Frailty in later life

Frailty in Later Life:

Focus on Assessment, Life Course and Context

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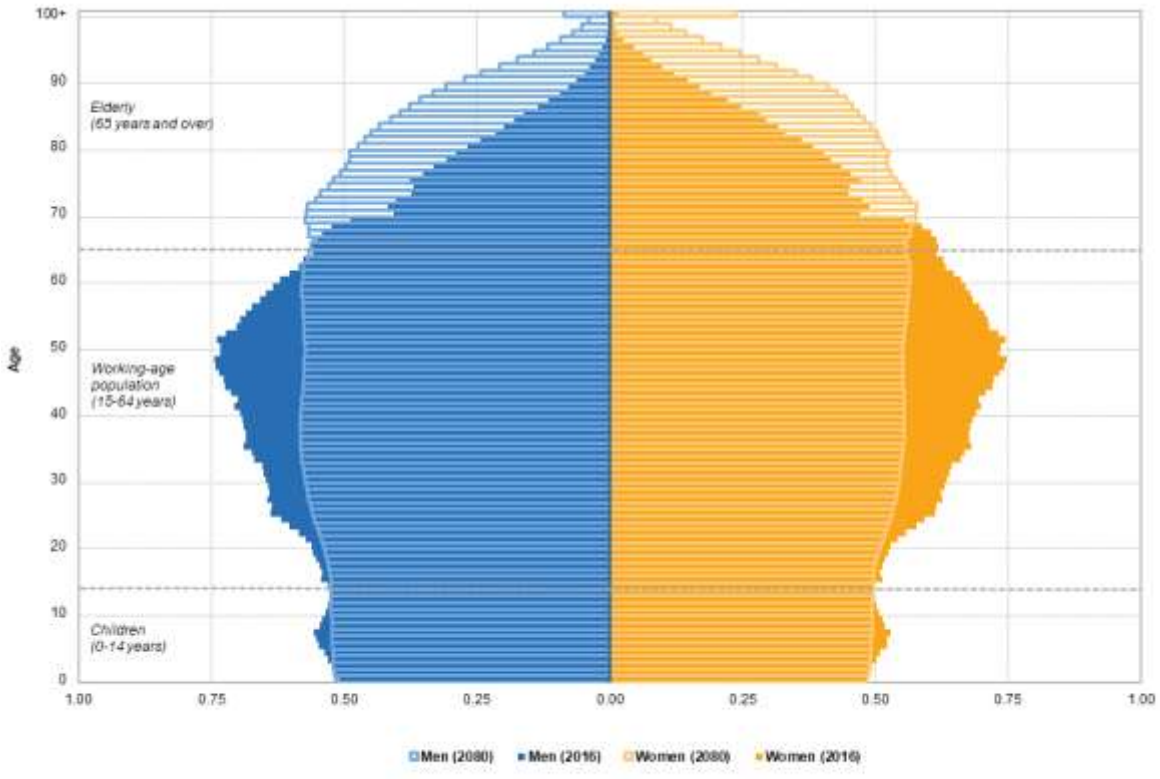
Chapter 1

General introduction

Aging society

Western societies are aging rapidly. This demographic shift is caused by a combination of factors [1]. First, western societies are characterized by an increased life expectancy and a decrease in the death rate [2]. On the one hand, the increase in life expectancy and the drop in the death rate are caused by discoveries in modern medicine, which enable people with chronic diseases to survive much longer, and a healthier lifestyle, but on the other hand, they are also caused by a large decrease in infant mortality [2, 3]. Second, after the Second World War, many western countries had a rise in birth rate marked as 'the baby boom' [1, 4, 5]. Consequently, the shape of the population pyramid is changing into a population condom (see Figure 1). Expectations with regard to the future population growth suggest that the educational attainment of females and access to contraception will hasten the decline in fertility and slow the population growth but will lead to an increase of the proportion of older adults in society [6].

Table 1: Population pyramid



Note: 2016, estimates. 2080: projections.
Source: Eurostat (online data codes: demo_pjan and proj_15npms)

At the beginning of 2018, the percentage of people of 65 years and older in the European Union (EU-28) was 19.7% [2]. Demographic studies indicate that this number will increase to approximately 30% in 2060 [2, 7]. Therefore, a more optimal and efficient organization of health care systems is needed.

The aging society (and demographic shift) has profound implications. For older adults, years gained can be overshadowed by functional, mental, and social decline. Several physical (e.g., heart disease, stroke) and cognitive problems (e.g., dementia) are among the many morbidities related to old age. The demographic shift also causes societal challenges, for instance, an increase in the need for long term care and a shrinking labor force while more people will be needed to care for older adults (dependency ratio) [7].

This aging society causes challenges but also offers opportunities. Aging pushes society into making use of its underused human potential. As people live longer, older persons have accumulated expertise, knowledge, and experience to an extent that was not common in earlier times [7]. Current policies put a lot of emphasis on facilitating 'healthy aging' and 'aging in place' [7, 8]. Healthy aging is defined as "The process of developing and maintaining the functional ability that enables well-being in older age and preserves autonomy" [9]. Functional ability means having the health-related capabilities that enable people to be and do what they prefer and value [8]. This includes having the ability to meet their basic needs; learn, grow, and make decisions; be mobile; build and maintain relationships; and contribute to society [8].

Aging in place is, according to the World Health Organization (WHO) (2015): "Meeting the desire and ability of people, through the provision of appropriate services and assistance, to remain living relatively independently in the community in his or her current home or an appropriate level of housing" [8]. Aging in place is considered and perceived as being better for an older person [8]. Older adults, themselves, mostly express their wish to live at home as long as possible as well [10, 11]. From a policy perspective, aging in place may also hold significant financial advantages in terms of health-care expenditures (WHO), although it should not be viewed as a good policy to simply minimize costs by failing to provide more costly alternatives. Recently, the WHO extended the concept of aging in place into aging in

the ‘right’ place, which means the ability to live in the place with the closest fit with the person’s needs and preferences, which may or may not be one’s own home [8].

Within the light of the concepts of healthy aging and aging well in place, the concept of frailty is very relevant. Research clearly shows that frailty is associated with adverse outcomes, including mortality, institutionalization, and hospitalization [12-16]. However, frailty is also related with outcomes like quality of life, life satisfaction, and well-being [17-21]. Consequently, frailty is a threat for healthy aging and aging well in place.

Concepts of the present dissertation

Frailty in later life: Conceptualization and operationalization

Frailty is an often-used concept by clinicians [22, 23]. The term 'frail elderly' was introduced to describe a particular and vulnerable segment of the older population [23]. The Federal Council on Aging (US), in 1978, defined frailty as "Persons, usually but not always over the age of 75, who because of an accumulation of various continuing problems often require one or several supportive services in order to cope with daily life" [24]. Nowadays, there is still no generally accepted definition, but there are three elements that all frailty definitions have in common [25]:

1) frailty is a geriatric syndrome associated with an increased risk of adverse health outcomes, such as functional decline, hospitalization, and mortality;

2) the increased risk of adverse health outcomes is the result of the loss of resources or reserve capacity;

3) frailty is a dynamic state that can change (improve or deteriorate) over time.

Meanwhile, various conceptualizations of frailty exist in current research.

The first, often designated as a unidimensional, biomedical conceptualization or physical frailty, emphasizing frailty as a biological/medical concept, is defined as "A medical syndrome with multiple causes and contributors that is characterized by diminished strength, endurance, and reduced physiologic function that increases an individual's vulnerability for developing increased dependency and/or death" [12]. This conceptualization of frailty is mostly operationalized by the Fried Phenotype with five criteria: weight loss, weakness, exhaustion, slowness, and low physical activity. Older adults meeting three or more criteria are classified as frail, while older adults meeting 1 or 2 criteria are classified as pre-frail. When an older adult does not meet any of the criteria, he/she is classified as robust [26]. This biomedical conceptualization of frailty is criticized because it does not include psychological, social, and cognitive factors [23, 27], since older adults do not experience frailty solely as a physical problem [28].

A second conceptualization of frailty is the deficit model of Rockwood et al. [29]. They operationalize frailty as an accumulation of deficits. In this approach, older adults are assessed

by the presence of a set of clinical deficits (e.g., physical status, memory, and mood) [29]. The mostly used operationalization of the present approach is the frailty index that includes 70 items.

A third conceptualization of frailty attempts to be integrative and has a multidimensional perspective on frailty. In addition to physical features such as strength or endurance, this approach emphasizes cognitive, social, and psychological factors, which is more in line with the perception and experiences of older adults themselves [7]. According to this integrative approach, frailty is described as "A dynamic state affecting an individual who experiences losses in one or more domains of human functioning, increasing the risk of adverse outcomes" [30]. In general, the integrative approach of frailty includes physical, cognitive, social, and psychological factors such as those measured by the Groningen Frailty Indicator (GFI) and the Tilburg Frailty Indicator (TFI) [31, 32]. Some researchers also point to the addition of environmental factors associated with frailty, such as the Comprehensive Frailty Assessment Instrument (CFAI) [27, 33, 34].

Studies show that the different methods to conceptualize and operationalize frailty result in widely differing prevalence figures of frailty. According to a systematic review, the prevalence of frailty in older adults ranges from 4.0% to 59.1% [35]. Therefore, one can assume that these differences between frailty measurements also could have a strong influence on the outcomes of a study. Since 'being frail' is often used as an inclusion criterion, the selected frailty measurement can have a major impact on the number and characteristics of the included study subjects [36]. Furthermore, one can expect that depending on the selected frailty assessment, differences can occur on who will be included and also with respect to the characteristics of the selected frail sample. Comparative studies with regard to the interrelatedness between frailty scales are rather scarce. In addition, the impact of the used frailty measurements on the characteristics of a selected 'frail sample' remains unclear. Therefore, a better understanding of the similarities and differences between these scales and instruments is needed.

