (Coelho-Júnior & Uchida, 2021). It should be noted that different assessment methods were used to determine these frail states. Another study considered a reverse in frailty severity, such as a change from a severe to a mild state (Hergott & Lovins, 2020). Common amongst these definitions is that a reversal requires an individual to be frail at the outset. Ways to assess frailty included the frailty phenotype, the frailty index and a study-specific checklist of various questions were the methods of determining frailty among participants. These findings highlight that, at present, there is no agreed-upon definition of reverse frailty. Conceptual clarity is needed, which could be achieved with a concept analysis.

5.2 Comparison of Dissertation Findings with Existing Research

5.2.1 Dominance of the frailty phenotypes

There is ongoing debate surrounding the definition of frailty in clinical settings (Hoogendijk et al., 2019; Lally & Crome, 2007; H. Lee et al., 2020). A central area of contention in literature is whether frailty should be based purely on biomedical factors or psychological,

environmental, social, and other factors (Arnadottir et al., 2020; Van Damme et al., 2021; Van Oostrom et al., 2017). These variations affect the ability to diagnose, measure progress or severity, measure the scope of the problem at a population level, conduct clinical interventions, and formulate healthcare policy. Most of our included studies (n=20, 60.6%) used Fried and colleagues' frailty definition, which aligns with other studies that have reported increased use of this definition (Bieniek et al., 2016; Hiltunen et al., 2021; H. Lee et al., 2020). We propose the following explanation for the phenotype's dominant use. First, the frailty phenotype analyzes many characteristics with adjustments for outliers like socioeconomic status, clinical and subclinical diseases, depressive symptoms, and disability at baseline (Fried et al., 2001). These determinants have been reported as risk factors perpetuating frailty (Yang & Chen, 2018). Therefore, addressing them might play a role in sustaining or reversing frailty in older adults.

We identified a few studies that looked at the correlation of frailty with memory, mood and depression using this phenotype (Cesari et al., 2015; Coelho-Júnior & Uchida, 2021; Kim et al., 2020; Tarazona-Santabalbina et al., 2016). Additionally, this phenotype is presumed highly predictive of frailty despite being limited to only physical variables (Fried et al., 2001; Zhang et al., 2020). Some studies relied on this predictive ability to predict hospitalization rates, falls, and health-related quality of life (HRQoL) (Abizanda et al., 2015; Arrieta et al., 2019; Kim et al., 2020; Tarazona-Santabalbina et al., 2016). Furthermore, the phenotype is a biological phenomenon explicitly different from comorbidity and disability, though often treated as synonymous (Espinoza et al., 2019; Kamaruzzaman S.B., 2018). As a result, clinicians can objectively confirm biometric issues and treat them by clinical means. Another component of this phenotype is that its criteria are straightforward, easy and inexpensive to apply (Fried et al., 2001; Laukli et al., 2021). The standardized clinical features, few assumptions, easy

applicability, and the fact that it only relies on reports of medical screening for participants could explain why this phenotype is prevalent in literature.

5.2.2 A lack of holistic care

In light of our FI conceptual model, we recognized that interventions for frailty should target more domains than the physical ones. Nevertheless, it was not surprising that over 80% of our included studies focused only on the physical domain of frailty, which is consistent with the dominance of the frailty phenotype. Another rationale for this finding may be because research on frailty is primarily on older populations (Clegg et al., 2013). This group presents unique challenges in physical functioning and cognitive/psychological impairment (Taylor et al., 2019). Research activities and evaluations often require participants to be agreeable, conscious, and willing to participate. While biomedical reports provide biomedical information and physical evaluations, cognitive impairments may make it difficult for individuals to provide informed consent and engage with study activities as required (Li et al., 2020).

While our included studies did not report any concerns with participant participation during the frailty screening stage, Pritchard et al. (2017) suggested that participants with psychological or cognitive impairments sometimes have difficulties completing frailty assessments. Hence, researchers might incorporate more physical factors into the inclusion criteria.

5.2.3 Limited use of social interventions

Social frailty or interventions that address it remains largely unexplored in the literature (Bunt et al., 2017; Figueroa et al., 2020). Seven of our 33 eligible studies (21.1%) studied interventions that addressed the social frailty of participants, indicating it is not an often-addressed dimension of frailty. Despite increased studies on social frailty (Bunt et al., 2017;

Figueroa et al., 2020; D. R. Lee et al., 2018; Nagai et al., 2020; Ye et al., 2021), Pek and colleagues note that this domain remains considerably underexplored compared to other domains, primarily the physical domain (Pek et al., 2020). We advocate for more interventions that address social frailty, considering the lived experiences of frail older adults to ensure they feel included in their care planning. The failure to address the social domain of frailty may increase an individual's vulnerability, resulting in a decline in cognitive and psychological function (Huang et al., 2021; Makizako et al., 2018). These adverse outcomes highlight the need to address social frailty. Addressing social frailty aims to enhance the functionality of frail older adults and promote healthy ageing. Ways to do this include improving social skills, increasing participation in social activities, and increasing trust in the community.

When we began this review, we expected to find more studies examining multiple aspects of frailty besides the physical component. Contrary to this expectation, physical frailty dominated while social domains were underrepresented in studies that showed frailty reversal as an outcome. The social domain may be equally important to the physical domain, as inadequate attention to this domain has been documented to lead to declines in cognitive and physiological performance. Thus, addressing the social domain is comparable to addressing the cognitive and physiological domains. Moreover, our review of the literature (chapter 2) identified the importance of addressing the psychological and cognitive domains in addition to the social and physical for maximum results.

Undoubtedly, frailty is multifaceted and standard interventions may be challenging to design and implement across the general adult population over 65. However, the fact remains that frailty interventions should be diverse regarding the targeted factors. It is encouraging that

the social domain is gaining traction in research, and we recommend that other domains (chapter 2) be given equal relevance to achieve a holistic outcome. The projected increase in the number of older adults makes frailty a much more significant concern, which needs strategies for it to be maintained or reversed. Though the concept of reversing frailty is not fully understood, adopting future studies to gain clarity, and implementing interventions to achieve this outcome is worthwhile.

5.3 Future Directions

The findings of this dissertation have implications for nursing practice, nursing education, nursing administration, research, and policy, as outlined below.

5.3.1 Nursing Practice

According to the professional standards established by the College of Nurses of Ontario (CNO), nurses are required to maintain a high level of critical thinking and knowledge at all times, and to continually improve the application of professional knowledge. (College of Nurses of Ontario, 2015) (REF). Nurses spend more time with patients than other interdisciplinary team members (Butler et al., 2018; Westbrook et al., 2011). Consequently, nurses familiar with frailty intervention studies like ours are better prepared to assess frail patients' risk factors and vulnerabilities, adjust their care accordingly, and determine interventions that benefit their patients based on their ongoing and past medical history. Nurses may also have loved ones who are ageing and frail; nurses informed of this study's findings can identify interventions that may benefit them and their loved ones and integrate them as applicable in discussion with their loved one's healthcare team.

5.3.2 Nursing Education

We highlighted some concerns expressed by older adults about not being included in discussions about frailty and interventions available to treat it (Durepos et al., 2021). The CNO guidelines promote patient-centred care as an essential component of nursing (College of Nurses of Ontario, 2021). Nurses must consider patients' individual needs and preferences and ensure patients are active participants in all aspects of their health care decisions. In this regard, it remains essential to reiterate patient-centred care in secondary and post-secondary nursing curriculums. In addition, in-*service* education can incorporate frailty intervention studies that help promote a healthy attitude toward ageing and frailty among nursing professionals. These approaches can curb the notion of discrimination that some older adults perceive because of their age and invoke change in the nursing practice. According to Avgerinou et al. (2021), the main barriers to identifying and managing frailty are related to the health care system. The most significant is a gap in geriatric training and education of specialists. The Canadian Nurses Association (CNA) refers to a nursing specialist as a registered nurse with a post-secondary nursing degree (Canadian Nurses Association, 2022). Thus, encouraging more nurses to have post-secondary education is critical to advancing nursing practice and improving patient care. In Canada, nurses wishing to specialize in geriatrics can obtain a certification in gerontology by obtaining extensive knowledge and skills in geriatrics and passing the CNA certification exam. This certification is nationally recognized as a nursing specialty credential (Canadian Nurses Association, 2022). Nurses may also pursue a master's or doctoral degree in nursing to become clinical nurse specialists in their respective specialty fields.

5.3.3 Nursing Administration

Nursing administrators aware of current frailty interventions studies can understand how to allocate resources, such as more time for nurses to implement and monitor the progression of interventions for frail older adults to begin with. Due to nursing shortages, nurses might have less room for additional time (Drennan & Ross, 2019). The importance of this component, however, does not diminish. They can also provide nurses with tools such as online training to identify and address potential frailty-related issues. For example, online frailty training modules from the Canadian Frailty Network can be readily available to nurses.

Furthermore, nursing administrators can help design policies and procedures related to frail patients by providing evidence-based information on how to best care for this population. To facilitate easy accessibility and to assess the effectiveness of interventions implemented to reverse frailty, frailty screening tools such as the clinical frailty scale (CFS) may be incorporated into nursing care plans. Developed from the Canadian Study of Health and Aging, the CFS is a validated clinical tool that assesses patients' level of dependence on care, and physical and cognitive abilities, among others (Moreno-Ariño et al., 2020). These components can also be obtained from patients' electronic medical records (EMR).

5.3.4 Research

It is encouraged that researchers examine different studies done on frailty interventions for older adults to identify research gaps and validate the effectiveness of some of the reported interventions. For example, in this study, we have demonstrated that the outcome of interventions might vary with individuals due to compounding factors such as underlying comorbidities. Therefore, there is a need to study the implementation and effectiveness of the interventions what achieved frailty reversal as an outcome.

We identified a limited body of literature on interventions addressing the social, cognitive, and psychological domains of frailty, along with some adverse consequences associated with neglecting these aspects. As researchers continue contributing to the frail literature, we encourage them to target multiple domains of frailty in the future as they develop strategies to improve the well-being of frail older adults.

Furthermore, reverse frailty is a relatively new concept that has not been fully explored. Although we discuss reverse frailty extensively, the scope of this review limits our ability to provide a true definition. For this reason, we propose a concept analysis.

Frailty intervention studies provide valuable insights into the mechanisms contributing to frailty, its consequences on health, and how to develop better strategies for promoting healthy ageing. It is therefore essential to conduct more qualitative studies that consider the lived experiences of frail older adults to guide strategies that promote healthy ageing.

5.3.5 Policy

The Canadian Frailty Network is mandated to advance frailty evidence-based studies to policy (Canadian Frailty Network, 2019). Before integrating the evidence generated from this scoping review into policy, there are a few considerations. First, frailty intervention studies should be designed with the target population. For example, interventions aimed at frail older adults living independently may differ from those aimed at frail older adults in long-term care settings. Second, once potential interventions are identified, there should be consideration of adapting these interventions to the specific challenges of a target population. In addition to explaining the rationale for tailoring frailty interventions for older adults (chapter 4), it has been reported that this approach has more potential to improve clinical results (Golas et al., 2021). This review provides evidence that it is challenging to consider a particular intervention ideal for everyone.

Many older adults often have comorbidities (Fan et al., 2021; Salive, 2013) and suffer from polypharmacy (Dagli & Sharma, 2014), which might impact the outcome of the interventions. Third, frailty interventions should be evaluated for their cost-effectiveness. Understanding whether the interventions are worth the cost for the individual and the healthcare system remains essential. Considering these points ensure that progressive policies protect and ensure the well-being of frail patients at different stages of their condition.

Conclusion

Per our scoping review and FI conceptual framework, frailty is more than a physical condition. Our findings suggest that reversing frailty is possible, yet this is not clearly defined. Another concern is the lack of consideration of frailty domains beyond the physical. Frailty's detrimental effects on health, society, and individuals reinforce the need for a holistic approach across all domains. Our study contributes to the frailty body of literature by presenting and explaining the necessity of tailoring frailty interventions for frail older adults. We also demonstrate how multi-domain frailty care approaches can enhance outcomes. Furthermore, we provide evidence suggesting that reverse frailty is possible and outline a rationale for further exploration of this idea.