When screening large populations, a short and feasible frailty screener is necessary. Therefore, frailty scales that include a long list of questions to measure the frailty level or

make use of performance-based measures can be difficult to conduct because they are time consuming and costly and often require well-trained assessors [26, 32]. Within this light, a two-step approach is suggested, with a short screening tool as an initial indicator in a sequential process towards a more comprehensive assessment [37]. Therefore, many researchers often simplify the initial frailty instrument by making it shorter or using questionnaires instead of performance-based measures. Such substitution questions are often suggested also for the two performance-based measures of the Fried frailty criteria. A review shows a large variation in how these performance-based measures are assessed [38]. Moreover, in most studies, the validity of these questions has not been tested or at least not been reported.

Since all these differences cause variations in the frailty prevalence estimates and in the predictive ability of the measurements, it is unclear which question (or set of questions) can adequately substitute the performance-based measures of the Fried frailty phenotype in the identification of frail older people. Therefore, there is need to test the psychometric properties of such replacement questions for performance-based tests.

Early detection and a proactive approach of frailty

In general, frailty is defined as a dynamic state that can change (improve or deteriorate) over time. There is evidence that frailty in an early state may be reversible [39]. However, the evidence for reversibility of frailty at a later stage is rather limited. Only a small group of older adults seems to benefit from intervention programs [40]. Therefore, early detection and a proactive frailty approach may be important. An approach that can facilitate early detection of frailty is to identify risk factors for frailty and to develop risk profiles. Previous studies mainly focused on profiles of physical frailty [41]. In response to this, Dury et al. (2017) used the Belgian Ageing Studies dataset (BAS) to observe risk factors for four different domains of frailty (i.e., physical, social, environmental, and psychological) stratified by sex [42]. Sociodemographic risk factors were age, marital status, relocated in the past 10 years, and country of birth. Socioeconomic risk factors were net household income and education [42]. These risk factors differ depending on the frailty domain and sex. Currently, it is not clear if selecting older people based on these risk factors is, indeed, an effective way of identifying frail older people in preventive home visits.

Findings from the social, psychological, epidemiological, and biological sciences show an interconnection of experiences in the younger life on health and aging in later life [43]. Having a low socio-economic status is a predictor for adverse health outcomes in adulthood [44]. In addition, there is evidence that life events (e.g., job loss) can have a negative effect on physical or mental health [45, 46]. Therefore, more focus on a life-course perspective may be helpful in acquiring a better understanding of the development of frailty and might give insights into strategies to detect/prevent frailty in time [47]. As outlined in the Minsk Declaration on the Life-course perspective in the Context of Health 2020, this approach recognizes that all stages of a person's life are intricately intertwined not only with each other but also with the lives of family members (past, present, and future) and other people in society. The WHO states that "It takes a temporal and societal perspective of the health of individuals and generations. Thereby, acknowledges a life course perspective that health and well-being depend on interactions between risk and protective factors throughout people's lives" [48]. Currently, only a few studies focus on or emphasize the life course perspective within the field of frailty research. There is evidence that childhood (hunger, poor health, and poor socioeconomic conditions), adulthood (little education and non-white-collar occupation), and current social conditions (insufficient income) are associated with higher odds of frailty [49]. A study has also found an association between life events and psychological frailty [50]. Kuh describes the importance that the life course perspective can have in frailty research [47]. Looking for important events/transitions in a lifetime in association with frailty in later life might be beneficial to develop a proactive strategy to prevent frailty and facilitate healthy aging and aging (well) in place [51-54]. Therefore, more research is needed to focus on frailty in the light of the life course perspective.

Frailty and complex interventions

Frailty is associated with adverse outcomes, such as hospitalization, mortality, and institutionalization [55]. Nevertheless, frailty is considered to be dynamic with the potential to improve. Therefore, developing interventions involves a critical step in decreasing adverse health outcomes in frail older adults [56]. So far, various types of interventions have been proposed, such as physical activity, psychosocial interventions, adequate health and social care provision, cognitive stimulation, optimizing nutrition, deprescribing in older people with polypharmacy, interventions based on information and communication technologies, and

more multifactorial interventions [57-59]. Most of these are complex interventions. The key features of a complex intervention are: 1) the number of interacting components and the number and complexity of behaviors required by those delivering or receiving the intervention, 2) the number of groups or organizational levels targeted by the intervention, 3) the number and variability of outcomes, and 4) the degree of flexibility or tailoring of the intervention permitted [60].

In complex interventions, the results are subject to mixed outcome patterns depending on the context in which an intervention is implemented. The role of implementers and the local setting may activate different mechanisms that may moderate the effect of an intervention [61]. It is argued that some contexts are supportive for an intervention while others are not [62]. However, it is still unclear how effective these interventions are in frail community-dwelling older adults, which types of interventions are more likely to be effective, and whether these interventions can be influenced by external factors. Therefore, a more in-depth analysis is needed in the effectiveness of complex interventions.

The D-SCOPE Project

The present doctoral dissertation is written in the frame of the D-SCOPE project (Detection - Support, Care for Older People: Prevention and Empowerment) [63]. D-SCOPE is a four-year international research project, financed by the Flemish government agency for Innovation by Science and Technology [IWT-140027 Strategisch Basis Onderzoek (SBO)] (2015-2018). The D-SCOPE consortium is a multidisciplinary group composed of researchers from five universities/colleges: Maastricht University, Universiteit Antwerpen, Hogeschool Gent, KU Leuven and Vrije Universiteit Brussel. The focus of D-SCOPE has been the targeted detection of frail older adults in their local environment. The project contributes to the development of new methodologies for the prevention of frailty in older adults, so they can age in their own homes in good quality of life. The D-SCOPE project starts from a multidimensional perspective on frailty, including physical, cognitive, psychological, social and environmental frailty and focuses on positive outcomes like mastery, life satisfaction and meaning in life. In order to achieve this, the D-SCOPE project was divided in three research phases. In the first phase, risk profiles were determined through data from the Belgian Ageing Studies. In the second phase, balancing factors and life events were explored by means of 121 individual interviews with frail older people. The third and last phase consisted of a randomized controlled trial (RCT) in three municipalities (Ghent, Knokke-Heist and Thienen) among 869 older adults. The respondents in the experimental group received a home visit from a social worker of the municipality and were referred to tailored care and support when needed.

Aims and research questions

In current policies, more and more focus is put on facilitating 'healthy aging' and 'aging (well) in place'. However, a better understanding of how to do this is needed. So, in this respect, attention for phenomena such as the conceptualization and operationalization of frailty, the life course of older adults, and (complex) interventions in frail older adults is important.

Therefore, the present dissertation has three objectives:

First, many frailty scales have been developed in the last two decades. It is unknown how these frailty scales are related to each other since comparative studies between these frailty scales are scarce and mainly focus on the predictability for adverse outcomes (e.g., mortality, hospitalization). Therefore, the first aim is to get a better understanding of the interrelatedness of the frailty measurements.

Second, frailty may be reversible when detected at an early stage (pre-frail). Therefore, early detection and a proactive approach are important. In this dissertation, we will study strategies that facilitate early detection and a proactive approach by means of studying risk factors but also focus on an earlier stage of a person's life.

Third, to prevent frailty, interventions are important. The last objective of the present dissertation is to expand our knowledge with regard to the effectiveness of interventions and the aspects that should be taken into account when doing a (complex) intervention study. Therefore, we focus on the context in which an intervention is implemented and to what extent the context may have an impact on the results.

Research Questions (RQ)

PART I: The relatedness of frailty conceptualizations and operationalizations (aim 1)

RQ 1 - What are the concordances and differences between a unidimensional (Fried Phenotype) and a multidimensional assessment (CFAI) of frailty? (*Chapter 2)*

RQ 2 - To what extent do the characteristics of 'frail participants' differ, depending on the used frailty measurement? *(Chapter 2)*

RQ 3 - What is the concordance between the two-overall operationalizations of the Fried scales? (*Chapter 3)*

PART II: Early detection and proactive approach of frailty (aim 2)

RQ 4 - Can a larger number of frail older adults be detected by means of preventive home visits by using risk factors as developed by Dury et al. (2017)? *(Chapter 4)*

RQ 5 - What is the relationship between the determining factors of retirement and frailty in later life? (*Chapter 5)*

RQ 6 - What is the relationship between age of retirement and frailty? (*Chapter 6)*

PART III: complex interventions in frailty studies (aim 3)

RQ 7 - What effect do interventions have on frail community-dwelling older adults in terms of mortality, hospitalization, formal health costs, accidental falls, and institutionalization? (*Chapter 7)*

RQ 8 - How do age, study time, approach of frailty and recruitment of participants influence the effect of an intervention to prevent adverse frailty outcomes in community-dwelling elderly? (*Chapter 7)*

RQ 9 - Are there relevant standardized web-based public data available in the three municipalities, participating in the D-SCOPE project? *(Chapter 8)*

RQ 10 - How can the contextual factors most likely to interact with the intervention and moderate its outcomes be determined? (*Chapter 8)*

The thesis is divided in three consecutive parts:

Part 1 is about the conceptualization and operationalization of frailty measurements and includes two chapters (RQ 1 to 3). Chapter 2 presents the results of a cross- sectional study that compares two frailty scales: the Fried Phenotype and the Comprehensive Frailty Assessment Instrument (CFAI). The relatedness between both scales is tested, as well as if the frail subjects have different characteristics. In chapter 3, in a cross-sectional study, it is examined whether six questions are able to replace performance-based measures of walking time and handgrip strength (two Fried Phenotype Criteria).

Part 2 focuses on early detection and the life course perspective and includes chapters 4, 5 and 6 (RQ 4 to 7). In chapter 4, the aim is to validate several risk factors for multidimensional frailty. Chapter 5 and 6 are both cross-sectional studies in which the focus is on the potential relation between the transition towards retirement on the one hand and the development of frailty in later life on the other hand. More specific, in chapter 5 the motivation of a person's retirement and its relation with frailty in later life is examined and in chapter 6, the association between age of retirement and frailty.

Part 3 includes chapter 7 and 8 and deals with the (complex) interventions (RQ 8 to 10). In chapter 7, the results of a systematic review and meta-analysis are presented. The effect of interventions (RCTs) in community-dwelling frail older adults are examined on adverse outcomes. In chapter 8, a 5-step approach is described to find relevant contextual factors that may moderate the effect of an intervention. This 5-step approach is also applied on the D-SCOPE trial in which a home visit is implemented in three municipalities.

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Chapter 2

Concordances and differences between a unidimensional and multidimensional assessment of frailty: a cross-sectional study

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Abstract

Background: Many instruments to identify frail older people have been developed. One of the consequences is that the prevalence rates of frailty vary widely dependent on the instrument selected. The aims of this study were 1) to examine the concordances and differences between a unidimensional and multidimensional assessment of frailty, 2) to assess to what extent the characteristics of a 'frail sample' differ depending on the selected frailty measurement because 'being frail' is used in many studies as an inclusion criterion.

Methods: A cross-sectional study was conducted among 196 community-dwelling older adults (≥60 years), which were selected from the census records. Unidimensional frailty was operationalized according to the Fried Phenotype (FP) and multidimensional frailty was measured with the Comprehensive Frailty Assessment Instrument (CFAI). The concordances and differences were examined by prevalence, correlations, observed agreement and Cohen's kappa. Differences between sample characteristics (e.g., age, physical activity, life satisfaction) were investigated with ANOVA and Kruskal-Wallis test.

Results: The mean age was 72.74 (SD 8.04) and 48.98% was male. According to the FP, 23.59% was not-frail, 56.92% pre-frail and 19.49% was frail. According to the CFAI, 44.33% was no-to-low frail, 37.63% was mild frail and 18.04% was high frail. The correlation between FP and the CFAI was r=0.46 and the observed agreement was 52.85%. The Cohen's kappa value was κ=0.35 (quadratic κ=0.45). In total, 11.92% of the participants were frail according to both measurements, 7.77% was solely frail according to the FP and 6.21% was solely frail according to the CFAI. The 'frail sample respondents' according to the FP had higher levels of life satisfaction and net income, but performed less physical activities in comparison to high frail people according to the CFAI.

Conclusion: The present study shows that the FP and CFAI partly measure the same 'frailty-construct', although differences were found for instance in the prevalence of frailty and the composition of the 'frail participants'. Since 'being frail' is an inclusion criterion in many studies, researchers must be aware that the choice of the frailty measurement has an impact on both the estimates of frailty prevalence and the characteristics of the selected sample.

Introduction

Frailty is an emerging concept, although no agreement exists about its definition [1, 2]. Consequently, many instruments for identifying frail older adults have been developed [3]. Initially, frailty was often designated as a unidimensional construct, defined as: “A medical syndrome with multiple causes and contributors that is characterized by diminished strength, endurance, and reduced physiologic function that increases an individual’s vulnerability for developing increased dependency and/or death” [4]. An example of such a (bio)medical, unidimensional approach to operationalize frailty is the Fried Phenotype (FP) [5]. Nowadays, some conceptual models of frailty attempt to be integrative [6]. Such an integrative approach has a multidimensional perspective, and in addition to physical features such as grip strength or endurance, social and/or psychological domains are also included [7, 8]. More recently, the environmental domain has been added as well [9]. An example of an integrative, multidimensional definition of frailty is: “A dynamic state affecting an individual who experiences losses in one or more domains of human functioning (physical, psychological, social), which is caused by the influence of a range of variables and which increases the risk of adverse outcomes” [2]. In line with this, the Comprehensive Frailty Assessment Instrument (CFAI) for instance, is an assessment with a multidimensional perspective on frailty [9].

Prior research showed that the different operationalizations of frailty have an important impact on the classification of older adults as frail or not-frail; as a consequence, the prevalence of frailty differs widely across studies depending on the used frailty assessment [10]. According to a systematic review, the prevalence estimates of frailty range from 4.0% till 59.1% [10]. In addition, a previous study, comparing four frailty scales in the same population, estimated a prevalence rate of frailty ranging between 22.2% (FP) and 64.8% (Tilburg Frailty Indicator, TFI) [11]. Furthermore, Ntanasi et al. compared five frailty scales whereby the prevalence ranged from 4.1% until 30.2%, but less than 1% was frail according to all scales. Depending on the used frailty scale the characteristics of the ‘frail sample’ had important differences. For instance, 50% of the ‘frail sample’ according to the FP was 80 years and over, while this was only 20.1% of the frail older persons as assessed according to the Groningen Frailty Index (GFI) [12]. A study of Aguayo and colleagues comparing 35 frailty measurements found considerably varying prevalence rates across studies (ranged 1.6% for men till 72.4% for women) [13].

Therefore, one can assume that these differences between frailty measurements also could have a strong influence on the outcomes of a study. Since 'being frail' is often used as an inclusion criterion, the selected frailty measurement may have a major impact on how many older adults will be included. Furthermore, one can expect that, depending on the selected frailty assessment, differences occur on who will be included and also with respect to the characteristics of the selected frail sample (e.g., differences in the average age of the sample). In the literature, many studies can be found which compared the predictive validity of different frailty-instruments or their risk factors [11, 12, 14]. However, the impact of the used frailty measurements on the characteristics of a selected 'frail sample' is not yet assessed and remains unclear.

The aim of this study was to examine the concordances and differences between a unidimensional (FP) and a multidimensional assessment (CFAI) of frailty and to assess to what extent the characteristics of 'frail participants' differ depending on the used frailty measurement. Since the FP solely focuses on the physical domain, while the CFAI adds measures within the psychological, social and environmental domain as well, one can assume that some agreement will be found because of the mutual physical domain and that differences will be found because of the additional domains.

Method

Study design

Data were gathered within the D-SCOPE project (Randomized Controlled Trial), which stands for Detection, Support and Care for Older adults: Prevention and Empowerment. The aim of D-SCOPE was to detect frail community-dwelling older adults who previously were unnoticed and to improve their access to tailored care and support [15]. Participants were selected from the census records of three municipalities in Flanders, the northern region of Belgium (Ghent, Knokke-Heist and Thienen) and were all community-dwelling older adults and aged ≥60 years. Participants were excluded from the study in case of hospitalization, when the participant or the informal caregiver indicated that the older adult was unable to participate, or when the interviewer noted that the older participant was unable to provide adequate answers (e.g., not being able to answer questions due to physical exhaustion or decreasing attention). To determine the numbers of participants needed for the present cross-sectional study, a sample

size calculation was conducted (see supplementary file 1: Sample size). Therefore, only a part of the D-SCOPE participants was asked to do the performance-based tests (Walk time and Handgrip strength) and were included in the present study [16]. Data collection was retrieved by two assessors (authors MVDE and AvdV) and started in March 2017 and lasted until September 2017. The details of the data collection method of D-SCOPE can be found elsewhere [15]. This study was reviewed and approved by the medical ethics committee of the Vrije Universiteit Brussel, Brussels, Belgium (reference number: B.U.N. 143,201,630,458). Written consent was obtained from all participants. The study adheres to the STROBE guidelines.

Frailty measurements

Fried's Phenotype of frailty was used to measure unidimensional frailty. According to the Fried Phenotype the following five criteria are used to determine the level of frailty: weight loss, exhaustion, low physical activity, slowness, and weakness [5]. Weight loss is measured by asking the following question: "In the past year, have you lost more than 5 kg unintentionally (i.e., not due to dieting or exercise)?" If yes, the participant was scored frail for the weight loss criterion. Exhaustion was determined using two questions of the CES–D Depression Scale, for which the following two statements had to be answered on a scale from 0 to 3: "Last week, I felt that everything I did was an effort"; and "Last week, I could not get going". Participants could answer with the options: 0 = rarely or none of the time (< 1 day), 1 = some or a little of the time (1 - 2 days), 2 = a moderate amount of the time (3 - 4 days), or 3 = most of the time. The participants answering '2' or '3' on at least one of these two questions were categorized as frail by the exhaustion criterion [17]. Low physical activity was measured by asking the participants whether they did any physical activities (e.g., walking, swimming, or cycling). The answer options were never, rarely, monthly or weekly [18]. Participants answering weekly were categorized as not-frail, the others as frail. For the performance-based measures slowness and weakness, all participants received standardized instructions. For the slowness criterion, participants were asked to walk 4.57 m (15 ft) at a normal pace, starting from a standing position. Equal to the original criteria from Fried and colleagues, depending on gender and height, a walk time below 6 or 7 seconds was categorized as not-frail, the others were considered as frail [5, 17]. Weakness (handgrip strength) was measured using a Saehan hand dynamometer (Saehan Corporation, South Korea). Participants were asked to squeeze

the dynamometer as hard as possible. Depending on gender and BMI, a different cut-off existed to categorize a person as (not-)frail [5]. In supplementary file 2, the protocol of the performance-based tests is described in detail. The result of each frailty criterion is dichotomized: frail (score 1) or not-frail (score 0). The final frailty sum scores range from 0 to 5. A score of 0 means a not-frail participant, participants with a score of 1 or 2 are considered pre-frail, and a score of 3–5 indicates that someone is frail [5].

The Comprehensive Frailty Assessment Instrument (CFAI) is self-report and was used to measure multidimensional frailty. This frailty measurement includes four domains: physical, social, psychological, and environmental [9]. The physical domain (4 items) assesses an older adult's functionality. An example of an item is "Walking up a hill or some stairs". The psychological domain (8 items) measures mood disorders and emotional loneliness such as "I feel unhappy and depressed". The social domain (4 items) assesses social loneliness and the potential social support network like "There are enough people whom I can rely on when I am in trouble". Finally, the environmental domain (5 items) evaluates the suitability of the physical housing environment, for instance, "My house is in a bad condition/poorly kept". All subscales range theoretically from 0 to 100 with higher scores indicating more severe levels of frailty. An overall score on the CFAI is calculated by summing the scores on each domain divided by the number of domains. A detailed description of the CFAI can be found in Supplementary file 3. The composition of the CFAI makes it possible to analyze the overall scale, including all the domains, but also on the domains separately. In what follows, CFAI is always used to indicate the overall scale including all the domains; otherwise, the specific domain is mentioned. A previous study determined the presence of three natural groups for the CFAI and its four domains: no-to-low frail, mild frail and high frail. The cut-offs of the CFAI are 0 - 21.89, 21.90 - 38.79 and 38.80 - 100, respectively (see supplementary file 3, Table C) [19].