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Appendices

Appendix A- List of Variables Used to Construct The 70-Item FI

- Changes in everyday activities
- Head and neck problems
- Poor muscle tone in neck
- Bradykinesia, facial
- Problems getting dressed
- Problems with bathing
- Problems carrying out personal grooming
- Urinary incontinence
- Toileting problems
- Bulk difficulties
- Rectal problems
- Gastrointestinal problems
- Problems cooking
- Sucking problems
- Problems going out alone
- Impaired mobility
- Musculoskeletal problems
- Bradykinesia of the limbs
- Poor muscle tone in limbs
- Poor limb coordination
- Poor coordination, trunk
- Poor standing posture
- Irregular gait pattern
- Falls
- Mood problems
- Feeling sad, blue, depressed
- History of depressed mood
- Tiredness all the time
- Depression (clinical impression)
- Sleep changes
- Restlessness
- Memory changes
- Short-term memory impairment
- Long-term memory impairment
- Changes in general mental functioning
- Onset of cognitive symptoms
- Clouding or delirium
- Paranoid features
- History relevant to cognitive impairment or loss
- Family history relevant to cognitive impairment or loss
- Impaired vibration
- Tremor at rest
- Postural tremor
- Intention tremor
- History of Parkinson's disease
- Family history of degenerative disease
- Seizures, partial complex
- Seizures, generalized
- Syncope or blackouts
- Headache
- Cerebrovascular problems
- History of stroke
- History of diabetes mellitus
- Arterial hypertension
- Peripheral pulses
- Cardiac problems
- Myocardial infarction
- Arrhythmia
- Congestive heart failure
- Lung problems
- Respiratory problems
- History of thyroid disease
- Thyroid problems
- Skin problems
- Malignant disease
- Breast problems
- Abdominal problems
- Presence of snout reflex
- Presence of the palmomental reflex
- Other medical history

Adapted from "A global clinical measure of fitness and frailty in elderly people" by K. Rockwood, X. Song, C. MacKnight, H. Bergman, D.B. Hogan, I. McDowell, and A. Mitnitski, 2005, *Canadian Medical Association Journal, 173*, p. 489–495. Copyright © 2005 CMA Media Inc

Appendix B-Breakdown on The Search Criteria and Strategy for Literature Review

Boolen Operators

Search Terms Used
frailty in the senior citizens OR frail older adult OR vulnerable senior citizens OR functionally impaired senior citizens OR impaired senior citizens.
AND nursing role, OR nurse management OR nurse responsibility
AND reverse frailty, OR increase functionality of senior citizens OR mange frailty
AND frailty interventions OR frailty reversal, OR reverse frailty

MeSH terms used

Concept 1	**Concept 2**	**Concept 3**
Frailty/ or frail elderly/ frail* vulnerab*	Aged/ aged, 80 and over/ geriatrics/ elderly* aged*	revers* chang* Improv*

Electronic Search Strategy from CINAHL for literature review

Number	**Query**	**Limiters/Expanders**	**Last Run Via**	**Results**
S16	S11 AND S15	Expanders-Apply related words; Apply equivalent subjects Search modes-	Interface- EBSCOhost Research Databases	122

		Boolean/Phrase	Search Screen-Advanced Search Database-CINAHL	
S15	reverse	Expanders-Apply related words; Apply equivalent subjects Search modes-Boolean/Phrase	Interface-EBSCOhost Research Databases Search Screen-Advanced Search Database-CINAHL	37,556
S14	S11 AND S13	Expanders-Apply related words; Apply equivalent subjects Search modes-Boolean/Phrase	Interface-EBSCOhost Research Databases Search Screen-Advanced Search Database-CINAHL	3,850
S13	Reverse or change or improve	Expanders-Apply related words; Apply equivalent subjects Search modes-Boolean/Phrase	Interface-EBSCOhost Research Databases Search Screen-Advanced Search Database-CINAHL	1,231,800

S12	S1 AND S2 AND S6 AND S11	Expanders-Apply related words; Apply equivalent subjects Search modes-Boolean/Phrase	Interface-EBSCOhost Research Databases Search Screen-Advanced Search Database-CINAHL	3
S11	Frailty or frail elderly or vulnerable elderly	Expanders-Apply related words; Apply equivalent subjects Search modes-Boolean/Phrase	Interface-EBSCOhost Research Databases Search Screen-Advanced Search Database-CINAHL	15,305
S10	S5 AND S9	Expanders-Apply related words; Apply equivalent subjects Search modes-Boolean/Phrase	Interface-EBSCOhost Research Databases Search Screen-Advanced Search Database-CINAHL	11
S9	Scoping review	Expanders-Apply related words; Apply equivalent subjects Search modes-Boolean/Phrase	Interface-EBSCOhost Research Databases Search Screen-Advanced Search	5,616

			Database-CINAHL	
S8	S5 AND S6	Expanders-Apply related words; Apply equivalent subjects Search modes-Boolean/Phrase	Interface-EBSCOhost Research Databases Search Screen-Advanced Search Database-CINAHL	152
S7	S5 AND S6	Expanders-Apply related words; Apply equivalent subjects Search modes-Boolean/Phrase	Interface-EBSCOhost Research Databases Search Screen-Advanced Search Database-CINAHL	166
S6	Nurse*intervention or nurse*care or nurse*role	Expanders-Apply related words; Apply equivalent subjects Search modes-Boolean/Phrase	Interface-EBSCOhost Research Databases Search Screen-Advanced Search Database-CINAHL	103,937
S5	S3 AND S4	Expanders-Apply related words; Apply equivalent subjects Search modes-	Interface-EBSCOhost Research Databases	11,801

		Boolean/Phrase	Search Screen-Advanced Search Database-CINAHL	
S4	Elderly or aged or older or elder or geriatric or elderly people or old people or senior or frailty	Expanders-Apply related words; Apply equivalent subjects Search modes-Boolean/Phrase	Interface-EBSCOhost Research Databases Search Screen-Advanced Search Database-CINAHL	1,110,339
S3	S1 AND S2	Expanders-Apply related words; Apply equivalent subjects Search modes-Boolean/Phrase	Interface-EBSCOhost Research Databases Search Screen-Advanced Search Database-CINAHL	43,718
S2	Nutrition or diet or food or nourishment or food intake or eating	Expanders-Apply related words; Apply equivalent subjects Search modes-Boolean/Phrase	Interface-EBSCOhost Research Databases Search Screen-Advanced Search Database-CINAHL	387,437

S1	Physical activit* or exercise* or physical exercise*	Expanders-Apply related words; Apply equivalent subjects Search modes-Boolean/Phrase	Interface-EBSCOhost Research Databases Search Screen-Advanced Search Database-CINAHL	247,971

Appendix C-Psychometric Properties of The Frailty Phenotype, The Frailty Index, and The Frailty Trait Scale

			Reliability			Validity			
Frailty Assessment instruments	Frailty Measures	Scale type	Internal consistency	Equivalence	Stability	Construct validity	Content validity	Criterion Validity	Mortality prediction
The frailty phenotype (FP)	Evaluates 5 main dimensions: -weakness, -loss of endurance, -slowness, -low physical activity, -loss of weight	Ordinal Scale (0-5) Not frail=0 Pre-frail= 1-2 Frail= ≥ 3	0	0	0	✓	0	✓	Yes

The frailty index (FI)	A measure of an 'accumulation of deficits' Including but not limited to: -social stressors, -cognitive dysfunction, -physical decline, -nutrition, -depression, -comorbidities.	Continuous Scale (0-1) non-frail= 0 - 0.10 vulnerable = 0.10-0.21 **frail = 0.22 0.44** frailest = ≥ 0.45	0	✓	✓	✓	✓	✓	Yes
Frailty Trait Scale (FTS)	Evaluates 7 domains: -energy balance and nutrition, -Activity, -Nervous system,	Continuous Scale (0–100) Robust = 0 100=max frail	0	0	0	✓	0	✓	yes

	-Vascular system, -Weakness, -Endurance, -Gait speed								

0, no data available: ✓, instrument fulfils the mentioned criterion (Faller et al., 2019; J. L. Sutton et al., 2016)

Reliability is the degree to which results can be reproduced by repeating the study under the same circumstances, internal consistency is a degree to which multiple items measuring the same general construct produce similar results, equivalence is when corresponding measurements are obtained on two or more forms of the test, and stability refers to the consistency of measurements across time on the same test (Salgado, 2015).

Construct validity evaluates whether a measurement tool represents what we are measuring, content validity determines whether a test represents all aspects of the construct, and criterion validity measures how closely the results of a test match those of another test (Hughes, 2017).

Appendix D-PRISMA-ScR Checklist of Study

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Reversing frailty in older adults: A scoping Review	Click here to enter text.
ABSTRACT			
Structured summary	2	Abstract presented in the manuscript section	ii
INTRODUCTION			
Rationale	3	In this study, the review process is explained in detail, with a conceptual framework for frailty identified, along with examples on the types of interventions implemented. These led to identifying the research questions, and the reason why a scoping review approach is credible (i.e., lack of a previous comprehensive review done in this area to map the evidence around interventions that achieve frailty reversal as an outcome)	Click here to enter text.
Objectives	4	The Questions being addressed are: What is the available literature on interventions that achieve frailty reversal as an outcome ? What does it mean to reverse frailty? They follow the PCC format of P-Population (older adults over 65yrs who are frail), C-Concept (reversing frailty), and C-Context (all contexts).	Click here to enter text.
METHODS			
Protocol and registration	5	Protocol developed, not registered	Not applicable
Eligibility criteria	6	Eligibility criteria clearly stated, along with its rationale	Click here to enter text.
Information sources*	7	Databases and grey literature sources used for the literature search identified but dates not included. These will be done for the actual study.	Click here to enter text.
Search	8	A full electronic search strategy for ovid-MEDLINE is provided, and it was developed and refined with the help of a liberian.	

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
Selection of sources of evidence†	9	The studies for the review were selected based on the inclusion criteria. Covidence software was used to facilitate the process	
Data charting process‡	10	We charted the data using google Forms and Microsoft Excel.	Click here to enter text.
Data items	11	Data items were sought based on the research question, need for quality appraisal, tracking missing data, and using the TIDIER checklist for reporting interventions.	
Critical appraisal of individual sources of evidence§	12	Appraisal done using the JBI checklist for critical appraisal	
Synthesis of results	13		
RESULTS			
Selection of sources of evidence	14	Section done and can be found on page number listed	
Characteristics of sources of evidence	15	Section done and can be found on page number listed	
Critical appraisal within sources of evidence	16	Section done and can be found on page number listed	
Results of individual sources of evidence	17	Section done and can be found on page number listed	
Synthesis of results	18		
DISCUSSION			
Summary of evidence	19	Section done and can be found on page number listed	
Limitations	20	Limitation of study due to limited number of databases used acknowledged.	
Conclusions	21	Section done and can be found on page number listed	
FUNDING			
Funding	22	Not Applicable	Not applicable

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyzes extension for Scoping Reviews (Tricco *et al.*, 2018)

Appendix E-Ovid MEDLINE Search Strategy for Manuscript

1 *frailty/

2 *frail elderly/

3 frail*.ti,ab,kf. /freq=3

4 aged/

5 "aged, 80 and over"/

6 geriatrics/

7 ((old* or aged or aging or ageing) adj2 (person* or people or adult* or population*)).ti,ab,kf.

8 (elder* or senior or seniors* or geriatric*).ti,ab,kf.

10 1 or 2 or 3

11 4 or 5 or 6 or 7 or 8

12 9 and 10 and 11

13 (frail* adj3 (revers* or improv* or chang* or interven* or modif* or reduc*)).ti,ab,kf.

14 10 and 11 and 13

Appendix F-Data Extraction Items of Manuscript

Extraction categories	Data items
Bibliography	Authors, journal title, year of publication, corresponding author contact.
Study characteristics	Aim of study, country of study, setting of the study, conceptual framework of frailty considered, domains of frailty considered.
Participant information	Age of participants, Specific health conditions, the total number enrolled in the study, the total number lost to follow-up, frail state of participants at the start of the study, sex of participants.
Intervention characteristics	Reversing/treating frailty mentioned, theory guiding intervention, types of Interventions, who performed an intervention, how was intervention provided, frequency of intervention, duration of follow-up post-intervention (months), outcome and outcome measures.
Quality Appraisal	JBI quality appraisal tool, study limitations.

Appendix G- Interpretation of Quality Assessment Scores

Interpretation of quality assessment scores

Study Design	Total score	Interpretation
Randomized Control Trial	13	10-13: Low risk of bias 6-9: Moderate risk of bias 0-5: High risk of bias
Quasi-Experimental study	9	8-9: Low risk of bias 4-7: Moderate risk of bias 0-3: High risk of bias
Cohort Study	11	9-11: Low risk of bias 5-8: Moderate risk of bias 0-4: High risk of bias
Case Series	10	8-10: Low risk of bias 5-7: Moderate risk of bias 0-4: High risk of bias
Case report	8	7-8: Low risk of bias 4-6: Moderate risk of bias 0-3: High risk of bias

Quality Assessment scores of individual studies

Author	Year	Research design	Score	Interpretation
Arrieta	2019	RCT	12	Low risk of bias
Brown	2000	RCT	8	Moderate risk of bias
Cameron	2013	RCT	7	Moderate risk of bias
Cesari	2015	RCT	8	Moderate risk of bias
Chin A Paw	2001	RCT	9	Moderate risk of bias
Coelho-Junior	2021	RCT	9	Moderate risk of bias
de Souto Barreto	2018	RCT	10	Low risk of bias
Fiatarone	1994	RCT	8	Moderate risk of bias
Imaoka	2016	RCT	8	Moderate risk of bias
Kim	2015	RCT	9	Moderate risk of bias
Lammes	2012	RCT	7	Moderate risk of bias
Li	2010	RCT	10	Low risk of bias
Liao	2019	RCT	12	Low risk of bias
Nagai	2018	RCT	9	Moderate risk of bias
Ng	2017	RCT	10	Low risk of bias
Ng	2015	RCT	10	Low risk of bias
Rydwik	2010	RCT	9	Moderate risk of bias
Sadjapong	2020	RCT	12	Low risk of bias
Sahin	2018	RCT	9	Moderate risk of bias
Seino	2017	RCT	10	Low risk of bias
Tarazona-Santabalbina	2016	RCT	12	Low risk of bias
Torres-Sánchez	2017	RCT	10	Low risk of bias
Vestergaard	2008	RCT	8	Moderate risk of bias
Cadore	2014	Case Series	9	Low risk of bias
Kim	2020	Case Series	8	Low risk of bias
Hergott	2020	Case Report	6	Moderate risk of bias
Larsen	2020	Cohort Studies	9	Low risk of bias
Takatori	2021	Cohort Studies	9	Low risk of bias
Abizanda	2015	Cohort Studies	7	Moderate risk of bias
Liu	2017	Quasi-Experimental Studies	8	Low risk of bias
Losa-Reyna	2019	Quasi-Experimental Studies	8	Low risk of bias
Oh	2021	Quasi-Experimental Studies	9	Low risk of bias
Ushijima	2021	Quasi-Experimental Studies	9	Low risk of bias

Appendix H-Articles Excluded with Reasons

Articles Excluded with Reasons (n=251)

Duplicate Study (n=15)

Title	Authors	Year	Journal	Volume	Issue	Pages
A systematic review of exercise programs for the frail elderly.	Paw MJM; van Uffelen JGZ; Riphagen II; van Mechelen W	2007	Long-Term Care Interface	8	6	14-19
Singapore frailty intervention trial: Effect of frailty reversal on reducing depressive symptoms	Nyunt, Ma Shwe Zin; Feng, Liang; Feng, Lei; Ng, Tze Pin; Niti, Mathew; Tan, Boon Yeow; Chan, Gribson; Chan, Sue Mei; Ann, Khoo Sue; Yap, Philip; Yap, Keng Bee	2014	Annals of the Academy of Medicine Singapore	43	10 SUPPL. 1	S29-S30
Study to assess the effects of a nutritional formula plus exercise intervention in the functional capacities of frail institutionalized elderly patients: ACTIVNES study	Abizanda, P.; Diez, M.; Perez, V.; Da Silva, A.; Estrella, J.; Araujo, K.; Barcons, N.; Tuset, A.	2014	European Geriatric Medicine	5	SUPPL. 1	S78
Findings in Clinical Trials and Studies Reported from	Francisco José Tarazona-	2016	Clinical Trials Week	15	5	426-33

University Hospital (A Multicomponent Exercise Intervention that Reverses Frailty and Improves Cognition, Emotion, and Social Networking in the Community-Dwelling Frail Elderly: A Randomized ...).(Clin	Santabalbina , Mari Carmen Gómez-Cabrera , Pilar Pérez-Ros , Francisco Miguel Martínez-Arnau , Helena Cabo , Konstantina Tsaparas , Andrea Salvador-Pascual , Leocadio Rodriguez-Mañas , José Viña					
Intervention for falls: Reduced exercise and vitamin D supplementation among the institutionalized frail elderly	Higuchi, Y.; Todo, E.; Hirasima, K.; Kitagawa, T.; Ueda, T.; Ando, S.; Yasuoka, M.; Mizuno, T.; Imaoka, M.; Nakamura, K.; Kurosaki, K.; Ikeuchi, M.; Shichikawa, D.; Masue, A.	2015	Physiotherapy (United Kingdom)	101	SUPPL. 1	eS641
Effects of Exercise and Milk Fat Globule Membrane (MFGM) Supplementation on Body Composition, Physical Function, and Hematological Parameters in Community-Dwelling Frail Japanese Women: A Randomized Double Blind,	Kim, H; Suzuki, T; Kim, M; Kojima, N; Ota, N; Shimotoyodome, A; Hase, T; Hosoi, E; Yoshida, H	2015	PLOS ONE	10	2	e0116256

Placebo-Controlled, Follow-Up Trial						
Physical exercise or micronutrient supplementation for the wellbeing of the frail elderly? A randomised controlled trial.	Chin A Paw MJM; de Jong N; Schouten EG; van Staveren WA; Kok FJ; Chin A Paw, M J M; de Jong, N; Schouten, E G; van Staveren, W A; Kok, F J	2002	British Journal of Sports Medicine	36	2	126-131
A PHYSICAL ACTIVITY INTERVENTION TO TREAT THE FRAILTY SYNDROME - RESULTS FROM THE LIFESTYLE INTERVENTIONS AND INDEPENDENCE FOR ELDERS-PILOT (LIFE-P) STUDY	Cesari, M; Vellas, B; Doss, H; Gill, TM; Newman, AB; King, AC; Church, T; Pahor, M	2013	GERONTOLOGIST	70	2	216-22
Systematic review of non-pharmacological interventions to treat well-defined sarcopenia and physical frailty	Lozano-Montoya, I.; Correa-Perez, A.; Abraha, I.; Cherubini, A.; Soiza, R.L.; O'Mahony, D.	2017	European Geriatric Medicine	8	Supplement 1	S112
Individualized home-based exercise and nutrition interventions improve frailty in older adults: a randomized controlled trial (vol 16, 119, 2019)	Hsieh, TJ; Su, SC; Chen, CW; Kang, YW; Hu, MH; Hsu, LL; Wu, SY; Chen, L; Chang, HY; Chuang, SY; Pan, WH; Hsu, CC	2019	INTERNATIONAL JOURNAL OF BEHAVIORAL NUTRITION AND PHYSICAL ACTIVITY	16	1	119

Effects of nutritional intervention and physical training on energy intake, resting metabolic rate and body composition in frail elderly. A randomised, controlled pilot study	Lammes, E.; Rydwik, E.; Akner, Gunnar	2012	Journal of Nutrition, Health and Aging	16	2	162-7
Is it possible to reverse frailty in patients with chronic obstructive pulmonary disease?	Wang, Z; Hu, XJ; Dai, QX	2020	CLINICS	75		e177
New Findings on Systolic Heart Failure from Columbia University Summarized (Can a Left Ventricular Assist Device in Individuals with Advanced Systolic Heart Failure Improve or Reverse Frailty?)	Mathew S. Maurer, , Evelyn Horn, Alex Reyentovich, Victoria Vaughan Dickson, Sean Pinney, Deena Goldwater, Nathan E. Goldstein, Omar Jimenez, Sergio Teruya, Jeff Goldsmith, Stephen Helmke, MPH, RCDS, Melana Yuzefpolskaya,, and Gordon R Reeves	2017	Medical Devices & Surgical Technology Week	65	11	2383–2390.
â€œI Donâ€™t Feel Like Myselfâ€• : Treating Frailty in the Elderly With Diet	Firnhaber, Gina C; Kolasa, Kathryn M	2016	Nutrition today (Annapolis)	51	6	281-289
Exercise as an intervention to reverse frailty: A randomized clinical trial	Gomez-Cabrera, Mari Carmen; Tarazona-Santabalbina, Francisco Jose;	2016	Free radical biology & medicine	96		S37-S37

	Cabo, Helena; Salvador-Pascual, Andrea; Escriva, Consuelo; Rodriguez-MaÃ±as, Leocadio; ViÃ±a, Jose					

Full Text not Available (n=27)

Title	Authors	Year	Journal	Volume	Issue	Pages
Sensible aging: using nutrient-dense foods and physical exercise with the frail elderly.	De Jong N	2001	Nutrition Today	36	4	202-207
Exercise Prescription Intervention Plan for Pre-frail and Frail Elderly in New Taipei City	Lin, HP; Tseng, YT; Lin, CH	2018	MEDICINE AND SCIENCE IN SPORTS AND EXERCISE	50	5	241-241
Acceptability of a community-based exercise and nutritional intervention in frail older adults	Jeyaseelan, Arveen; O'Donoghue, Patrick; Bambrick, Padraig; Mulcahy, Riona; Pope, George; O'Regan, Niamh; Cooke, John; Byrne, Thomas; Harrison, Michael	2020	European Geriatric Medicine	11	SUPPL 1	S220

Exercise as an intervention to reverse frailty: A randomized clinical trial	Gomez-Cabrera, Mari Carmen; Tarazona-Santabalbina, Francisco Jose; Cabo, Helena; Salvador-Pascual, Andrea; Escriva, Consuelo; Rodriguez-MaÃ±as, Leocadio; ViÃ±a, Jose	2016	Free radical biology & medicine	96		S37
Personalized multicomponent physical exercise program for the prevention and reversal of frailty in the elderly	Millan, F; Carretero, A; Garcia-Dominguez, E; Garcia-Correas, A; Garcia-Dominguez, C; De la Rosa, A; Arc-Chagnaud, C; Olaso-Gonzalez, G; Gomez-Cabrer, M; Vina, J	2021	FREE RADICAL BIOLOGY AND MEDICINE	165		
Transitional states in frailty: Implications for end of life support in heart failure	Lee, Jenny S. W.	2019	Heart Asia	11	Supplement 1	A5
Impact of nutritional supplementation and nordic walking in frail older patients in geriatrics department of tertiary care hospital in India	Kandel, R.; Chatterjee, P.; Kumar, V.; Gopalan, V.; Ambashtha, A.; Jathar, S.; Dey, A.B.	2014	European Geriatric Medicine	5	SUPPL. 1	S127-S128

Reversibility of frailty in LVAD and heart transplant patients	Macdonald, Peter S.	2019	Heart Asia	11	Supplement 1	A4-A5
Correction to: Individualized home-based exercise and nutrition interventions improve frailty in older adults: a randomized controlled trial...Hsieh TJ, et al. Individualized home-based exercise and nutrition interventions improve frailty in older adults:	Hsieh, Tsung-Jen; Su, Shin-Chang; Chen, Chun-Wei; Kang, Yaw-Wen; Hu, Ming-Hsia; Hsu, Li-Lin; Wu, Szu-Yun; Chen, Likwang; Chang, Hsing-Yi; Chuang, Shao-Yuan; Pan, Wen-Harn; Hsu, Chih-Cheng	2019	International Journal of Behavioral Nutrition & Physical Activity	16	1	136
The ex-frail CKD trial: A pilot randomised controlled trial of a home-based exercise programme for pre-frail and frail, older adults with chronic kidney disease	Brady, Mark; Dhaygude, Ajay; Nixon, Andrew; Bampouras, Theodoros; Gooch, Helen; Young, Hannah; Finlayson, Kenneth; Pendleton, Neil; Mitra, Sandip	2020	Nephrology Dialysis Transplantation	35	SUPPL 3	P095
Can an LVAD reverse the frailty phenotype in advanced heart failure?	Jimenez, O.G.; Teruya, S.; Alvarez, J.; Maurer, M.; Horn, E.; Pinney, S.; Goldwater, D.; Reyntovich, A.; Dickson, V.; Gordon, R.	2016	Journal of the American Geriatrics Society	64	SUPPL. 1	S216

The effect of task-oriented activities in the pre-frail older people	Savvakis, Ioannis; Stratidaki, Eirini; Aravantinou-Karlatou, Antonia; Patelarou, Athina; Kleisiaris, Christos; Adamakidou, Theodoula; Panagiotakis, Simeon	2020	European Geriatric Medicine	11	SUPPL 1	S217
Short-and long-term effects of a tailored multicomponent exercise programme on functional capacity in older adults living in nursing homes: pilot results from the heal study	Courel-Ibanez, J.; Munoz-Gomez, M.D.M.; Garcia Conesa, S.; Buendia Romero, A.; Gomez Vazquez, S.	2020	Osteoporosis International	31	SUPPL 1	S602
A multifactorial interdisciplinary intervention reduces frailty, increases function and is cost-effective in older adults who are frail: Randomised controlled trial	Cameron, I.D.; Fairhall, N.; Sherrington, C.; Lord, S.; Susan, K.	2015	Physiotherapy (United Kingdom)	101	SUPPL. 1	eS371-eS372
Does a multifactorial interventional programme on falls prevention in older fallers improve frailty outcomes? Preliminary results from the Malaysian falls assessment	Tan, P.J.; Khor, H.M.; Saedon, N.I.; Kamaruzzaman, S.B.; Tan, M.P.	2017	Age and Ageing	46	Supplement 2	

intervention trial (MYFAIT)						
DEFRAIL (diet and exercise for frailty): The effect of a novel multi-component group exercise program and protein supplementation on frailty in older adults	Bambrick, Padraig; Mulcahy, Riona; Cooke, John; Byrne, Thomas; Harrison, Michael; Phelan, Niamh; Grant, Emma	2020	European Geriatric Medicine	11	SUPPL 1	S223
Frailty and clinical outcomes of transcatheter aortic valve replacement	Cheema, A.	2018	Cardiology (Switzerland)	140	Supplement 1	175
Promoting active ageing through a physical exercise program aimed at reducing frailty and risk of falling among older adults.	Alhambra-BorrÃ¡s, Tamara; Valia-Cotanda, Elisa; Dura-Ferrandis, Estrella; GarcÃ©s-Ferrer, Jordi; Quel-TejÃ³n, BelÃ©n	2017	International Journal of Integrated Care (IJIC)	17	5	1-8
[Intervention effects of inclusive support in an "exercise and a nutritional community-based prevention program" for pre-frail elderly individuals].	Fukasaku, Takako; Okuno, Junko; Tomura, Shigeo; Seino, Satoshi; Kim, Mi-Ji; Yabushita, Noriko; Okura, Tomohiro; Tanaka, Kiyoji; Yanagi, Hisako	2011	[Nihon koshu eisei zasshi] Japanese journal of public health	58	6	420-32
Using a group exercise program to improve the flexibility of frail older adults living in long-term care institutions	Lazowski, DA; Ecclestone, NA; Paterson, DH; Fitzgerald, C; Jones, G; TudorLocke, CE	1997	JOURNAL OF AGING AND PHYSICAL ACTIVITY	5	4	376-376

Meta-analysis of Primary Care Interventions to Address Frailty Among Adults Aged 65+...67th Annual & Scientific Meeting of the Irish Gerontological Society, Innovation, Advances and Excellence in Ageing, September 26-28, 2019, Cork, Ireland	Macdonald, Steve; Travers, John; Eidı́n Nı́ Shé; Bailey, Jade; Romero-Ortuno, Roman; Keyes, Michael; O'Shea, Diarmuid; Cooney, Marie Therese	2019	Age & Ageing	48		iii17-iii65
Training and de-training effects: One year follow-up of a 3-month resistance exercise program in the pre-frail elderly	Wu, H.-H.; Tseng, T.-J.; Gi, B.-H.; Lin, T.-Y.; Lin, P.-S.; Liao, T.-H.	2015	Physiotherapy (United Kingdom)	101	SUPPL. 1	eS882
Effect of Exercise Intervention on Frailty, Muscular Function, and Self-Efficacy in Daily Activities of Life for the Elder Population	Chen, YL; Huang, CH; Chang, YS	2016	JOURNAL OF AGING AND PHYSICAL ACTIVITY	24		S87-S87
EFFECT OF DIETARY AND EXERCISE INTERVENTIONS IN SARCOPENIC, PRE-FRAIL AND FRAIL OLDER ADULTS	Hida, A; Anton, S; Mankowski, R; Layne, A; Solberg, L; Mainous, A; Buford, T	2017	ANNALS OF NUTRITION AND METABOLISM	71		869-869
Modest functional exercise protocol with frail elders improves functional capacity: a series of case studies.	Blain A; McKnight J; Hutchinson K; Lowe S; Fitzpatrick D	2004	Journal of Geriatric Physical Therapy	27	3	113-113

Effects of an exercise protocol in frail and pre-frail elderly	Amaro, R.; Alegria, N.; Ramalhinho, M.; Afonso, G.; Morais, D.; Pereira, F.; Araujo, G.; Miguel, S.; Santos, O.	2016	European Geriatric Medicine	7	Supplement 1	S151
Nutrition, or Nutrition and Exercise? A Systematic Review of Interventions in Frail Elderly People	Saleh, RA; Lirette, S; Elisson, J; Wright, M; Cleinman, A	2015	JOURNAL OF THE AMERICAN GERIATRICS SOCIETY	63		S61-S61