Characteristics of participants

Participants were asked their date of birth and net monthly income. Meaning in life was evaluated with a short version of the Meaning in Life Questionnaire [20]. Life satisfaction was measured by using the Satisfaction with Life Scale, a validated scale which measures global life satisfaction [21]. To assess mastery, a questionnaire with 4 items was used which evaluates

to what extent people feel they exert control over existing circumstances of their lives [22]. In addition, 1 self-constructed item assesses mastery in relation to others [23]. Social inclusion was measured by using 1 item from the Community Integration Measure: to what extent they feel like part of the community [24]. Aging well in place was assessed using a self-constructed question: to what extent the older participant feels he/she lives at home in a qualitative way. Feeling frail was assessed by 1 item: to what extent the older participant feels frail [15].

Statistical analyses

To describe the sample, univariate analyses were conducted. To assess concordances and differences between the FP and the CFAI several tests were applied. First, differences in mean scores for the CFAI and the four CFAI-domains according to the three levels of the FP were examined by means of Analysis of Variance (ANOVA). As post-hoc, the Tukey HSD test was conducted to find differences in mean between pairs. Second, the strength of the association between the FP and both the CFAI and its subdomains was assessed by calculating Spearman correlation coefficients. Stronger correlations indicate concordance between the concepts that are measured, lower correlations indicate differences. No definite cut-offs exist, however Reid et al. suggested that different tests of the same construct should have correlation coefficients of more than 0.30, therefore, >0.30 was used as the cut-off [25]. Third, the observed agreement and the Cohen's kappa value (interrater reliability) between the FP and the CFAI (and domains) were computed [26]. Since both frailty scales are ordinal, a weighted (Linear and Quadratic) Cohen's kappa value was analyzed. The interpretation of the weighted Cohen's kappa value was divided as follows: ≤0, no agreement; 0.01 to 0.20, none to slight; 0.21 to 0.40, fair; 0.41 to 0.60, moderate; 0.61 to 0.80, substantial; 0.81 to 1.00, almost perfect [27]. Since 'being frail' is an inclusion criterion in many studies, it was decided to compare the characteristics (as mentioned above) of the frail sample according to the FP with the frail sample of the CFAI. ANOVA was conducted for continuous variables and the Kruskal-Wallis tests for ordinal variables. Missing data were excluded pairwise. Statistical significance was set at $p < 0.05$ for all analyses, which were performed using SPSS 24 (IBM SPSS Statistics for Windows, IBM Corp., Armonk, NY).

Results

In total, 196 people aged 60 years or older participated in the study. The mean age was 72.74 years old (SD 8.04, range 60 - 93) and 48.98% was male. The characteristics of the sample are described in Table 1. According to the FP measurement, 19.49% of the participants was frail, while 18.04% of the participants was high frail according to the CFAI. According to the CFAI 44.33% of the sample was no-to-low frail, while 23.59% was not-frail according to FP.

Table 1: Socio-demographic characteristics of the sample (N=196)

		Mean (SD)	N (%)
Age		72.74 (8.04)	
Gender			
	Male		96 (48.98)
	Female		100 (51.02)
Marital status			
	Married		61 (31.12)
	Never married		14 (7.14)
	Divorced		42 (21.43)
	Cohabited		26 (13.27)
	Widow(ed)		53 (27.04)
Highest level of education			
	No/primary		8 (4.10)
	Lower secondary		58 (29.74)
	Higher secondary		77 (39.49)
	Higher education		52 (26.67)
Relocated past 10 years			
	Yes		97 (49.49)
	No		99 (50.51)
Origin (country of birth)			
	Belgium		176 (89.80)
	Other		20 (10.20)
	500 - 999 €		10 (6.13)
Net income	1000 - 1499 €		63 (38.65)
	1500 - 1999 €		32 (19.63)
	2000 € and more		58 (35.58)
Fried Phenotype (unidimensional)			
	Not-frail		46 (23.59)
	Pre-frail		111 (56.92)
	Frail		38 (19.49)
CFAI* (multidimensional)			
	No to low frail		86 (44.33)
	Mild frail		73 (37.63)
	High frail		35 (18.04)

Note: CFAI = Comprehensive Frailty Assessment Instrument

Table 2 shows that frail participants according to FP, scored significantly higher on the CFAI and the CFAI-domains physical and psychological frailty compared to people who were not-frail or pre-frail. No such differences were found for the CFAI-domains environmental and social frailty.

Table 2: The CFAI mean scores (total and per domain) according to the Fried Phenotype distribution

	N	Fried Phenotype			P-value
		Not-frail (mean±SD)	Pre-frail (mean±SD)	Frail (mean±SD)	
CFAI	193	19.35±10.88[1]	23.84±11.61[2]	41.05±14.28[12]	p<0.000
CFAI Physical	195	6.25±13.11[34]	22.07±30.61[35]	61.84±32.22[45]	p<0.000
CFAI Psychological	193	14.96±16.32[6]	16.46±15.52[7]	36.95±22.92[67]	p<0.000
CFAI Social	195	46.61±18.70	45.38±18.04	51.21±20.48	ns
CFAI Environmental	195	9.57±13.16	10.99±12.23	14.21±14.64	ns

Note: Anova test. According to the Levene's Statistic, the variance of CFAI Physical and CFAI psychological were not equal instead the Welch test and Brown-Forsythe test were used to determine the p-value. As post-hoc, the Tukey HSD test was conducted to find differences in mean between pairs (see the superscripts). Superscripts with the same number indicate a significant mean difference between two pairs of groups. The CFAI and its domains are a continuous scale (0-100). For the psychological domain, there were missing data for two participants, and for the Fried Phenotype one participant had missing data. ns = non-significant

Table 3 presents the results of the Spearman correlation analysis, observed agreement and Cohen's kappa value. The Spearman correlation between the FP and the CFAI was R = 0.46, which was mainly attributed to by the physical domain (R = 0.52), and to a lesser extent by the psychological domain (R = 0.34). The correlations between the FP and the social and environmental domain were R = 0.05 and R = 0.13, respectively. The observed agreement between the FP and the CFAI was 52.85%, the Cohen's kappa value was linear weighted = 0.35 and quadratic weighted = 0.45. Supplementary file 4 presents the number of participants for the different levels of frailty according to the FP and the CFAI and its domains.

Table 3: Measurements for differences and concordances between the Fried Phenotype and the CFAI and its domains

	Fried Phenotype			
	Spearman correlation	Observed agreement	Weighted kappa value	Quadratic weighted kappa value
CFAI	R=0.46	52.85%	0.35	0.45
CFAI Physical	R=0.52	44.62%	0.25	0.39
CFAI Psychological	R=0.32	39.38%	0.18	0.28
CFAI Social	R=0.05	40.05%	0.04	0.06
CFAI Environmental	R=0.13	48.72%	0.13	0.14

Note: Spearman correlation: The same construct should have correlation coefficients greater than 0.30. The interpretation of the weighted Cohen's kappa coefficient is divided as follows: < 0, no agreement; 0.01 to 0.20, none to slight; 0.21 to 0.40, fair; 0.41 to 0.60, moderate; 0.61 to 0.80, substantial; 0.81 to 1.00, almost perfect.

In total, 23 participants (11.92%) were frail according to both the FP and the CFAI, 15 participants (7.77%) were solely frail according to FP, and 12 participants (6.21%) were solely high frail according to the CFAI (see supplementary file 4, Table F, for the subdomains of the CFAI). The characteristics of the frail samples differed, depending on the used frailty measurement (Table 4). For instance, life satisfaction was significantly lower in the respondents who were high frail according to the CFAI compared to people who were frail according to the FP. The high frail sample according to the CFAI tended to have a lower income in comparison to the frail sample of the FP; with regard to physical activities, the frail FP-sample tended to perform less physical activities than the high frail sample according to the CFAI. For the characteristics age, meaning in life, social inclusion, and feeling frail no significant differences between groups were found.

Table 4: Characteristics of the frail samples according to the frailty measurements (CFAI and Fried Phenotype)

			Solely CFAI High frail N=12	CFAI and FP (High-) frail N=23	Solely FP Frail N=15	p-value
Age	mean		70.00	75.04	76.67	0.141
Sense of Mastery (0 - 5)	mean		3.36	2.94[1]	3.76[1]	0.003*
Meaning in Life (0 - 5)	mean		3.67	3.53	3.87	0.427
Life Satisfaction (0 - 5)	mean		2.82[2]	3.07[3]	3.92[23]	0.001*
Social Inclusion (0 - 5)	mean		3.58	3.87	4.38	0.199
Aging Well in Place (0 - 5)	mean		4.17	3.74[4]	4.53[4]	0.081¥
Feeling Frail (0 - 5)	mean		3.25	3.17	2.73	0.465
Net income	N					0.021
		500 - 999 €	2	2	0	
		1 000 - 1 499 €	9	10	4	
		1 500 - 1 999 €	0	4	5	
		2 000 € or more	1	5	4	
Physical activities	N					0.001
		Never	2	18	11	
		Rarely	1	2	0	
		Monthly	1	1	0	
		Weekly	8	2	4	

Note: Continuous variables were tested by ANOVA (Post hoc: Tukey HSD), while ordinal variables were tested by the Kruskal-Wallis test (post hoc Kendall tau). CFAI=Comprehensive Frailty Assessment Index, FP= Fried Phenotype. *=$p < 0.05$ is considered significant. ¥= $p < 0.10$ is considered a trend. Superscripts with the same number indicate a significant (mean) difference between two pairs of groups. Net income and physical activity are significant different between solely CFAI and the two other groups (solely FP/CFAI and FP). Except age, all continuous scales ranged from 0 indicating a low level of … (e.g., mastery), till 5 indicating a high level of … (e.g., mastery).

Discussion

This study aimed to examine the concordances and differences between a unidimensional (FP) and a multidimensional assessment (CFAI) of frailty and to assess to what extent the characteristics of 'frail participants' differ depending on the used frailty measurement. The results show that FP and CFAI measure partly the same 'frailty-construct', with a fair (linear weighted Cohen's kappa) to moderate (quadratic weighted Cohen's kappa) resemblance. Both scales (FP and CFAI) indicate that 18% to 19% of the participants belong to the highest level of frailty. Although the frailest group in both scales (FP and CFAI) overlaps only partially for instance, 7.77% was solely frail according to FP and not according to the CFAI. Besides differences in 'frailty status' between the samples, the present results also show some differences between the characteristics of these 'frail samples'.

With regard to the first aim, the results show that the overlap between CFAI and FP seems mainly due to the physical domain of the CFAI and to a lesser extent to the psychological

domain. Because the FP includes several physical elements, like physical activity, walk time and handgrip strength, the relation with the CFAI's physical domain was expected [5]. In addition, an association with the psychological domain of the CFAI can be expected since exhaustion is also seen as a characteristic of depressive symptoms [28].

Differences between both frailty measurements were found. For instance, more participants were categorized as no-to-low frail according to the CFAI compared to the FP. In addition, some participants were frail according to FP and not according to the CFAI and vice versa. This is confirmed by previous research. For instance, a prior study of Ntanasi et al. (2018) examined the overlap of 'frail participants' using 5 frailty scales; the results show only a small overlap (0.7%), while some instruments indicated a frailty prevalence of 30.2% [12]. Further, low correlations were found between the FP and the social and environmental domain of the CFAI. Since both domains are not included in the FP, a weak or no association was expected. The inclusion of extra domains in the CFAI is probably also the reason why the Cohen's kappa value between the FP and the CFAI was only fair (linear weighted) to moderate (quadratic weighted). However, differences were also found between the physical domain of the CFAI and the FP; here the interrater reliability was only fair. This difference can be due to the use of performance-based tests (FP) versus self-reporting questions (CFAI) [29-31].

Concerning the characteristics of the 'frail samples', it was shown that depending on the used frailty measurement the characteristics of the study samples differed. Since the FP is focusing on physical frailty, one could expect that the frail sample according to the FP would be physically weaker in comparison with the frail sample of the CFAI, since the other domains in the CFAI will downsize the importance of the physical domain. This can explain why frail participants according to the FP were older and physically less active. Although, it must be pointed out that physical activity is one of the criteria of the FP (see supplementary file 5: physical activity). The frail CFAI-sample seems to have lower levels of life satisfaction and social inclusion. Furthermore, the frail CFAI-sample also seems to have a lower income. This is consistent with previous research that found that income was a risk factor for multidimensional frailty and not for unidimensional frailty (as measured with the FP) [12].

Strengths and Limitations

A strength of the present study is the difference in focus in comparison with other studies. Whereby previous research often aims to assess the predictive validity of different frailty

instruments or to find similarities in frailty instruments, the present study objective is to find concordances and differences between two frailty instruments [11, 12]. Thereby one frailty scale is not considered to be better or worse than the other, but to have an added value depending on the context.

This study has some limitations as well. First, the criterion 'low physical activity' was not operationalized in exactly the way it was initially proposed in the FP; this may have affected the results [5]. Secondly, the sample to assess to what extent the characteristics of 'frail participants' differ depending on the used frailty measurement, was rather small. Thirdly, only a small set of characteristics was assessed, and variables such as multi-morbidity, or total number of drugs used, were not available [32].

Implications and future research

Many frailty measurements exist, each with their specific qualifications. Consequently, differences occur between frailty measurements, for instance in the classification of older adults and the prevalence of frailty. Since the choice of a specific frailty measurement has an impact on the selected sample and the characteristics of the sample, we assume that the outcomes of a (intervention) study can differ as well depending on the used frailty measurement. We also assume that both approaches of frailty examined in the present study can be useful for distinct purposes, or contexts. For instance, an intervention study focusing on preventing the incidence of falls or the improvement of physical activity will probably make the best use of an approach in which particular physical elements of frailty are included. The selected sample will be physically weaker (e.g., presence of sarcopenia, performing less physical activities) when a physical unidimensional approach is used compared to a multidimensional approach of frailty in which social, psychological and environmental domains are included and may downsize the importance of the physical domain. In case of an intervention study focusing on aging (well) in place, one can assume that a multidimensional approach of frailty will probably have a higher likelihood to recruit the targeted sample population. Since aging well in place is partly determined by the social network of older adults [33], a multidimensional approach of frailty including a social domain will probably be able to recruit better those older adults at risk for institutionalization, for example because of a lacking social network; less persons of this group may be recruited in a unidimensional physical approach of frailty [34]. To achieve a maximum effect of an intervention, we assume that the

ability to recruit the targeted sample is essential. However, more research is needed to find evidence for both approaches of frailty to be useful for distinct purposes or contexts.

Researchers must be aware that different methods to operationalize and measure frailty may have important consequences for the outcomes of a study. Therefore, more research including both a unidimensional and a multidimensional approach in larger samples is warranted. A better understanding of the similarities and differences in frailty approaches and their consequences for the effectiveness of interventions and which approach is recommendable for which purpose will offer healthcare professionals a better framework, which they can apply to improve the care for frail older adults.

Conclusion

The present study shows that the FP and CFAI partly measure the same construct, although differences were found in the prevalence of frailty and the composition of the 'frail participants'. Since 'being frail' is an inclusion criterion in many studies, researchers must be aware that the choice of the frailty measurement has an impact on both the estimates of frailty prevalence and the characteristics of the selected sample.

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Supplementary File 1: Sample size

Analysis:	A priori: compute required sample size	
Input:	Tail(s)	= two
	Correlation ρ H1	= 0.3
	α err prob	= 0.05
	Power (1-β err prob)	= 0.95
	Correlation ρ H0	= 0
Output:	Lower critical r	= -0.1671877
	Upper critical r	= 0.1671877
	Total sample size	= 138
	Actual power	= 0.9504014

Supplementary File 2: Protocol performance-based tests Fried Phenotype

- Weight loss was measured by asking: In the last year, have you lost more than 10 pounds unintentionally (i.e., not due to dieting or exercise)? If yes, then the participant was scored frail for weight loss criterion.
- Exhaustion was determined using the CES–D Depression Scale, for which the following two statements were read by one of the two assessors: (a) last week, I felt that everything I did was an effort; and (b) last week, I could not get going. Participants could answer with the options: 0 = rarely or none of the time (< 1 day), 1 = some or a little of the time (1 - 2 days), 2 = a moderate amount of the time (3 - 4 days), or 3 = most of the time. The participants answering '2' or '3' on at least one of these two questions are categorized as frail by the exhaustion criterion.
- Low physical activity was measured by asking the participants whether they did any sports activities (e.g., walking, swimming, or cycling). The answer options were never, rarely, monthly or weekly. Participants answering weekly were categorized as not-frail, the others as frail.

For both performance-based measures, all participants received standardized Instructions.

- Slowness: participants were asked to walk 4.57 m (15 ft) at a normal pace, starting from a standing position. No encouragement was given by the assessor. A walking aid was permitted if necessary. The test was performed three times, and each time the time they needed was measured. For analyses, the average time was used. To indicate the distance, a rope was used.
- Weakness (handgrip strength) was measured using a Saehan hand dynamometer (Saehan Corporation, South Korea). Participants were asked to press as hard as possible on the dynamometer. Three measurements per hand were conducted alternately with a minimum of 30 seconds rest between each attempt. Results were averaged per hand, and the highest average score (either left or right hand, it did not matter whether this was their 'dominant hand'), was used for analyses. Before doing the handgrip strength test, participants were asked to practice first. Participants were seated upright in a chair without armrests or standing, the shoulder and forearm in neutral position, and the elbow in 90° flexion. The handle position of the

dynamometer was determined in such a way that the intermediate phalanges were on the front side of the handle. Participants were verbally encouraged.

For the cut-off values of the performance-based Fried measures, it is necessary to measure weight and height, in order to calculate the Body Mass Index (BMI). Cut-off values for both performance-based measures were used as described by Fried and colleagues. To measure the weight of the participants both researchers used a scale of the brand OMRON, and participants were weighted twice. The average body weight was calculated and used in the analysis. To measure body length, participants were asked to stand against a wall as straight as possible (without shoes). A book with a hard cover was placed on the respondent's head and a post-it was used to mark the respondent's body length. Using a ruler, the body length was measured. This procedure was performed three times, and the average body length was used in the analysis. The assessors were trained to conduct the data collection by author LOhV.

Cut-offs performance-based tests Fried Phenotype

- Walk Time, stratified by gender and height (gender-specific cutoff a medium height).