Non-English or French (n= 10)

Title	Authors	Year	Journal	Volume	Issue	Pages
[Physical exercise in the frail elderly: an update].	Casas Herrero, Alvaro; Cadore, Eduardo L; Martinez Velilla, Nicolas; Izquierdo Redin, Mikel	2015	Revista espanola de geriatria y gerontologia	50	2	74-81
[A systematic review of intervention programs for frail elderly people enrolled in the Japanese social long-term care insurance system].	Ukawa, Shigekazu; Tamakoshi, Akiko; Sakamoto, Ai	2015	[Nihon koshu eisei zasshi] Japanese journal of public health	62	1	3-19
[Interventions for frailty and sarcopenia in community-dwelling elderly women].	Kim, Hunkyung	2012	Nihon Ronen Igakkai zasshi. Japanese journal of geriatrics	49	6	726-30

Effect of strength exercise with elastic bands and aerobic exercise in the treatment of frailty of the elderly patient with type 2 diabetes mellitus.	Garcia Diaz, Eduardo; Alonso Ramirez, Javier; Herrera Fernandez, Nuria; Peinado Gallego, Concha; Perez Hernandez, Domingo de Guzman	2019	Endocrinologia, diabetes y nutricion	66	9	563-570
[Effects of an intervention program for community-dwelling elderly to improve frailty and dietary habits].	Kawabata, Teruko; Takemi, Yukari; Murayama, Hiroshi; Nishi, Mariko; Shimizu, Yumiko; Narita, Miki; Kim, Mi-Ji; Shinkai, Shoji	2015	[Nihon koshu eisei zasshi] Japanese journal of public health	62	4	169-81
Nutritional, Physical, Cognitive, and Combination Interventions and Frailty Reversal among Older Adults: A Randomized Controlled Trial	Braun, T	2016	PHYSIOSCIENCE	12	4	165-U61
[Effectiveness of physical exercise on fitness in frail older adults: A systematic review of randomised trials].	Viladrosa, Maria; Casanova, Carles; Ghiorghies, Angela Claudia; Jurschik, Pilar	2017	Revista espanola de geriatria y gerontologia	52	6	332-341
Physical exercise as an efficient intervention in frail elderly persons	Herrero, AC; Izquierdo, M	2012	ANALES DEL SISTEMA SANITARIO DE NAVARRA	35	1	69-85
[Effects of a multifactorial intervention for improving frailty on risk of long-term care insurance certification, death, and long-term care cost among community-dwelling older adults: A quasi-experimental	Yokoyama, Yuri; Seino, Satoshi; Mitsutake, Seigo; Nishi, Mariko; Murayama, Hiroshi; Narita, Miki; Ishizaki,	2020	[Nihon koshu eisei zasshi] Japanese journal of public health	67	10	752-762

study using propensity score matching].	Tatsuro; Nofuji, Yu; Kitamura, Akihiko; Shinkai, Shoji					
Physical exercise as an efficient intervention in frail elderly persons physical exercise as an efficient intervention in frail elderly persons	Casas Herrero, A.; Izquierdo, M.	2012	Anales del Sistema Sanitario de Navarra	35	1	69-85

Pre and frail outcome reported combined (n= 23)

Title	Authors	Year	Journal	Volume	Issue	Pages
Home-based exercise for people living with frailty and chronic kidney disease: A mixed-methods pilot randomised controlled trial	Nixon, AC; Bampouras, TM; Gooch, HJ; Young, HML; Finlayson, KW; Pendleton, N; Mitra, S; Brady, ME; Dhaygude, AP	2021	PLOS ONE	16	7	e0251652
Integrated care for geriatric frailty and sarcopenia: a randomized control trial	Chan, DC; Tsou, HH; Chang, CB; Yang, RS; Tsauo, JY; Chen, CY; Hsiao, CF; Hsu, YT; Chen, CH; Chang, SF; Hsiung, CA; Kuo, KN	2017	JOURNAL OF CACHEXIA SARCOPENIA AND MUSCLE	8	1	78-88
Individualized home-based exercise and nutrition interventions improve frailty in older adults: a randomized controlled trial.	Hsieh, Tsung-Jen; Su, Shin-Chang; Chen, Chun-Wei; Kang, Yaw-Wen; Hu, Ming-Hsia; Hsu, Li-Lin; Wu, Szu-Yun; Chen, Likwang; Chang, Hsing-Yi;	2019	International Journal of Behavioral Nutrition & Physical Activity	16	1	119

	Chuang, Shao-Yuan; Pan, Wen-Harn; Hsu, Chih-Cheng					
A Randomized Controlled Pilot Exercise and Protein Effectiveness Supplementation Study (EXPRESS) on Reducing Frailty Risk in Community-Dwelling Older People.	Jadczak, Agathe Daria; Visvanathan, Renuka; Barnard, Robert; Luscombe-Marsh, Natalie	2021	Journal of nutrition in gerontology and geriatrics	40	1	26-45
Chair-based exercise programs in institutionalized older women: Salivary steroid hormones, disabilities and frailty changes	Furtado, GE; Carvalho, HM; Loureiro, M; Patricio, M; Uba-Chupel, M; Colado, JC; Hogervorst, E; Ferreira, JP; Teixeira, AM	2020	EXPERIMENTAL GERONTOLOGY	130		110790
Effect of various exercises on frailty among older adults with subjective cognitive concerns: a randomised controlled trial.	Huang, Chi Hsien; Umegaki, Hiroyuki; Makino, Taeko; Uemura, Kazuki; Hayashi, Takahiro; Kitada, Tomoharu; Inoue, Aiko; Shimada, Hiroyuki; Kuzuya, Masafumi	2020	Age & Ageing	49	6	1011-1019
How to Improve the Functional Capacity of Frail and Pre-Frail Elderly People? Health, Nutritional Status and Exercise Intervention. The EXERNET-Elder 3.0 Project	Fernandez-Garcia, AI; Gomez-Cabello, A; Moradell, A; Navarrete-Villanueva, D; Perez-Gomez, J; Ara, I; Pedrero-Chamizo, R; Subias-Perie, J; Muniz-Pardos, B; Casajus, JA; Vicente-Rodriguez, G	2020	SUSTAINABILITY	12	15	6246

Cognitive Effects of Multi-Domain Interventions Among Pre-Frail and Frail Community-Living Older Persons: Randomized Controlled Trial.	Tze Pin Ng; Ling Hui Audrey Ling; Liang Feng; Ma Shwe Zin Nyunt; Lei Feng; Niti, Mathew; Boon Yeow Tan; Chan, Gribson; Khoo, Sue Anne; Sue Mei Chan; Yap, Philip; Keng Bee Yap; Ng, Tze Pin; Ling, Ling Hui Audrey; Feng, Liang; Nyunt, Ma Shwe Zin; Feng, Lei; Tan, Boon Yeow; Chan, Sue Mei; Yap, Keng Bee	2018	Journals of Gerontology Series A: Biological Sciences & Medical Sciences	73	6	806-812
Effects of horticultural therapy: Perspectives of frail and pre-frail older nursing home residents	Lo, SKL; Lam, WYY; Kwan, RYC; Tse, MMY; Lau, JKH; Lai, CKY	2019	NURSING OPEN	6	3	1230-1236
Effects of dehydroepiandrosterone (DHEA) on cardiovascular risk factors in older women with frailty characteristics	Kleppinger, A.; Burleson, J.A.; Kenny, A.M.; Feinn, R.; Brindisi, J.; Boxer, R.S.	2010	Age and Ageing	39	4	451-458
The effect of the group-based Otago exercise program on frailty among nursing home older adults with cognitive impairment.	Feng, Hong; Zou, Zhijie; Zhang, Qing; Wang, Liang; Ouyang, Yan-Qiong; Chen, Zhongwan; Ni, Zhao	2021	Geriatric Nursing	42	2	479-483
Effectiveness of combined exercise and nutrition interventions in prefrail or frail older hospitalised patients: a	Han, CY; Miller, M; Yaxley, A; Baldwin, C; Woodman, R; Sharma, Y	2020	BMJ OPEN	10	12	e040146

systematic review and meta-analysis						
Adherence Is More Than Just Being Present: Example of a Lay-Led Home-Based Programme with Physical Exercise, Nutritional Improvement and Social Support, in Prefrail and Frail Community-Dwelling Older Adults	Lackinger, C; Grabovac, I; Haider, S; Kapan, A; Winzer, E; Stein, KV; Dorner, TE	2021	INTERNATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH	18	8	4192
Effects of a Multicomponent Exercise Program, a Detraining Period and Dietary Intake Prediction of Body Composition of Frail and Pre-Frail Older Adults from the EXERNET Elder 3.0 Study	Moradell, A; Navarrete-Villanueva, D; Fernandez-Garcia, AI; Sagarra-Romero, L; Marin-Puyalto, J; Perez-Gomez, J; Gesteiro, E; Ara, I; Casajus, JA; Gomez-Cabello, A; Rodriguez, GV	2020	SUSTAINABILITY	12	23	9894
Randomized Comparison of Exercise Intervention Versus Usual Care in Older Adult Patients with Frailty After Acute Myocardial Infarction.	Sanchis, Juan; Sastre, Clara; Ruescas, Arantxa; Ruiz, Vicente; Valero, Ernesto; Bonanad, Clara; GarcÃa-Blas, Sergio; FernÃ¡ndez-Cisnal, AgustÃn; GonzÃ¡lez, Jessika; MiÃ±ana, Gema; NÃºÃ±ez, Julio	2021	American Journal of Medicine	134	3	383-383

Effects of a Primary Care-Based Multifactorial Intervention on Physical and Cognitive Function in Frail, Elderly Individuals: A Randomized Controlled Trial.	Romera-Liebana, Laura; Orfila, Francesc; Segura, Josep Maria; Real, Jordi; Fabra, Maria LluÃ¯sa; MÃ¶ller, Mercedes; Lancho, Santiago; Ramirez, Anna; Marti, Nuria; Cullell, Montserrat; Bastida, Nuria; Martinez, Dolors; GinÃ©, Maria; CendrÃ³s, Patricia; Bistuer, Anna; Perez, Elena; Fabregat, Maria Assumpta; Foz, GonÃ§al	2018	Journals of Gerontology Series A: Biological Sciences & Medical Sciences	73	12	1688-1674
Effects of exercise training on frailty in community-dwelling older adults: results of a randomized, controlled trial.	Binder EF; Schechtman KB; Ehsani AA; Steger-May K; Brown M; Sinacore DR; Yarasheski KE; Holloszy JO	2002	Journal of the American Geriatrics Society	50	12	1921-1928
Impact of a lay-led home-based intervention programme on quality of life in community-dwelling pre-frail and frail older adults: a randomized controlled trial.	Kapan, A.; Winzer, E.; Haider, S.; Titze, S.; Schindler, K.; Lackinger, C.; Dorner, T. E.	2017	BMC Geriatrics	17	1	154
Effects and feasibility of exercise therapy combined with branched-chain amino acid supplementation on muscle strengthening in frail	Ikeda, Takashi; Aizawa, Junya; Nagasawa, Hiroshi; Gomi, Ikuko; Kugota, Hiroyuki; Nanjo, Keigo; Jinno, Tetsuya; Masuda, Tadashi; Morita, Sadao	2016	Applied Physiology, Nutrition & Metabolism	41	4	438-445

and pre-frail elderly people requiring long-term care: a crossover trial.						
Protein Supplementation Improves Physical Performance in Frail Elderly People: A Randomized, Double-Blind, Placebo-Controlled Trial.	Tieland, Michael; van de Rest, Ondine; Dirks, Marlou L.; van der Zwaluw, Nikita; Mensink, Marco; van Loon, Luc J.C.; de Groot, Lisette C.P.G.M.	2012	Journal of the American Medical Directors Association	13	8	720-726
Efficacy of multidomain interventions to improve physical frailty, depression and cognition: data from cluster-randomized controlled trials	Taiwan Hlth Promotion Intervention; Chen, LK; Hwang, AC; Lee, WJ; Peng, LN; Lin, MH; Neil, DL; Shih, SF; Loh, CH; Chiou, ST	2020	JOURNAL OF CACHEXIA SARCOPENIA AND MUSCLE	11	3	650-662
Effects of Resistance Exercise Training on Cognitive Function and Physical Performance in Cognitive Frailty: A Randomized Controlled Trial.	Yoon, D. H.; Lee, Jun-Young; Song, Wook	2018	Journal of Nutrition, Health & Aging	22	8	944-951
A realist review to understand the efficacy and outcomes of interventions designed to minimise, reverse or	Gwyther, Holly; Bobrowicz-Campos, Elzbieta; Luis Alves ApÃ³stolo, JoÃ£o; Marcucci, Maura; Cano, Antonio; Holland, Carol	2018	Health Psychology Review	12	4	382-404

prevent the progression of frailty.						

Wrong patient population <65yrs/frail state not mentioned (n= 87)

Title	Authors	Year	Journal	Volume	Issue	Pages
THE EFFECT OF PHYSICAL EXERCISE ON FRAIL OLDER PERSONS: A SYSTEMATIC REVIEW	Silva, RB; Aldoradin-Cabeza, H; Eslick, GD; Phu, S; Duque, G	2017	JOURNAL OF FRAILTY & AGING	6	2	91-96
Reversibility of Frailty after Lung Transplantation	Montgomery, E; Macdonald, PS; Newton, PJ; Chang, S; Wilhelm, K; Jha, SR; Malouf, M	2020	JOURNAL OF TRANSPLANTATION	37	4	S249
Dehydroepiandrosterone combined with exercise improves muscle strength and physical function in frail older women.	Kenny AM; Boxer RS; Kleppinger A; Brindisi J; Feinn R; Burleson JA	2010	Journal of the American Geriatrics Society	58	9	1707-1714
Possible Sarcopenia and Impact of Dual-Task Exercise on Gait Speed, Handgrip Strength, Falls, and Perceived Health	Merchant, RA; Chan, YH; Hui, RJY; Lim, JY; Kwek, SC; Seetharaman, SK; Au, LSY; Morley, JE	2021	FRONTIERS IN MEDICINE	8		
Nutrition and Frailty: Opportunities for	Ni Lochlainn, Mary; Cox, Natalie J.; Wilson,	2021	Nutrients	13	7	2349-2349

Prevention and Treatment.	Thomas; Hayhoe, Richard P. G.; Ramsay, Sheena E.; Granic, Antoneta; Isanejad, Masoud; Roberts, Helen C.; Wilson, Daisy; Welch, Carly; Hurst, Christopher; Atkins, Janice L.; MendonÃ§a, Nuno; Horner, Katy; Tuttiett, Esme R.; Morgan, Yvie; Heslop, Phil; Williams, Elizabeth A.; Steves, Claire J.; Greig, Carolyn					
Exercise and/or Dietary Varieties and Incidence of Frailty in Community-Dwelling Older Women: A 2-Year Cohort Study.	Osuka, Yosuke; Kojima, N.; Yoshida, Y.; Kim, M.; Won, CW.; Suzuki, T.; Kim, H.	2019	Journal of Nutrition, Health & Aging	23	5	425-430
Effects of passive exercise training on physical and psychological variables of elderly participants living in long-term care: a cross sectional study.	Brenner, Ingrid	2009	Perspectives (Gerontological Nursing Association (Canada))	33	4	7-14
Obesity and Physical Frailty in Older Adults: A Scoping Review of Lifestyle Intervention Trials.	Porter Starr, Kathryn N.; McDonald, Shelley R.; Bales, Connie W.	2014	Journal of the American Medical Directors Association	15	4	240-250

Effects of lower limb resistance exercise on muscle strength, physical fitness, and metabolism in pre-frail elderly patients: a randomized controlled trial.	Lai, Xiaoxing; Bo, Lin; Zhu, Hongwei; Chen, Baoyu; Wu, Zhao; Du, Hongdi; Huo, Xiaopeng	2021	BMC geriatrics	21	1	447
A multicomponent frailty intervention for socioeconomically vulnerable older adults: a designed-delay study	Jang, IY; Jung, HW; Park, H; Lee, CK; Yu, SS; Lee, YS; Lee, E; Glynn, RJ; Kim, DH	2018	CLINICAL INTERVENTIONS IN AGING	13		1799-1814
Tai Chi is an effective form of exercise to reduce markers of frailty in older age	Kasim, NF; van Zanten, JV; Aldred, S	2020	EXPERIMENTAL GERONTOLOGY	135		110925
Involving older people in co-designing an intervention to reverse frailty and build resilience.	Travers, John; Romero-Ortuno, Roman; Ni She, Eidin; Cooney, Marie-Therese	2021	Family practice	39	1	200-206
Frailty and exercise interventions Evidence and barriers for exercise programs	Freiberger, E; Kemmler, W; Siegrist, M; Sieber, C	2016	ZEITSCHRIFT FUR GERONTOLOGIE UND GERIATRIE	49	7	606-611
Feasibility, safety, acceptability, and functional outcomes of playing Nintendo Wii Fit PlusTM for frail older adults: A	Gomes, Gisele Cristine Vieira; SimÃµes, Maria do Socorro; Lin, Sumika Mori; Bacha, JÃ©ssica Maria Ribeiro; Viveiro, Larissa Alamino	2018	Maturitas	118		20-28

randomized feasibility clinical trial.	Pereira; Varise, Eliana Maria; Carvas Junior, Nelson; Lange, Belinda; Jacob Filho, Wilson; Pompeu, JosÃ© Eduardo					
Nonpharmacological interventions to treat physical frailty and sarcopenia in older patients: a systematic overview - the SENATOR Project ONTOP Series	Lozano-Montoya, I; Correa-Perez, A; Abraha, I; Soiza, RL; Cherubini, A; O'Mahony, D; Cruz-Jentoft, AJ	2017	CLINICAL INTERVENTIONS IN AGING	12		721-740
Effects of exercise programs on falls and mobility in frail and pre-frail older adults: a multicenter randomized controlled trial.	Faber MJ; Bosscher RJ; Paw MJC; van Wieringen PC	2006	Archives of Physical Medicine & Rehabilitation	87	7	885-896
A Multicomponent Intervention Program to Improve Physical Function and Frailty in Vulnerable Older Adults: A Designed-Delay Intervention Study	Jang, I; Jung, H; Lee, Y; Lee, E; Kim, D	2018	JOURNAL OF THE AMERICAN GERIATRICS SOCIETY	13		1799–1814
LIFE-SUSTAINING INTERVENTIONS IN FRAIL ELDERLY PERSONS - TALKING ABOUT CHOICES	KELLOGG, FR; CRAIN, M; CORWIN, J; BRICKNER, PW	1992	ARCHIVES OF INTERNAL MEDICINE	152	11	2317-2320

The effects of exercise on strength and physical performance in frail older people: A systematic review	Katharine CM Nash	2012	Reviews in Clinical Gerontology	22	4	274-285
A primary care approach to frailty and sarcopenia	Woo, Jean	2019	Aging Medicine and Healthcare	10	Supplement 1	2
Does Home-Based Exercise Improve the Physical Function of Prefrail Older Women?	Garcia, RNSD; Costa, SN; Garcia, EDSD; Bento, PCB	2021	REJUVENATION RESEARCH	24	1	13-Jun
Interventions to prevent, delay or reverse frailty in older people: a journey towards clinical guidelines.	Marcucci, Maura; Damanti, Sarah; Germini, Federico; Apostolo, Joao; Bobrowicz-Campos, Elzbieta; Gwyther, Holly; Holland, Carol; Kurpas, Donata; Bujnowska-Fedak, Maria; Szwamel, Katarzyna; Santana, Silvina; Nobili, Alessandro; D'Avanzo, Barbara; Cano, Antonio	2019	BMC Medicine	17	1	193-193
Interventions to improve the outcomes of frail people having surgery: A systematic review	McIsaac, DI; Jen, T; Mookerji, N; Patel, A; Lalu, MM	2017	PLOS ONE	12	12	e0190071
A multicomponent exercise intervention to improve physical	Cordes, Thomas; Bischoff, Laura L.; Schoene, Daniel;	2019	BMC Geriatrics	19	1	369

functioning, cognition and psychosocial well-being in elderly nursing home residents: a study protocol of a randomized controlled trial in the PROCARE (prevention and occupational health in long-t	Schott, Nadja; Voelcker-Rehage, Claudia; Meixner, Charlotte; Appelles, Luisa-Marie; Bebenek, Michael; Berwinkel, Andre; Hildebrand, Claudia; JÃ¶llenbeck, Thomas; Johnen, Bettina; Kemmler, Wolfgang; Klotzbier, Thomas; Korbus, Heide; Rudisch, Julian; Vogt, Lutz; Weigelt, Matthias; Wittelsberger, Rita; Zwingmann, Katharina					
Cost analysis of a community-based exercise and nutritional intervention in frail older adults	Walsh, Joseph; Bambrick, Padraig; Pope, George; O'Regan, Niamh; Harrison, Michael; Byrne, Thomas; Mulcahy, Riona; Cooke, John	2020	European Geriatric Medicine	11	SUPPL 1	S223
Feasibility of a community-based Functional Power Training program for older adults	Tan, QLL; Chye, LMY; Ng, DHM; Chong, MS; Ng, TP; Wee, SL	2018	CLINICAL INTERVENTIONS IN AGING	13		309-316
Effect of an integrated care model for pre-frail and frail older people living in community.	Yu, Ruby; Tong, Cecilia; Woo, Jean	2020	Age & Ageing	49	6	1048-1055

Motoric cognitive risk syndrome, physio-cognitive decline syndrome, cognitive frailty and reversibility with dual-task exercise	Merchant, RA; Chan, YH; Hui, RJY; Tsoi, CT; Kwek, SC; Tan, WM; Lim, JY; Sandrasageran, S; Wong, BLL; Chen, MZ; Ng, SE; Morley, JE	2021	EXPERIMENTAL GERONTOLOGY	150		111362
A case of chronic dizziness and frailty that improved with a combination of exercise and medical guidance	Kawamura, Koki; Kondo, Izumi; Nakada, Takafumi; Sugiura, Saiko; Uchida, Yasue	2021	Equilibrium Research	80	2	104-111
MANAGEMENT OF FRAILTY AT INDIVIDUAL LEVEL: NARRATIVE REVIEW OF PHYSICAL ACTIVITY FROM THE EUROPEAN PERSPECTIVE OF JOINT ACTION ON FRAILTY - JA ADVANTAGE	Strojnik, V; Gabrovec, B	2019	ZDRAVSTVENO VARSTVO	58	2	84-90
The effects of exercise on strength and physical performance in frail older people: a systematic review.	Nash, Katharine CM	2012	Reviews in Clinical Gerontology	22	4	274-285
Randomized controlled trial to evaluate effectiveness of exercise therapy (Takizawa	Makita, Mitsuyo; Nakadaira, Hiroto; Yamamoto, Masaharu	2006	Environmental health and preventive medicine	11	5	221-7

Program) for frail elderly.						
Delaying and reversing frailty: a systematic review of primary care interventions	Travers, J; Romero-Ortuno, R; Bailey, J; Cooney, MT	2019	BRITISH JOURNAL OF GENERAL PRACTICE	69	678	E61-E69
Reversal of age-associated frailty by controlled physical exercise: The pre-clinical and clinical evidences	Millan, F.; Salvador-Pascual, A.; Correas, A.G.; Olaso-Gonzalez, G.; De la Rosa, A.; Carretero, A.; Gomez-Cabrera, M.C.; Vina, J.; Arc-Chagnaud, C.	2019	Sports Medicine and Health Science	1	1	33-39
The Atlanta FICSIT study: two exercise interventions to reduce frailty in elders.	Wolf SL; Kutner NG; Green RC; McNeely E	1993	Journal of the American Geriatrics Society	41	3	329-332
Social isolation and loneliness as related to progression and reversion of frailty in the Survey of Health Aging Retirement in Europe (SHARE).	Jarach, Carlotta Micaela; Tettamanti, Mauro; Nobili, Alessandro; D'avanzo, Barbara	2021	Age & Ageing	50	1	258-262
The Home-based Older People's Exercise (HOPE) trial: a pilot randomised controlled trial of a home-based exercise intervention for older people with frailty.	Clegg, Andrew; Barber, Sally; Young, John; Iliffe, Steve; Forster, Anne	2014	Age & Ageing	43	5	687-695

Is It Time to Begin a Public Campaign Concerning Frailty and Pre-frailty? A Review Article	Sacha, J; Sacha, M; Sobon, J; Borysiuk, Z; Feusette, P	2017	FRONTIERS IN PHYSIOLOGY	8		484
Adherence to and effectiveness of an individually tailored home-based exercise program for frail older adults, driven by mobility monitoring: design of a prospective cohort study	Geraedts, HAE; Zijlstra, W; Zhang, W; Bulstra, S; Stevens, M	2014	BMC PUBLIC HEALTH	14		570
Reversing Frailty Levels in Primary Care Using the CARES Model.	Theou, Olga; Park, Grace H.; Garm, Antonina; Song, Xiaowei; Clarke, Barry; Rockwood, Kenneth	2017	Canadian Geriatrics Journal	20	3	105-111
Metaâ€• analysis and GRADE profiles of exercise interventions for falls prevention in longâ€• term care facilities.	Schoberer, Daniela; Breimaier, Helga E.	2020	Journal of Advanced Nursing (John Wiley & Sons, Inc.)	76	1	121-134
Mediterranean diet intervention alters the gut microbiome in older people reducing frailty and improving health status: the NU-AGE 1-year dietary intervention	Ghosh, TS; Rampelli, S; Jeffery, IB; Santoro, A; Neto, M; Capri, M; Giampieri, E; Jennings, A; Candela, M; Turroni, S; Zoetendal, EG; Hermes, GDA; Elodie, C; Meunier, N; Brugere,	2020	GUT	69	7	1218-1228

across five European countries	CM; Pujos-Guillot, E; Berendsen, AM; De Groot, LCPGM; Feskins, EJM; Kaluza, J; Pietruszka, B; Bielak, MJ; Comte, B; Maijo-Ferre, M; Nicoletti, C; De Vos, WM; Fairweather-Tait, S; Cassidy, A; Brigidi, P; Franceschi, C; O'Toole, PW					
Frailty predicts adverse outcomes in older people with diabetes.	Ulley, Joanna; Abdelhafiz, Ahmed H.	2017	Practitioner	261	1800	17-20
Cognitive Frailty and Its Association with All-Cause Mortality Among Community-Dwelling Older Adults in Taiwan: Results from I-Lan Longitudinal Aging Study.	Liu, Li-Kuo; Chen, Chia-Hung; Lee, Wei-Ju; Wu, Yi-Hui; Hwang, An-Chun; Lin, Ming-Hsien; Shimada, Hiroyuki; Peng, Li-Ning; Loh, Ching-Hui; Arai, Hidenori; Chen, Liang-Kung	2018	Rejuvenation Research	21	6	510-517
The pulmonary rehabilitation regimen: a treatment for frailty and â€˜inflammagingâ€™?	Tanner, A; Vassallo, M; Kwan, JSK; Allen, SC	2018	British Journal of Hospital Medicine (17508460)	79	8	432-437
The role of prehabilitation in frail surgical patients: A systematic review	Milder, DA; Pillinger, NL; Kam, PCA	2018	ACTA ANAESTHESIOLOGICA SCANDINAVICA	62	10	1356-1366