Men	
Height ≤ 173 cm	7 seconds
Height > 173 cm	6 seconds
Women	
Height ≤ 159 cm	7 seconds
Height > 159 cm	6 seconds

- Grip Strength, stratified by gender and body mass index (BMI) quartiles:

Men	
BMI ≤ 24	≤ 29
BMI 24.1–26	≤ 30
BMI 26.1–28	≤ 30
BMI > 28	≤ 32
Women	
BMI ≤ 23	≤ 17
BMI 23.1–26	≤ 17.3
BMI 26.1–29	≤ 18
BMI > 29	≤ 21

Supplementary File 3: The Comprehensive Frailty Assessment Instrument (CFAI)

1. Have the following activities been hampered by your state of health? If so, for how long?

	Not at all	3 months or less	More than 3 months
Less demanding activities like carrying shopping bags			
Walking up a hill or some stairs			
Bending or lifting			
Going for a walk			

2. Considering the last few weeks, to which extent do you agree with the following

1 = not at all 3 = more than usual
2 = not more than usual 4 = considerably more than usual

	1	2	3	4
I feel unhappy and depressed				
I feel like I'm losing my self-confidence				
I feel like I cannot cope with problems				
I feel like I'm under constant pressure				
I feel like I'm not worth anything anymore				

3. To which extent do you agree with the following statements?

1 = I completely disagree 4 = I agree
2 = I disagree 5 = I completely agree
3 = I neither agree nor disagree

	1	2	3	4	5
I experience a general sense of emptiness					
I miss having people around me					
I often feel rejected					
There are enough people whom I can rely on when I am in trouble					
I know many people whom I can totally trust					
There are enough people with whom I feel a bond					
My house is in a bad condition/poorly kept					
My house is not very comfortable					
It is difficult to heat my house					
There is insufficient comfort in my house					
I do not like my neighborhood					

4. Suppose you are unable to carry out the activities you usually do in terms of housekeeping for a certain length of time; whom would you be able to appeal to? (More than one answer may be given)

Partner	
Son	
Daughter-in-law	
Daughter	
Son-in-law	
Grandchild	
Sister or brother (in-law)	
Family	
Neighbors	
Friends	

Calculation of the scores of the CFAI:

The purpose of the CFAI was not only to assess four domains of frailty, but also to give equal weight to the four domains. Table A gives an overview of those domains, their measurements, their scores, their weight within the domain (WWD) and the weight of the domain within the total score of the CFAI (DWWT). Table B contains the formulas for calculating the domain and total scores that are presented in Table A.

Table A: CFAI-domains, measurements and weights

CFAI	**DWWT**	**Measurements**	**Min-max**	**WWD**
CFAI Physical domain	25%	Physical items	0 - 8	100%
CFAI Psychological domain	25%			
		Mood disorders	0 - 15	50%
		Emotional loneliness	0 - 12	50%
CFAI Social domain	25%			
		Social loneliness	0 - 12	50%
		Social support network	0 - 10	50%
CFAI Environmental domain	25%	Actual housing/environment	0 - 20	100%

Table B: Formulas for calculating the subdomains of the CFAI

CFAI	**Formula**
CFAI Physical domain	[Physical items]*100/8
CFAI Psychological domain	[mood disorders]*50/15 + [emotional loneliness]*50/12
CFAI Social domain	[social loneliness]*50/12 + [social support network]*50/10
CFAI Environmental domain	[actual housing/environment]*100/20

Table C: Cut-offs CFAI

	No/Low frail	Mild frail	High frail
CFAI	0.00 thru 21.89	21.90 thru 38.79	38.80 thru 100.00
Physical domain	0.00 thru 24.99	25.00 thru 75.00	75.01 thru 100.00
Psychological domain	0.00 thru 19.99	20.00 thru 45.84	45.85 thru 100.00
Social domain	0.00 thru 37.49	37.50 thru 64.15	64.16 thru 100.00
Environmental domain	0.00 thru 4.99	5.00 thru 30.00	30.01 thru 100.00

Supplementary File 4: Observed agreement between Fried Phenotype and CFAI

Table A: Number of participants with different levels of frailty according to the Fried Phenotype and CFAI total

			Fried Phenotype			
			No	Pre-frail	Frail	Total
CFAI	No/low frail	N	31	51	4	86
	Mild frail	N	13	48	11	72
	High frail	N	2	10	23	35
	Total	N	46	109	38	193

Table B: Number of participants with different levels of frailty according to the Fried Phenotype and CFAI Physical

			Fried Phenotype			
			No	Pre-frail	Frail	Total
CFAI Physical	No/low frail	N	37	64	4	105
	Mild frail	N	9	40	24	73
	High frail	N	0	7	10	17
	Total	N	46	111	38	195

Table C: Number of participants with different levels of frailty according to the Fried Phenotype and CFAI Psychological

			Fried Phenotype			
			No	Pre-frail	Frail	Total
CFAI Psychological	No/low frail	N	34	72	10	116
	Mild frail	N	10	30	16	56
	High frail	N	2	7	12	21
	Total	N	46	109	38	193

Table D: Number of participants with different levels of frailty according to the Fried Phenotype and CFAI Social

			Fried Phenotype			
			No	Pre-frail	Frail	Total
CFAI Social	No/low frail	N	13	36	9	58
	Mild frail	N	25	58	18	101
	High frail	N	8	17	11	36
	Total	N	46	111	38	195

Table E: Number of participants with different levels of frailty according to the Fried Phenotype and CFAI Environmental

			Fried Phenotype			
			No	Pre-frail	Frail	Total
CFAI Environmental	No/low frail	N	24	42	12	78
	Mild frail	N	19	65	20	104
	High frail	N	3	4	6	13
	Total	N	46	111	38	195

Table F: The percentage of participants frail according to the Fried Phenotype, the CFAI or both frailty measurements

	Fried Phenotype	Fried Phenotype and CFAI	CFAI
Frailty	7.77%	11.92%	6.21%
Physical domain	14.36%	5.13%	3.59%
Psychological domain	13.47%	6.22%	4.66%
Social domain	13.85%	5.64%	12.82%
Environmental domain	16.41%	3.08%	3.59%

Supplementary File 5: Physical activity

Since physical activity is a part of the Fried Phenotype, an additional analysis whereby the item physical activity was not included in the Fried Phenotype was done. The table below presents these results. If physical activity was not included, 27 persons met three or four criteria of the Fried Phenotype. The ANOVA suggested that there is a significant difference between the three groups ($p = 0.01531$) indicating that persons frail according to FP performed less physical activity.

Table A: Physical activity

	Solely CFAI High frail N=12	CFAI and FP (High-) frail N=17	Solely FP Frail N=10
Never	2	13	6
Rarely	1	1	0
Monthly	1	1	0
Weekly	8	2	4

Note: $p < 0.05$

Chapter 3

Validation of replacement questions for slowness and weakness to assess the Fried Phenotype: cross-sectional study

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Abstract

Background: When screening large populations performance-based measures can be difficult to conduct because they are time consuming and costly, and require well-trained assessors. The aim of the present study is to validate a set of questions replacing the performance-based measures slowness and weakness as part of the Fried frailty Phenotype (FRIED-P).

Methods: A cross-sectional study was conducted among community-dwelling older adults (≥60 years) in three Flemish municipalities. The Fried Phenotype (FRIED-P) was used to measure physical frailty. The two performance-based measures of the Fried Phenotype (slowness and weakness) were also measured by means of six substituting questions (FRIED-Q). These questions were validated through sensitivity, specificity, Cohen's kappa value, observed agreement, correlation analysis, and the Area Under the Curve (AUC, ROC-curve).

Results: 196 older adults participated. According to the FRIED-P, 19.5% was frail, 56.9% was pre-frail and 23.6% was non-frail. For slowness, the observed sensitivity was 47.0%, the specificity was 96.5% and the AUC was 0.717. For weakness, the sensitivity was 46.2%, the specificity was 83.7%, and the AUC was 0.649. The overall Spearman correlation between the FRIED-P and the FRIED-Q was r=0.721 with an observed agreement of 76.6% (weighted linear Cohen's kappa value = 0.663, quadratic Cohen's kappa value = 0.738).

Conclusions: The concordance between the FRIED-P and FRIED-Q was substantial, characterized by a very high specificity but a moderate sensitivity. This alternative operationalization of the Fried Phenotype – i.e., including six replacement questions instead of two performance-based tests – can be considered to apply as a screening tool to screen physical frailty in large populations.

Introduction

Physical frailty is a state of increased vulnerability, which can evolve into disability and other adverse outcomes [1-5]. However, frailty in older adults is often not identified [3, 6, 7]. Large-scale screening may be helpful to identify frail older persons [8]. However, to implement large-scale screening, an easy to apply frailty screener is necessary [3]. One of the most frequently used scales to assess frailty is the Fried Phenotype [9, 10]. According to the Fried Phenotype, a person is frail when he or she meets at least three of the following criteria: unintentional weight loss, slowness, weakness, exhaustion, and low physical activity [11]. Slowness and weakness are both assessed with performance-based measures. When large populations of older people are screened, performance-based measures can be difficult to conduct because they are time consuming, costly, and require well-trained assessors [12]. Consequently, the replacement of these performance-based measures by self-report questions may be helpful in the development of an easy to apply frailty-screening tool, which may enable to screen large populations [6, 10]. Although the two performance-based criteria (slowness and weakness) of the Frailty Phenotype were already replaced by questions in a few earlier studies [13, 14], still little is known about which question (or set of questions) are most valid to substitute the performance-based measures [10]. In most of the studies in which self-report questions were used, the validity of these questions was not tested, or at least no tests were reported, while these modifications may have an important impact on its classification and predictive ability [10, 15].

Nonetheless, a recent study did test the psychometric properties of six self-report questions in order to replace the performance-based measurements slowness and weakness [15]. In this study by Op het Veld and colleagues, participants were recruited from different settings in the Netherlands: a community center for older people, clients of a physical therapy practice, people admitted to a hospital, and people attending day care facilities. It was aimed to include 50 persons per frailty stage (i.e., frail, pre-frail, non-frail). Regarding the psychometric properties, this study showed an observed agreement of 71.1% between a Fried Phenotype with performance-based measures and a Fried Phenotype without performance-based measures but including self-report questions and a Cohen's kappa = 0.55 [11, 15].