Multicomponent exercise and the hallmarks of frailty: Considerations on cognitive impairment and acute hospitalization	Cadore, EL; de Asteasu, MLS; Izquierdo, M	2019	EXPERIMENTAL GERONTOLOGY	122		10-14
Review of Interventions for the Frailty Syndrome and the Role of Metformin as a Potential Pharmacologic Agent for Frailty Prevention	Espinoza, SE; Jiwani, R; Wang, J; Wang, CP	2019	CLINICAL THERAPEUTICS	41	3	376-386
A comparison of functional outcomes following a physical activity intervention for frail older adults in personal care homes.	Taylor LF; Whittington F; Hollingsworth C; Ball M; King SV; Diwan S; Rosenbloom C; Patterson V; Neel A	2003	Journal of Geriatric Physical Therapy	26	1	7-11
Physical Exercise as Therapy for Frailty	Aguirre, LE; Villareal, DT	2015	FRAILTY: PATHOPHYSIOLOGY, PHENOTYPE AND PATIENT CARE	83		83-92
The effects of exercise on the quality of life of frail older adults: A preplanned meta-analysis of the FICSIT trials	FICSIT Grp; Schechtman, KB; Ory, MG	2001	ANNALS OF BEHAVIORAL MEDICINE	23	3	186-197
EXERCISE TRAINING AND NUTRITIONAL SUPPLEMENTATION	FIATARONE, MA; ONEILL, EF; RYAN, ND; CLEMENTS, KM;	1994	NEW ENGLAND JOURNAL OF MEDICINE	330	25	1769-1775

FOR PHYSICAL FRAILTY LN VERY ELDERLY PEOPLE	SOLARES, GR; NELSON, ME; ROBERTS, SB; KEHAYIAS, JJ; LIPSITZ, LA; EVANS, WJ					
Effects of a group-based exercise program on the mood state of frail older women after discharge from hospital.	Timonen, L; Rantanen, T; Timonen, T E; Sulkava, R	2002	International Journal of Geriatric Psychiatry	17	12	1106-1111
Health Benefits of beta-Hydroxy-beta-Methylbutyrate (HMB) Supplementation in Addition to Physical Exercise in Older Adults: A Systematic Review with Meta-Analysis	Courel-Ibanez, J; Vetrovsky, T; Dadova, K; Pallares, JG; Steffl, M	2019	NUTRIENTS	11	9	2082
Randomized Controlled Trial on the Effects of a Combined Intervention of Computerized Cognitive Training Preceded by Physical Exercise for Improving Frailty Status and Cognitive Function in Older Adults	Yu, R; Leung, G; Woo, J	2021	INTERNATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH	18	4	1396

THE ATLANTA FICSIT STUDY - 2 EXERCISE INTERVENTIONS TO REDUCE FRAILTY IN ELDERS	WOLF, SL; KUTNER, NG; GREEN, RC; MCNEELY, E	1993	JOURNAL OF THE AMERICAN GERIATRICS SOCIETY	41	3	329-332
Primary care interventions to address physical frailty among community-dwelling adults aged 60 years or older: A meta-analysis	Macdonald, SHF; Travers, J; She, EN; Bailey, J; Romero-Ortuno, R; Keyes, M; O'Shea, D; Cooney, MT	2020	PLOS ONE	15	2	e0228821
Exergaming as a Physical Exercise Strategy Reduces Frailty in People With Dementia: A Randomized Controlled Trial.	Karssemeijer, Esther G.A.; Bossers, Willem J.R.; Aaronson, Justine A.; Sanders, Lianne M.J.; Kessels, Roy P.C.; Olde Rikkert, Marcel G.M.	2019	Journal of the American Medical Directors Association	20	12	1502-1502
Effects of in-hospital exercise on frailty in patients with hepatocellular carcinoma	Tsuchihashi, Jin; Koya, Shunji; Hirota, Keisuke; Koga, Noboru; Narao, Hayato; Tomita, Manabu; Kawaguchi, Takumi; Nakano, Dan; Tsutsumi, Tsubasa; Torimura, Takuji; Hashida, Ryuki; Matsuse, Hiroo; Yoshio, Sachiyo; Sanada, Taku; Notsumata, Kazuo	2021	Cancers	13	2	194

Effects of Home-Based Exercise on Frailty in Patients With End-Stage Renal Disease: Systematic Review	Yoo, J; Ruppar, T; Wilbur, J; Miller, A; Westrick, JC		BIOLOGICAL RESEARCH FOR NURSING	24	1	48-63
Relationships of exercise with frailty, depression, and cognitive function in older women	Jeoung, BJ	2014	JOURNAL OF EXERCISE REHABILITATION	10	5	291-294
Association between Diet Quality and Frailty Prevalence in the Physicians' Health Study.	Ward, Rachel E.; Orkaby, Ariela R.; Chen, Jiaying; Hshieh, Tammy T.; Driver, Jane A.; Gaziano, J. Michael; Djousse, Luc	2020	Journal of the American Geriatrics Society	68	4	770-776
Effectiveness of a Community-Based Muscle Strengthening Exercise Program to Increase Muscle Strength Among Pre-frail Older Persons in Malaysia: A Pilot Study	Adnan, RNER; Din, HM; Ashari, A; Minhat, HS	2021	FRONTIERS IN PUBLIC HEALTH	9		610184
Physical frailty and its associated factors among elderly nursing home residents in China.	Liu, Weiwei; Puts, Martine; Jiang, Fen; Zhou, Chuyi; Tang, Siyuan; Chen, Sanmei	2020	BMC Geriatrics	20	1	294
Delaying and reversing frailty: A systematic review of primary care interventions	Travers, John; Cooney, Therese; Romero-Ortuno, Roman; Bailey, Jade	2018	Age and Ageing	69	678	e61-e69

BE WELL: RESULTS OF A NUTRITION, EXERCISE, AND WEIGHT MANAGEMENT INTERVENTION AMONG FRAIL OLDER ADULTS	Kogan, AC; Hart, B; Gonzalez, J; Enguidanos, S	2011	GERONTOLOGIST	32	7	889-901
Protocolized exercise improves frailty parameters and lower extremity impairment: A promising prehabilitation strategy for kidney transplant candidates	Lorenz, EC; Hickson, LJ; Weatherly, RM; Thompson, KL; Walker, HA; Rasmussen, JM; Stewart, TL; Garrett, JK; Amer, H; Kennedy, CC	2020	CLINICAL TRANSPLANTATION	34	9	e14017
Can a Left Ventricular Assist Device in Individuals with Advanced Systolic Heart Failure Improve or Reverse Frailty?	Maurer, Mathew S.; Horn, Evelyn; Reyentovich, Alex; Dickson, Victoria Vaughan; Pinney, Sean; Goldwater, Deena; Goldstein, Nathan E.; Jimenez, Omar; Teruya, Sergio; Goldsmith, Jeff; Helmke, Stephen; Yuzefpolskaya, Melana; Reeves, Gordon R.	2017	Journal of the American Geriatrics Society	65	11	2383-2390
Effects of whey protein nutritional supplement on muscle function among community-dwelling frail older	Kang, Lin; Gao, Ying; Liu, Xiaohong; Liang, Yinghui; Chen, Yiwen; Liang, Yanhong; Zhang,	2019	Archives of Gerontology & Geriatrics	83		7-12

people: A multicenter study in China.	Lu; Chen, Wei; Pang, Haiyu; Peng, Li-Ning					
Effects of Protein Supplementation Combined with Exercise Intervention on Frailty Indices, Body Composition, and Physical Function in Frail Older Adults.	Liao, Chun-De; Lee, Pi-Hsia; Hsiao, Dun-Jen; Huang, Shih-Wei; Tsauo, Jau-Yih; Chen, Hung-Chou; Liou, Tsan-Hon	2018	Nutrients	10	12	1916
Effectiveness of exercise interventions on physical function in community-dwelling frail older people: an umbrella review of systematic reviews.	Jadczak, Agathe D.; Makwana, Naresh; Luscombe-Marsh, Natalie; Visvanathan, Renuka; Schultz, Timothy J.	2018	JBI Database of Systematic Reviews & Implementation Reports	16	3	752-775
Multidomain Intervention for Reversal of Cognitive Frailty, Towards a Personalized Approach (AGELESS Trial): Study Design	Ponvel, P; Shahar, S; Singh, DKA; Ludin, AFM; Rajikan, R; Rajab, NF; Ai-Vyrn, C; Din, NC; Ibrahim, N; Subramaniam, P; Haron, H; Ismail, A; Sharif, R; Ramasamy, K; Majeed, AA; Ali, NM; Mohamad, M; Noah, SAM; Ibrahim, AM; Safien, AM; Khalid, NM; Fadzil, NHM; Mangialasche, F; Kivipelto, M	2021	JOURNAL OF ALZHEIMERS DISEASE	82	2	673-687

Functional resistance activities to impact frailty: A protocol for a randomized controlled trial involving home care aide and frail older adult dyads	Danilovich, MK; Diaz, L; Ciolinio, JD; Corcos, DM	2017	CONTEMPORARY CLINICAL TRIALS COMMUNICATIONS	7		28-32
Effects of exercise on frailty in patients with hepatocellular carcinoma	Kawaguchi, Takumi; Nakano, Dan; Torimura, Takuji; Koya, Shunji; Hirota, Keisuke; Tsuchihashi, Jin; Koga, Noboru; Narao, Hayato; Tomita, Manabu; Hashida, Ryuki; Matsuse, Hiroo; Sanada, Taku; Notsumata, Kazuo	2020	Hepatology International	14	Supplement 1	S398
"pre-habilitation" of frail candidates for lung transplantation using a mobile health enabled home-based intervention is feasible and safe	Singer, J.P.; Soong, A.; Hays, S.; Kukreja, J.; Bracha, A.; Chin, G.; Wolters, P.J.; Peters, M.; Bruun, A.; Garvey, C.M.	2017	American Journal of Respiratory and Critical Care Medicine	32	6	e13274
Changes in health parameters in older lay volunteers who delivered a lifestyle-based program to frail older people at home	Grabovac, I; Haider, S; Winzer, E; Kapan, A; Schindler, KE; Lackinger, C; Dorner, TE	2018	WIENER KLINISCHE WOCHENSCHRIFT	130	21-22	637-644
Effects of exercise interventions on frailty	Lin, Shu-Yuan	2021	Disability and health journal		101306633	101105

in pre-maturely aging adults with intellectual disabilities- a preliminary study.						
Community-Based Peer-Led Intervention for Healthy Ageing and Evaluation of the 'HAPPY' Program.	Merchant, Reshma A.; Tsoi, C. T.; Tan, W. M.; Lau, W.; Sandrasageran, S.; Arai, H.	2021	Journal of Nutrition, Health & Aging	25	4	520-527
Getting fit for hip and knee replacement: a protocol for the Fit-Joints pilot randomized controlled trial of a multi-modal intervention in frail patients with osteoarthritis.	Negm, Ahmed M; Kennedy, Courtney C; Ioannidis, George; Gajic-Veljanoski, Olga; Lee, Justin; Thabane, Lehana; Adachi, Jonathan D; Marr, Sharon; Lau, Arthur; Atkinson, Stephanie; Petruccelli, Danielle; DeBeer, Justin; Winemaker, Mitchell; Avram, Victoria; Deheshi, Benjamin; Williams, Dale; Armstrong, David; Lumb, Barry; Panju, Akbar; Richardson, Julie; Papaioannou, Alexandra	2018	Pilot and feasibility studies	4	101676536	127
Effectiveness of Community-Delivered Functional Power Training Program for	Tou, NX; Wee, SL; Seah, WT; Ng, DHM; Pang, BWJ; Lau, LK; Ng, TP	2021	PREVENTION SCIENCE	22	8	1048-1059

Frail and Pre-frail Community-Dwelling Older Adults: a Randomized Controlled Study						
The effects of a home-based exercise program on physical function in frail older adults.	Matsuda PN; Shumway-Cook A; Ciol MA	2010	Journal of Geriatric Physical Therapy	33	2	78-84
Effects of a 12-Week Exercise Training Program on Physical Function in Institutionalized Frail Elderly.	Ferreira, Cristiane Batisti; Teixeira, PÃ¢mela dos Santos; Alves dos Santos, Geiane; Dantas Maya, Athila Teles; Americano do Brasil, Paula; Souza, VinÃcius Carolino; CÃ³rdova, ClÃ¡udio; Ferreira, Aparecido Pimentel; Lima, Ricardo Moreno; NÃ³brega, OtÃ¡vio de Toledo	2018	Journal of Aging Research			
Treating frailty--a practical guide.	Fairhall, Nicola; Langron, Colleen; Sherrington, Catherine; Lord, Stephen R; Kurrle, Susan E; Lockwood, Keri; Monaghan, Noeline; Aggar, Christina; Gill, Liz; Cameron, Ian D	2011	BMC Medicine	9	1	83-83

New Chronic Obstructive Pulmonary Disease Study Findings Have Been Reported from Qinghai University Affiliated Hospital (Is it possible to reverse frailty in patients with chronic obstructive pulmonary disease?)	Zhe Wang, Xiaojing Hu, and Qingxiang Dai	2020	Health & Medicine Week	75		e1778
Exercise as an intervention for frailty.	Liu CK; Fielding RA; Liu, Christine K; Fielding, Roger A	2011	Clinics in Geriatric Medicine	27	1	101-110
Finding new strength. Exercising can help the frail elderly improve quality of life.	Wagner, L	1998	Provider (Washington, D.C.)	24	3	69-70
The effect of self-directed exercise programonphysical function of older adults with frailty	Song, W.; Woo, S.; Oh, S.; Kim, H.; Kim, D.; Kim, J.	2012	Journal of Science and Medicine in Sport	15	SUPPL.1	S80

Wrong Study (n= 51)

Title	Authors	Year	Journal	Volume	Issue	Pages
Effects of physical exercise interventions in frail older adults: a	de Labra, Carmen; Guimaraes-Pinheiro, Christyanne; Maseda, Ana;	2015	BMC Geriatrics	15		154

systematic review of randomized controlled trials.	Lorenzo, Trinidad; MillÃ¡n-Calenti, JosÃ© C.					
Home Exercise Interventions in Frail Older Adults	Stookey, AD; Katzel, LI	2020	CURRENT GERIATRICS REPORTS	9	3	163-175
Interventions Against Disability in Frail Older Adults: Lessons Learned from Clinical Trials.	FougÃ¨re, Bertrand; Morley, J. E.; Little, M. O.; de Souto Barreto, P.; Cesari, M.; Vellas, B.	2018	Journal of Nutrition, Health & Aging	22	6	676-688
Frailty: role of nutrition and exercise.	Kelaiditi, Eirini; van Kan, Gabor Abellan; Cesari, Matteo	2014	Current Opinion in Clinical Nutrition & Metabolic Care	17	1	32-39
Long-term effect of a multicomponent intervention on physical performance and frailty	Lee, H.; Jang, I.; Oh, G.; Jung, H.; Kim, D.	2020	Journal of the American Geriatrics Society	68	SUPPL 1	S140
Falling through the cracks: a case study of how a timely integrated approach can reverse frailty.	Freer, Karen	2020	British Journal of Community Nursing	25	8	382-387
Frailty, Exercise and Nutrition	Michel, JP; Cruz-Jentoft, AJ; Cederholm, T	2015	CLINICS IN LIVER DISEASE	19	3	375-+
Effects of multi-domain interventions in (pre)frail elderly on frailty, functional, and cognitive status: a systematic review	Dedeyne, L; Deschodt, M; Verschueren, S; Tournoy, J; Gielen, E	2017	CLINICAL INTERVENTIONS IN AGING	12		873-896

Physical Exercise for Frailty and Cardiovascular Diseases	Ricci, NA; Cunha, AIL	2020	FRAILTY AND CARDIOVASCULAR DISEASES: RESEARCH INTO AN ELDERLY POPULATION	1216		115-129
Effects of resistance bands exercise for frail older adults: A systematic review and meta-analysis of randomised controlled studies	Saragih, ID; Saragih, IS; Batubara, SO; Yang, YP; Lin, CJ	2022	JOURNAL OF CLINICAL NURSING			43-61
Interventions to prevent or reduce the level of frailty in community-dwelling older adults: a scoping review of the literature and international policies.	PUTS, MARTINE T. E.; TOUBASI, SAMAR; ANDREW, MELISSA K.; ASHE, MAUREEN C.; PLOEG, JENNY; ATKINSON, ESTHER; AYALA, ANA PATRICIA; ROY, ANGELIQUE; MONFORTE, MIRIAM RODRÃ• GUEZ; BERGMAN, HOWARD; MCGILTON, KATHY	2017	Age & Ageing	46	3	383-392
Do home-based exercise interventions improve outcomes for frail older people? Findings from a systematic review.	Clegg, Andrew P; Barber, Sally E; Young, John B; Forster, Anne; Iliffe, Steve J	2012	Reviews in Clinical Gerontology	22	1	68-78

The functional effects of physical exercise training in frail older people: a systematic review.	Chin A Paw MJM; van Uffelen JGL; Riphagen I; van Mechelen W	2008	Sports Medicine	38	9	781-793
The effect of exercise on quality of life and activities of daily life in frail older adults: A systematic review of randomised control trials	Campbell, E; Petermann-Rocha, F; Welsh, P; Celis-Morales, C; Pell, JP; Ho, FK; Gray, SR	2021	EXPERIMENTAL GERONTOLOGY	147		
Exercise prescription to reverse frailty.	Bray, Nick W.; Smart, Rowan R.; Jakobi, Jennifer M.; Jones, Gareth R.	2016	Applied Physiology, Nutrition & Metabolism	41	10	1112-1116
Therapeutic interventions for frail elderly patients: part I. Published randomized trials.	Bibas, Lior; Levi, Michael; Bendayan, Melissa; Mullie, Louis; Forman, Daniel E; Afilalo, Jonathan	2014	Progress in Cardiovascular Diseases	57	2	134-143
Therapeutic Interventions for Frail Elderly Patients: Part II. Ongoing and Unpublished Randomized Trials.	Bendayan, Melissa; Bibas, Lior; Levi, Michael; Mullie, Louie; Forman, Daniel E; Afilalo, Jonathan	2014	Progress in Cardiovascular Diseases	57	2	144-151
Physical therapy treatment on frailty syndrome: systematic review.	Arantes PMM; Alencar MA; Dias RC; Dias JMD; Pereira LSM	2009	Brazilian Journal of Physical Therapy	13	5	365-375

Geroprotectors: A role in the treatment of frailty	Trendelenburg, AU; Scheuren, AC; Potter, P; Muller, R; Bellantuono, I	2019	MECHANISMS OF AGEING AND DEVELOPMENT	180		20-Nov
Outcomes of coordinated and integrated interventions targeting frail elderly people: a systematic review of randomised controlled trials.	Eklund K; Wilhelmson K	2009	Health & Social Care in the Community	17	5	447-458
Reversible Cognitive Frailty, Dementia, and All-Cause Mortality. The Italian Longitudinal Study on Aging.	Solfrizzi, Vincenzo; Scafato, Emanuele; Seripa, Davide; Lozupone, Madia; Imbimbo, Bruno P.; D'Amato, Angela; Tortelli, Rosanna; Schilardi, Andrea; Galluzzo, Lucia; Gandin, Claudia; Baldereschi, Marzia; Di Carlo, Antonio; Inzitari, Domenico; Daniele, Antonio; SabbÃ , Carlo; Logroscino, Giancarlo; Panza, Francesco	2017	Journal of the American Medical Directors Association	18	1	89.e1-89.e8
The role of nutrition and physical activity in frailty: A review	O'Connell, ML; Coppinger, T; McCarthy, AL	2020	CLINICAL NUTRITION ESPEN	35		1-11
A randomized, controlled trial of quadriceps resistance exercise and vitamin D in frail older people: the Frailty Interventions	Latham NK; Anderson CS; Lee A; Bennett DA; Moseley A; Cameron ID	2003	Journal of the American Geriatrics Society	51	3	291-299

Trial in Elderly Subjects (FITNESS)						
Assessing the feasibility and impact of specially adapted exercise interventions, aimed at improving the multi-dimensional health and functional capacity of frail geriatric hospital inpatients: protocol for a feasibility study	Doody, P; Lord, JM; Greig, CA; Whittaker, AC	2019	BMJ OPEN	9	11	e031159
New Evidence: Mediterranean: Diet Supports Healthy Aging: Popular eating pattern may help reduce frailty in older adults.	Tufts University	2018	Tufts University Health & Nutrition Letter	36	2	
The effects of a multi-component intervention on the functional capacity, lower-body muscle strength, balance and gait in frail community-dwelling older people: a randomised controlled trial protocol.	Iosimuta, Natalia C. R.; Pessanha, Fernanda P. A. S; Alves, Natalia; Marques, Larissa T.; Porto, Jaqueline M.; Freire, Renato C.; Ferriolli, Eduardo; de Abreu, Daniela C. C.	2020	European Journal of Physiotherapy	22	5	262-273
Outcomes in a multicomponent exercise programme in frail community-dwelling individuals	Anton, I.; Andueza, E.; Raposo, S.; Embil, X.; Yanguas, J.	2016	European Geriatric Medicine	7	Supplement 1	S115

Introducing an exercise intervention to reverse frailty and build resilience in primary care consultations	Travers, John; Romero-Ortuno, Roman; Cooney, Marie-Therese	2020	European Geriatric Medicine	11	SUPPL 1	S215
Exercise Prescription Intervention Plan for Pre-frail and Frail Elderly in New Taipei City: 1015 Board #276 May 30 3:30 PM - 5:00 PM...American College of Sports Medicine Annual Meeting, May 29-June 2, 2018, Minneapolis, Minnesota	Lin, Hui-Ping; Tseng, Yu-Ting; Lin, Chi-Hung		Medicine & Science in Sports & Exercise	50		241-241
Rethink rehabilitation to reverse frailty		2016	Respiratory Therapeutics Week			105
Avoiding frailty as you age: nutritional, physical, and cognitive modifications can help reverse or prevent the condition.(NUTRITION & FITNESS)	Yancy, William S., Jr	2017	Duke Medicine Health News	23	9	6
Can good nutrition, physical training and mental exercises reverse physical frailty in the elderly?	National University of Singapore	2017	Science Daily			
Frailty Intervention Trial (FIT)	Fairhall N; Aggar C; Kurrle SE; Sherrington C; Lord S;	2008	BMC Geriatrics	8		27-27

	Lockwood K; Monaghan N; Cameron ID					
Good nutrition, physical training and mental exercises can reverse physical frailty in the elderly	National University of Singapore	2017	Science Daily			
Protocol for the PREHAB study-Pre-operative Rehabilitation for reduction of Hospitalization After coronary Bypass and valvular surgery: a randomised controlled trial	Stammers, AN; Kehler, DS; Afilalo, J; Avery, LJ; Bagshaw, SM; Grocott, HP; Legare, JF; Logsetty, S; Metge, C; Nguyen, T; Rockwood, K; Sareen, J; Sawatzky, JA; Tangri, N; Giacomantonio, N; Hassan, A; Duhamel, TA; Arora, RC	2015	BMJ OPEN	5	3	e007250
Lifestyle interventions for frail obese older adults	Waters, Debra	2019	Aging Medicine and Healthcare	10	Supplement 1	3
Muscle strength training for reversing frailty: how strong is the evidence?.	Nunan, David	2019	BMJ evidence-based medicine	24	5	199-200
Study protocol of a randomised controlled trial to examine the impact of a complex intervention in pre-frail older adults.	Teh, Ruth; Kerse, Ngaire; Waters, Debra L.; Hale, Leigh; Pillai, Avinesh; Leilua, Evelingi; Tay, Esther; Rolleston, Anna; Edlin, Richard; Maxted, Eruera; Heppenstall, Claire; Connolly, Martin J.	2019	Aging Clinical & Experimental Research	31	10	1407-1417

Biology of frailty: Modulation of ageing genes and its importance to prevent age-associated loss of function	Vina, J; Tarazona-Santabalbina, FJ; Perez-Ros, P; Martinez-Arnau, FM; Borras, C; Olaso-Gonzalez, G; Salvador-Pascual, A; Gomez-Cabrera, MC	2016	MOLECULAR ASPECTS OF MEDICINE	50		88-108
Individualized intervention for frail non-dialysis elderly patients with chronic kidney disease: protocol for a randomized controlled trial.	Chang, Jing; Gao, Yun; Fang, Xiang-Yang; Zhao, Su-Mei; Hou, Yuan-Ping; Sun, Qian-Mei	2020	BMC Geriatrics	20	1	8-Jan
A Multi-Domain Intervention Protocol for the Potential Reversal of Cognitive Frailty: "WE-RISE" Randomized Controlled Trial	Murukesu, RR; Singh, DKA; Shahar, S; Subramaniam, P	2020	FRONTIERS IN PUBLIC HEALTH	8		471
An evaluation of the effectiveness of a multi-modal intervention in frail and pre-frail older people with type 2 diabetes--the MID-Frail study: study protocol for a randomised controlled trial.	RodrÃguez-MaÃ±as, Leocadio; Bayer, Antony J; Kelly, Mark; Zeyfang, Andrej; Izquierdo, Mikel; Laosa, Olga; Hardman, Timothy C; Sinclair, Alan J; Moreira, Severina; Cook, Justin	2014	Trials	15	1	34-34
CONQUERING FRAILTY WITH A MULTI-	Aumayr, G	2017	IDIMT-2017 - DIGITALIZATION IN MANAGEMENT,	46		211-216

PERSPECTIVE APPROACH			SOCIETY AND ECONOMY			
Frailty in olders of a day program outpatients centre	Cruz Santaella, A.; Garcia Castellanos, M.; Torrijos Montalban, A.; Moreno Gonzalez, A.; Cifuentes Caceres, R.; Ortega Herrera, M.; Lozano Serrano, V.	2011	European Geriatric Medicine	2	SUPPL. 1	S113-S114
Diet and Exercise for FRAILty (DEFRAIL): protocol for a study to examine the effect of a novel community-based group exercise and nutritional intervention, designed to reverse frailty in older adults.	Bambrick, Padraig; Phelan, Niamh; Grant, Emma; Byrne, Thomas; Harrison, Michael; Mulcahy, Riona; Cooke, John	2021	BMJ open	11	6	e042408
Protocol for a randomised controlled trial of a primary care intervention to Reverse Frailty and Enhance Resilience through Exercise and dietary protein Education (REFEREE) in community-dwelling adults aged 65 and over.	Travers, John; Romero-Ortuno, Roman; Power, Dermot; Doran, Peter; Langan, John; MacNamara, Fergal; McCormack, Darren; McDermott, Christopher; McEntire, Jude; McKiernan, Joanne; Vencken, Sebastian; Murphy, Andrew W; Murphy, Patrick J; Ni She, Eidin; O'Shea, Diarmuid; Cooney, Marie-Therese	2020	HRB open research	3	101754913	91
Efficacy of a primary care geriatric intervention model in reversing frailty-	Ferreira, Miguel Marques	2018	European Geriatric Medicine	9	Supplement 1	S92

protocol of a randomized clinical trial						
The effect of comprehensive assessment and multi-disciplinary management for the geriatric and frail patient: A multi-center, randomized, parallel controlled trial.	Yao, Simin; Zheng, Peipei; Ji, Liwei; Ma, Zhao; Wang, Lijuan; Qiao, Linlin; Wan, Yuhao; Sun, Ning; Luo, Yao; Yang, Jiefu; Wang, Hua	2020	Medicine	99	46	e22873-e22873
The EX-FRAIL CKD trial: a study protocol for a pilot randomised controlled trial of a home-based EXercise programme for pre-frail and FRAIL, older adults with Chronic Kidney Disease	Nixon, AC; Bampouras, TM; Gooch, HJ; Young, HML; Finlayson, KW; Pendleton, N; Mitra, S; Brady, ME; Dhaygude, AP	2020	BMJ OPEN	10	6	e035344
PREHAB study: a protocol for a prospective randomised clinical trial of exercise therapy for people living with frailty having cancer surgery	McIsaac, DI; Saunders, C; Hladkowicz, E; Bryson, GL; Forster, AJ; Gagne, S; Huang, A; Lalu, M; Lavallee, LT; Moloo, H; Nante, J; Power, B; Scheede-Bergdah, C; Taljaard, M; van Walraven, C; McCartney, CJL	2018	BMJ OPEN	8	6	
Barriers to enrollment in an exercise intervention for pre-frail	Martinchek, M.; Huisingh-Scheetz, M.; Thompson, K.; Pachwicewicz, P.; Ferguson, M.	2016	Journal of the American Geriatrics Society	64	SUPPL. 1	S277

and frail thoracic surgery patients						

Wrong Type of Intervention/ Frail Population (n= 38)