Whereby the study of Op het Veld and colleagues was explorative, the aim of the present study is to validate and to confirm the psychometric properties of this set of six self-report questions (13). However, some differences in setting between both studies occur. The present

validation study is done in a Flemish sample, while Op het Veld and colleagues conducted their study in the Netherlands, whereby the present sample is larger. While the study of Op het Veld and colleagues was organized in several settings (e.g., a community center for older people, clients of a physical therapy practice, people admitted to a hospital, and people attending day care facilities) whereby the older adults visit the care provider, the present study must be placed in the context of the D-SCOPE framework which aims to detect frail older adults proactively (care providers visiting older adults,). The recruitment in the present study is based on census records (and risk factors) and without aims with regard to frailty stages of the sample.

The research questions of the present study are: 1) what is the concordance between slowness operationalized by doing a 15 ft walk time test and slowness operationalized by four self-report questions; 2) what is the concordance between weakness measured by means of a handgrip strength test and weakness operationalized by two self-report questions; 3) what is the concordance between the two-overall operationalizations of the Fried scales; and 4) what is the ability of the Fried Phenotype with no performance-based tests to discriminate between non-frail and/or frail older adults if we take the Fried Phenotype with performance-based test as a gold standard?

Method

Study design

For this cross-sectional study, data were gathered as baseline wave within the D-SCOPE project [16]. D-SCOPE stands for Detection, Support and Care for Older adults: Prevention and Empowerment. The aim of D-SCOPE was to detect frail community-dwelling older adults who previously were unnoticed and to improve their access to tailored care and support. The details of the data collection method of D-SCOPE have been published elsewhere [16]. To determine the numbers of participants needed, a sample size calculation was conducted a priori (see Online Resource 1: Sample size) [17]. This resulted in a required minimum of 138 participants to be able to show a statistically significant effect ($p < 0.05$) by means of a correlation of 0.30. Participants had to be community-dwelling and 60 years or older and were selected from the census records, based on risk profiles (e.g., age, gender, marital status, country of birth) developed by Dury and colleagues [16, 18]. Participants were excluded from the study in case of hospitalization, when inability to participate was indicated by the

participant or his/her informal caregiver, or when the interviewer noted that the older participant was unable to provide adequate answers (e.g., not being able to answer questions due to physical exhaustion or distraction). The present study took place in three Flemish municipalities Ghent, Knokke-Heist and Thienen in Belgium. To minimize intra- and inter-assessor variability the collection of the data was performed by two trained interviewers (authors MCJVdE and AVdV). Data collection started in March 2017 and ended in September 2017. This study was reviewed and approved by the Medical Ethics Committee of the Vrije Universiteit Brussel, Brussels, Belgium (reference number: B.U.N. 143,201,630,458). Written consent was obtained from all participants. The study adheres to the STROBE guidelines.

Frailty measurements

Fried's Phenotype of physical frailty was used to measure frailty [11]. The Fried Phenotype uses five criteria to determine the level of frailty: weight loss, exhaustion, low physical activity, slowness, and weakness [11]. Slowness and weakness were measured both in a performance-based way as proposed by Fried and colleagues [11], and additionally by using the six replacement questions as proposed by Op het Veld and colleagues (see supplementary file 1: development of the replacement questions) [15]. A detailed description of the performance-based measurements and its cut-offs are given in Online Resource 3: frailty measurement [11, 15]. Each frailty criterion was recoded in a dichotomous score: frail (score 1) or non-frail (score 0). The final frailty sum scores range from 0 to 5 and classify persons into non-frail (score 0), pre-frail (score 1 - 2) or frail (score 3 - 5). In what follows, the Fried Phenotype with performance-based measures is called FRIED-P, and the Fried Phenotype replacing the performance-based measures by six questions is called FRIED-Q. Table 1 presents an overview of the criteria and descriptions for both FRIED-P and FRIED-Q.

Table 1: Fried Phenotype: FRIED-P including performance-based measures for weakness and slowness and FRIED-Q including self-report questions for weakness and slowness

	FRIED-P	FRIED-Q
Weight loss	In the last year, have you lost more than 10 pounds unintentionally?	In the last year, have you lost more than 10 pounds unintentionally?
Exhaustion	How often in the last week did you feel this way? (a) I felt that everything I did was an effort (b) I could not get going	How often in the last week did you feel this way? (a) I felt that everything I did was an effort (b) I could not get going
Low physical activity	Do you do sports activities (e.g., walking, swimming, or cycling)?	Do you do sports activities (e.g., walking, swimming, or cycling)?
Weakness	Participants were asked to squeeze as hard as possible on the dynamometer (Saehan).	1) Do you have trouble watering plants with a spray bottle? 2) Do you feel like you have less hand strength than other people your age?
Slowness	Participants were asked to walk time/15 feet.	1) When the doorbell rings, do you usually get there in time to open the door? 2) Do you walk more slowly than you'd like? 3) Do you have enough time to cross the street on foot when the traffic light turns green? 4) Do you encounter problems in daily life due to poor balance?

An item was positive if: (a) weight loss was answered with yes; (b) exhaustion was answered with 3-4 days or more a week to either of these questions; (c) low physical activity was answered with monthly or less; (d) weakness was answered yes on at least one question; and (e) slowness was scored 3 or higher. For slowness every question was assigned a score 1, except question 2 which was assigned a score of two since it contributed substantially more to the total score than any of the other questions. The scores were summed (0-5), the cut-off score is 3.

Statistical analyses

To describe the population, univariate descriptive statistics were conducted. To get an impression whether the items of slowness and the items of weakness are related, the mean inter-item correlations were calculated for both measurements. A low inter-item correlation suggests that the items are hardly related to each other and might not be suitable for measuring a single construct. A high inter-item correlation suggests that the items tend to be very similar to each other, almost to the point that they are redundant. Optimal mean inter-item correlation values range from 0.2 to 0.4 [19].

In research question 1 and 2 we examine the concordance between the performance-based test (‘gold standard’, handgrip strength and walk time) and the replacement questions, to have a better understanding of the concordance if several tests were applied: sensitivity, specificity, observed agreement, Cohen’s kappa (interrater reliability); the performance of the model for both handgrip strength and walk time was quantified as the area under the receiver operating characteristic curve (AUC) [20-22].

To measure the AUC, the scores on the replacement question of handgrip strength and walk time were used as test variable and the score on the performance-based test was used as state variable.

To measure the concordance between the FRIED-P and the FRIED-Q (research question 3), the spearman correlation and observed agreement were computed. Since the Fried Phenotype has three categories, frail, prefrail and non-frail a weighted Cohen's kappa value (linear and quadratic) was calculated, whereby the FRIED-P was used as the 'gold standard'.

To measure the ability of the FRIED-Q to discriminate between non-frail and/or frail people (research question 4) the sensitivity, specificity, Cohen's kappa, observed agreement and Area Under the Receiver Operating Characteristic-curve (AUC) were measured against the FRIED-P.

The interpretation of the (Cohen's) kappa value was divided as follows: < 0: poor; 0 to 0.20: slight; 0.21 to 0.40: fair; 0.41 to 0.60: moderate; 0.61 to 0.80: substantial; 0.81 to 1.00: almost perfect [23]. The Area Under the Curve (AUC, ROC-curve) was interpreted as follows: 90 - 100 = excellent; 80 - 90 = good; 70 - 80 = fair; 60 - 70 = poor; 50 - 60 = fail [24]. Cases with missing data were excluded pairwise. The statistical analyses were performed using SPSS 24 (IBM SPSS Statistics for Windows, IBM Corp., Armonk, NY).

Results

In total, 196 participants participated in the study with an average age of 72.7 (SD 8.0) and of which 49.0% was male. The characteristics of the population are further described in Table 2. According to the FRIED-P 19.5% was frail, 56.9% was pre-frail and 23.6% was non-frail (not tabulated). According to the FRIED-Q 14.6% was frail, 52.1% was pre-frail and 33.3% was non-frail (not tabulated). For the four questions related to slowness the mean inter-item correlation was 0.266, which is between the range of the optimal inter-item correlation. The mean inter-item correlation value for weakness was 0.221, which is also between the range of the optimal inter-item correlation.

Table 2: Descriptive statistics of the study sample (N=196)

		Mean (SD)	N (%)
Age		72.7 (8.0)	
Range Age		60-95	
Gender			
	Male		96 (49.0)
	Female		100 (51.0)
Marital status			
	Married		61 (31.1)
	Never married		14 (7.1)
	Divorced		42 (21.4)
	Cohabiting		26 (13.3)
	Widow(ed)		53 (27.0)
Education			
	No/primary		8 (3.1)
	Lower secondary		58 (29.7)
	Higher secondary		77 (39.5)
	Higher education		52 (26.7)
Relocated past 10 years			
	Yes		97 (49.5)
	No		99 (50.5)
Origine			
	Flemish		176 (89.8)
	Other		20 (10.2)

The AUC for slowness was 0.717, which can be defined as fair. The replacement questions for slowness had a sensitivity of 47.0% and a specificity of 96.5% (see Table 3). The observed agreement was 75.5%. The Cohen's kappa value was κ = 0.464, and was defined as moderate.

Table 3: The psychometric properties of slowness for the FRIED-Q compared to the FRIED-P

			Performance-based test 15 ft Walk time +	-	Total	Positive predictive value	Negative predictive value
Replacement questions	+	N	39	4	43		
		%	47.0%	3.5%	21.9%	90.7%	
Slowness	-	N	44	109	153		
		%	53.0%	96.5%	78.1%		71.2%
	Total	N	83	113	196		
	Sensitivity	%	47.0%				
	Specificity	%		96.5%			

Note: FRIED-P stands for the Fried Phenotype with slowness and weakness operationalized as performance-based tests. FRIED-Q stands for The Fried Phenotype with slowness and weakness operationalized as self-report questions. + indicates a participant's slowness was higher than the cut-off determined by Fried Phenotype or had a higher score than the cut-off on the replacement questions determined by Op het Veld and colleagues (see Online Resource 2), - indicates a participant's slowness was lower than the cut-off determined by Fried Phenotype or had a lower score than the cut-off on the replacement questions determined by Op het Veld and colleagues.