Title	Authors	Year	Journal	Volume	Issue	Pages
Effects of Home-Based Physical Exercise on Days at Home and Cost-Effectiveness in Pre-Frail and Frail Persons: Randomized Controlled Trial.	Suikkanen, Sara A.; Soukkio, Paula K.; Aartolahti, Eeva M.; Kautiainen, Hannu; KÃ¤Ã¤riÃ¤, Sanna M.; Hupli, Markku T.; SipilÃ¤, Sarianna; PitkÃ¤lÃ¤, Kaisu H.; Kukkonen-Harjula, Katriina T.	2021	Journal of the American Medical Directors Association	22	4	773-779
Preoperative Home-Based Physical Therapy Versus Usual Care to Improve Functional Health of Frail Older Adults Scheduled for Elective Total Hip Arthroplasty: A Pilot Randomized Controlled Trial.	Oosting, Ellen; Jans, Marielle P.; Dronkers, Jaap J.; Naber, Roelfrieke H.; Dronkers-Landman, Christa M.; Appelman-de Vries, Suzan M.; van Meeteren, Nico L.	2012	Archives of Physical Medicine & Rehabilitation	93	4	610-616
Home-based preoperative rehabilitation (prehab) to improve physical function and reduce hospital length of stay	Waite, Iain; Deshpande, Ranjit; Baghai, Max; Massey, Tania; Wendler, Olaf; Greenwood, Sharlene	2017	Journal of Cardiothoracic Surgery	12		1-7

for frail patients undergoing coronary artery bypass graft and valve surgery.						
The Characteristic of a Simple Exercise Program under the Instruction of Physiotherapists-For General Elderly People and Frail Elderly People	Nakagawa, K; Inomata, N; Konno, Y; Nakazawa, R; Hagiwara, K; Sakamoto, M	2008	JOURNAL OF PHYSICAL THERAPY SCIENCE	20	4	197-203
The effects of exercise and protein-energy supplements on body composition and muscle function in frail elderly individuals: a long-term controlled randomised study	Bonnefoy, M; Cornu, C; Normand, S; Boutitie, F; Bugnard, F; Rahmani, A; Lacour, JR; Laville, M	2003	BRITISH JOURNAL OF NUTRITION	89	5	731-738
Feasibility and effectiveness of a cosmetic intervention program for institutionalized older women in Japan.	Hayakawa, Yohko; Shoji, Ikuko; Kumon, Hiroko; Tokita, Masumi; Kamata, Masazumi; Arao, Takashi	2016	Preventive medicine reports	4	101643766	242-7
A home-based exercise program focused on proprioception to reduce falls in frail and pre-frail community-dwelling older adults.	PÃ©rez-Ros, Pilar; Vila-Candel, Rafael; MartÃnez-Arnau, Francisco Miguel	2020	Geriatric Nursing	41	4	436-444

Older persons with signs of frailty in a home-based physical exercise intervention: baseline characteristics of an RCT.	Suikkanen, Sara; Soukkio, Paula; PitkÃ¤lÃ¤, Kaisu; KÃ¤Ã¤riÃ¤, Sanna; Kautiainen, Hannu; SipilÃ¤, Sarianna; Kukkonen-Harjula, Katriina; Hupli, Markku	2019	Aging Clinical & Experimental Research	31	10	1419-1427
Effect of a multifactorial interdisciplinary intervention on mobility-related disability in frail older people: randomised controlled trial.	Fairhall, Nicola; Sherrington, Catherine; Kurrle, Susan E; Lord, Stephen R; Lockwood, Keri; Cameron, Ian D	2012	BMC Medicine	10	1	120-120
Effects of Whole-Body Vibration Training on the Physical Function of the Frail Elderly: An Open, Randomized Controlled Trial.	Wadsworth, Daniel; Lark, Sally	2020	Archives of Physical Medicine & Rehabilitation	101	7	1111-1119
Effects of exercise training added to ongoing hormone replacement therapy on bone mineral density in frail elderly women.	Villareal DT; Binder EF; Yarasheski KE; Williams DB; Brown M; Sinacore DR; Kohrt WM	2003	Journal of the American Geriatrics Society	51	7	985-990
The effects of a life goal-setting technique in a preventive care program for frail community-dwelling older people: a cluster	Yoshimi Yuri; Shinichi Takabatake; Tomoko Nishikawa; Mari Oka; Taro Fujiwara; Yuri, Yoshimi; Takabatake, Shinichi; Nishikawa, Tomoko; Oka, Mari; Fujiwara, Taro	2016	BMC Geriatrics	16		1-11

nonrandomized controlled trial.						
A pilot randomized controlled trial to improve geriatric frailty.	Chan, Ding-Cheng Derrick; Tsou, Hsiao-Hui; Yang, Rong-Sen; Tsauo, Jau-Yih; Chen, Ching-Yu; Hsiung, Chao Agnes; Kuo, Ken N	2012	BMC Geriatrics	12	1	58-58
Additive Role of a Potentially Reversible Cognitive Frailty Model and Inflammatory State on the Risk of Disability: The Italian Longitudinal Study on Aging	Italian Longitudinal Study Aging; Solfrizzi, V; Scafato, E; Lozupone, M; Seripa, D; Giannini, M; Sardone, R; Bonfiglio, C; Abbrescia, DI; Galluzzo, L; Gandin, C; Baldereschi, M; Di Carlo, A; Inzitari, D; Daniele, A; Sabba, C; Logroscino, G; Panza, F	2017	AMERICAN JOURNAL OF GERIATRIC PSYCHIATRY	25	11	1236-1248
Progressive functional wii-hab in pre-frail older adults	Daniel, K.M.; Cason, C.; Ray, C.	2011	Journal of the American Geriatrics Society	59	SUPPL. 1	S157
Nutritional interventions to prevent and treat frailty.	Cruz-Jentoft, Alfonso J.; Woo, Jean	2019	Current Opinion in Clinical Nutrition & Metabolic Care	22	3	191-195
Effectiveness of a community-wide intervention for population-level frailty and functional health in older adults: A 2-year cluster nonrandomized controlled trial.	Seino, Satoshi; Tomine, Yui; Nishi, Mariko; Hata, Toshiki; Fujiwara, Yoshinori; Shinkai, Shoji; Kitamura, Akihiko	2021	Preventive Medicine	149		N.PAG-N.PAG

Effectiveness of interventions to prevent pre-frailty and frailty progression in older adults: a systematic review.	ApÃ³stolo, JoÃ£o; Cooke, Richard; Bobrowicz-Campos, Elzbieta; Santana, Silvina; Marcucci, Maura; Cano, Antonio; Vollenbroek-Hutten, Miriam; Germini, Federico; D'Avanzo, Barbara; Gwyther, Holly; Holland, Carol	2018	JBI Database of Systematic Reviews & Implementation Reports	16	1	140-232
Effectiveness of an individually tailored home-based exercise rogramme for pre-frail older adults, driven by a tablet application and mobility monitoring: a pilot study	Geraedts, HAE; Dijkstra, H; Zhang, W; Ibarra, F; Far, IK; Zijlstra, W; Stevens, M	2021	EUROPEAN REVIEW OF AGING AND PHYSICAL ACTIVITY	18	1	
Effectiveness of an intervention to prevent frailty in pre-frail community-dwelling older people consulting in primary care: a randomised controlled trial.	SERRA-PRAT, M.; SIST, X.; DOMENICH, R.; JURADO, L.; SAIZ, A.; ROCES, A.; PALOMERA, E.; TARRADELLES, M.; PAPIOL, M.	2017	Age & Ageing	46	3	401-407
Effects of elastic band exercise on the frailty states in pre-frail elderly people.	Chen, Rujie; Wu, Qingwen; Wang, Dongyan; Li, Zhou; Liu, Howe; Liu, Guangtian; Cui, Ying; Song, Linlin	2020	Physiotherapy Theory & Practice	36	9	1000-1008
Effectiveness of an intervention to prevent frailty in pre-frail community-dwelling	Serra-Prat, M; Sist, X; Domenich, R; Jurado, L; Saiz, A; Roces, A; Palomera, E; Tarradelles, M; Papiol, M	2017	AGE AND AGEING	46	3	401-407

older people consulting in primary care: a randomised controlled trial						
MULTI-COMPONENT EXERCISE WITH HIGH-INTENSITY, FREE-WEIGHT, FUNCTIONAL RESISTANCE TRAINING IN PRE-FRAIL FEMALES: A QUASI-EXPERIMENTAL, PILOT STUDY	Bray, NW; Jones, GJ; Rush, KL; Jones, CA; Jakobi, JM	2020	JOURNAL OF FRAILTY & AGING	9	2	111-117
Association between frailty and delirium in older adult patients discharged from hospital	Verloo, H; Goulet, C; Morin, D; von Gunten, A	2016	CLINICAL INTERVENTIONS IN AGING	11		55-63
Rodent models of frailty and their application in preclinical research	Banga, S; Heinze-Milne, SD; Howlett, SE	2019	MECHANISMS OF AGEING AND DEVELOPMENT	179		1-10
Frailty and Sarcopenia in Older Patients Receiving Kidney Transplantation	Gandolfini, I; Regolisti, G; Bazzocchi, A; Maggiore, U; Palmisano, A; Piotti, G; Fiaccadori, E; Sabatino, A	2019	FRONTIERS IN NUTRITION	6		169
"I Don't Feel Like Myself".	Firnhaber, Gina C.; Kolasa, Kathryn M.	2016	Nutrition Today	51	6	281-289
Allicin Reversed the Process of Frailty in	Liu, Yang; You, Meigui; Shen, Jianwei; Xu, Yaping;	2020	Journals of Gerontology Series A: Biological	75	5	821-825

Aging Male Fischer 344 Rats With Osteoporosis.	Li, Lin; Wang, Dongtao; Yang, Yajun		Sciences & Medical Sciences			
Voluntary Aerobic Exercise Reverses Frailty in Old Mice.	Graber, Ted G; Ferguson-Stegall, Lisa; Liu, Haiming; Thompson, LaDora V	2015	Journals of Gerontology Series A: Biological Sciences & Medical Sciences	70	9	1045-1058
Effectiveness of an intervention in multicomponent exercise in primary care to improve frailty parameters in patients over 70â€‰years of age (MEFAP-project), a randomised clinical trial: rationale and study design.	Castell, M. V.; GutiÃ©rrez-Misis, A.; SÃ¡nchez-MartÃ-nez, M.; Prieto, M. A.; Moreno, B.; NuÃ±ez, S.; Triano, R.; de Antonio, M. P.; Mateo, C.; Cano, M. D.; Garrido, A.; Julian, R.; Polentinos, E.; Rodriguez-Barrientos, R.; Otero Puime, A.	2019	BMC Geriatrics	19	1	9-Jan
Frail older adultsâ€™ perceptions of an in-hospital structured exercise intervention.	Oâ€™Hare, Louise; Savage, Eileen; McCullagh, Ruth; Bantry White, Eleanor; Fitzgerald, Eilis; Timmons, Suzanne	2017	Physiotherapy	103	4	478-484
Effectiveness of the PROMUFRA program in pre-frail, community-dwelling older people: A randomized controlled trial.	Barrachina-Igual, JoaquÃn; MartÃnez-Arnau, Francisco M.; PÃ©rez-Ros, Pilar; Flor-Rufino, Cristina; Sanz-Requena, Roberto; Pablos, Ana	2021	Geriatric Nursing	42	2	582-591
Frail older adults' perceptions of an in-hospital structured exercise intervention	Broderick, L.; Savage, E.; McCullagh, R.; Bantry-White, E.; Timmons, S.	2013	Irish Journal of Medical Science	182	SUPPL. 6	S240

Implementation and Evaluation of a Fall Risk Screening Strategy Among Frail Older Adults for the Primary Care Setting: A Study Protocol	Meekes, WMA; Leemrijse, CJ; Korevaar, JC; Henquet, JMAE; Nieuwenhuis, M; van de Goor, LAM	2020	CLINICAL INTERVENTIONS IN AGING	15		1625-1636
Corrigendum: Effectiveness of interventions to prevent pre-frailty and frailty progression in older adults: A systematic review (JBI Database of Systematic Reviews and Implementation Reports (2018) 16:1 (140-232) DOI: 10.11124/JBISRIR-2017-003382)	Apostolo, Joao; Bobrowicz-Campos, Elzbieta; Cooke, Richard; Gwyther, Holly; Holland, Carol; Santana, Silvina; Marcucci, Maura; Germini, Federico; Cano, Antonio; Vollenbroek-Hutten, Miriam; D'Avanzo, Barbara	2018	JBI Database of Systematic Reviews and Implementation Reports	16	5	1282-1283
Functional and cognitive impairment prevention through early physical activity for geriatric hospitalized patients: study protocol for a randomized controlled trial.	MartÃnez-Velilla, NicolÃ¡s; Casas-Herrero, Alvaro; Zambom-Ferraresi, FabrÃ-cio; SuÃ¡rez, Nacho; Alonso-Renedo, Javier; ContÃn, Koldo Cambra; de Asteasu, Mikel LÃ³pez-SÃ¡ez; Echeverria, Nuria Fernandez; LÃ¡zaro, MarÃa Gonzalo; Izquierdo, Mikel	2015	BMC Geriatrics	15	1	9-Jan
Extracellular vesicles from young mice improve physiological	Borras, C.	2021	European Journal of Clinical Investigation	51	SUPPL 1	123

functions and reverse frailty in aged mice						
Approach to frailty in the elderly in primary care and the community.	Christine Yuanxin Chen; Peiying Gan; Choon How How; Chen, Christine Yuanxin; Gan, Peiying; How, Choon How	2018	Singapore Medical Journal	59	5	240-245