The AUC for weakness was 0.649, which can be defined as poor. The replacement questions for weakness had a sensitivity of 46.2% and a specificity of 83.7% (see Table 4). The observed agreement was 73.6%. The Cohen's kappa value was κ = 0.308, and thus defined as fair.

Table 4: The psychometric properties of weakness for the FRIED-Q compared to the FRIED-P

			Performance-based test Dynamometer +	Performance-based test Dynamometer -	Total	Positive predictive value	Negative predictive value
Replacement questions	+	N	24	23	47		
		%	46.2%	16.3%	24.4%	51.1%	
Weakness	-	N	28	118	146		
		%	53.8%	83.7%	75.6%		80.8%
	Total	N	52	141	193		
	Sensitivity	%	46.2%				
	Specificity	%		83.7%			

Note: FRIED-P stands for the Fried Phenotype with slowness and weakness operationalized as performance-based tests. FRIED-Q stands for The Fried Phenotype with slowness and weakness operationalized as self-report questions. + indicates a participant's weakness was lower than the cut-off determined by the Fried Phenotype or had a higher score than the cut-off on the replacement questions determined by Op het Veld and colleagues (see Online Resource 2), - indicates a participant's weakness was higher than the cut-off determined by the Fried Phenotype or had a lower score than the cut-off on the replacement questions determined by Op het Veld and colleagues.

The observed agreement of the three frailty stages between FRIED-P and FRIED-Q was 76.6%. The Cohen's kappa value was substantial (unweighted κ = 0.607, weighted Linear κ = 0.663, weighted Quadratic κ = 0.738). The Spearman correlation between the FRIED-P and FRIED-Q (5 items) was r = 0.721.

When distinguishing between frail and non-frail/pre-frail older adults, the FRIED-Q had a sensitivity of 64.9% and a specificity of 97.4% against the FRIED-P (Table 5). The observed agreement was 91.1% and the area under the curve = 0.811 (ROC) was good. The Cohen's kappa value was substantial (κ = 0.686).

When distinguishing between non-frail and frail/pre-frail older adults, the FRIED-Q had a sensitivity of 84.2% and a specificity of 89.1% against FRIED-P (see also Table 5). The observed agreement was 85.5% and the area under the curve = 0.867 (ROC) was good. The Cohen's kappa value was substantial (κ = 0.647).

Table 5: Ability of FRIED-Q to discriminate between frail and non-frail older adults as compared to the FRIED-P

Ability of FRIED-Q to discriminate between frail and pre-frail/non-frail							
			FRIED-P				
			Frail	Non-/ pre-frail	Total	Positive predictive value	Negative predictive value
FRIED-Q	Frail	N	24	4	28		
		%	64.9%	2.6%	14.6%	85.7%	
	Non-/ pre-frail	N	13	151	164		
		%	35.1%	97.4%	85.4%		92.1%
	Total	N	37	155	192		
	Sensitivity	%	64.9%				
	Specificity	%		97.4%			
Ability of FRIED-Q to discriminate between non-frail and pre-frail/frail							
			FRIED-P				
			(Pre-)Frail	Non-frail	Total	Positive predictive value	Negative predictive value
FRIED-Q	(Pre-)Frail	N	123	5	128		
		%	84.2%	10.9%	66.7%	96.1%	
	Non-frail	N	23	41	64		
		%	15.8%	89.1%	33.3%		64.1%
	Total	N	146	46	192		
	Sensitivity	%	84.2%				
	Specificity	%		89.1%			

Note: FRIED-P stands for the Fried Phenotype with slowness and weakness operationalized as performance-based tests. FRIED-Q stands for The Fried Phenotype with slowness and weakness operationalized as self-report questions.

Discussion

In the present study, the psychometric properties of a set of six questions replacing the performance-based measures for slowness and weakness as part of the FRIED Phenotype were validated. The concordance between FRIED-P (including performance-based measures for slowness and weakness) and FRIED-Q (including self-report questions for slowness and weakness) was substantial. The FRIED-Q is very well in discriminating physically non-frail older adults (specificity 89.1%) but somewhat less in discriminating frail older adults (sensitivity 64.9%). At an item level, slowness and weakness are characterized by a low sensitivity (47.0% and 46.2%, respectively) but high specificity (96.5% and 83.7%, respectively).

The observed agreement (76.6% versus 71.1%) and Cohen's kappa value (0.607 versus 0.55) of the total scales (research question 3) are slightly better in comparison with the results of Op het Veld et al. [15]. However, the current study found (slowness and weakness) higher specificity (96.5% versus 86.1%, and 83.7% versus 71.9%, respectively) but lower sensitivity (47.0% versus 69.2% and 46.2% versus 73.2%, respectively) rates at item level. This indicates

that the replacement questions have the ability to correctly identify those without physical frailty, whereas their ability to correctly identify those with physical frailty seems to be less adequate compared with the results of the study of Op het Veld and colleagues [15, 22]. A first plausible explanation for the differences may be related to the composition of the sample. In the present study, 19.5% of the population was frail, 56.9% was pre-frail and 23.6% was non-frail, while in the study of Op het Veld and colleagues much less people were pre-frail (40.7%) and much more people were non-frail (38.5%) [15]. A second explanation could be related to the way participants were recruited. In the present study, older adults were selected from the census records based on risk factors, while in the study of Op het Veld et al. older adults were recruited from different settings, such as clients of a physical therapy practice, people admitted to a hospital, and people attending daycare facilities [15]. A previous study, for example, showed that self-reported levels of disability were higher after the completion of performance-based tests [25]. One can assume that participants undergoing physical therapy will experience physical limitations in real time and be aware of it. This may have influenced their perceptions of their level of daily functioning.

The concordance between the Fried Phenotype performance-based measures (slowness and weakness) and the set of replacement questions at item level is fair. In previous studies, discrepancies between self-report measures and performance-based tests were found. For instance, the results in a prior systematic review indicated a correlation-range between 0.60 and 0.86 when the same construct was measured in two different ways [26]. As far as we know, only two other studies reported psychometric properties with regard to the replacement of Fried's performance-based measures with questions. Johansen and colleagues used the Physical Function scale of the SF-36 as a substitution for the two performance-based measures together and found an overall agreement of 72.5% [27]. In an earlier attempt to operationalize the Fried Phenotype into an easy to apply screening tool (GFST), Cherubini and colleagues reported an observed agreement of 70.64% and a Cohen's kappa value of 0.45 [6]. However, Cherubini and colleagues added extra items like living alone and memory complaints [6]. Consequently, it is difficult to compare the results of both studies with the present study.

When distinguishing between non-frail older adults and frail older adults, the total FRIED-Q was marked by a high specificity (89.1%) but a rather low sensitivity (64.9%). This indicates that people might overestimate their own physical performance while filling in the FRIED-Q.

For instance, 44 participants reported no slowness (FRIED-Q), while they were slow according to the walk time test. On the other hand, only a small number of people (four participants) underestimated their own walk speed (slowness). Previous research found several confounding factors for overestimating own physical competences, such as perceived physical competence, perceived health status, personal control or mastery and depressive symptomatology [28-30]. For instance, Ferrer and colleagues describe that a person rating his/her health as poor is more likely to overreport functional limitation, while a person that perceives his/her health as good tends to underreport functional limitations. Consequently, one can assume that the present sample perceived their health as good or had a high level of mastery. However, this was not assessed, since this was not the aim of the current study.

In the present study the prevalence is higher than in comparison with previous research. There are several plausible reasons which can explain why the prevalence of frailty is higher: 1) in the present study, older adults were selected from the census records based on risk factors for frailty. Therefore, the prevalence of frailty will be higher and not representative for the population; 2) differences in inclusion and exclusion criteria, for instance, in the SHARE survey the sample was aged 50 years and over, while in the D-SCOPE project people had to be 60 years or older [31]; 3) a previous systematic review of Theou et al. showed that modifications in the Fried Phenotype can have an impact on the prevalence of frailty. Since low physical activity is also modified in the present study, this could have an impact on the prevalence of frailty [10].

Strengths and Limitations

This study has several strengths and limitations. A strength of the present study is that it replicates the study of Op het Veld and colleagues in a larger sample, whereby it was performed in a different setting and region (Flemish region in Belgium) [15]. Consequently, the present results indicate that this set of questions to replace the performance-based test can be used in different settings/countries. Secondly, the performance-based measurements were carried out under a strict protocol, the same as described in the study of Op het Veld and colleagues [15]. The two assessors in the present study (authors MCJVdE and AVdV) were also trained by Op het Veld. Therefore, we consider that the assessor variability was minimized, which makes a valid comparison between the two studies more likely. A limitation of the present study is the operationalization of the item physical activity, which is different

in comparison with the study of Fried and colleagues, and Op het Veld and colleagues [11]. Fried and colleagues used a short version of the Minnesota Leisure Time Activity questionnaire; Op het Veld used an adjusted version of the Short Questionnaire to Assess Health-enhancing physical activity (SQUASH), while in the present study we asked: "Do you do sports activities (e.g., walking, swimming, or cycling)" [32, 33]. This difference in operationalization might have affected the observed agreement of the three frailty stages between FRIED-P and FRIED-Q and the Cohen's kappa value.

Implications and future research

The substantial concordance between the FRIED-P and the FRIED-Q suggests the usefulness of the latter to screen frailty in a large population since the FRIED-Q is easier to apply in comparison with the FRIED-P. The high specificity is an advantage when the objective is to exclude non-frail persons, for instance in (research) projects where being frail is often an inclusion criterion. However, the FRIED-Q does not detect all frail older adults (according the Fried Phenotype) and can be considered as a step in a sequential process to detect frailty in large populations. This sequential process should reduce the number of false positives and false negatives. For instance, most older adults (aged 75 and over) in Europe consult their GP frequently. If large screening of frailty becomes a responsibility of general practitioners, there are occasions to screen the patient frequently. In case of doubt the performance-based tests can still be applied as a second order. Future research is needed to validate these set of substitution questions in other languages and settings.

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Supplementary File 1: Development of the replacement questions (Op het Veld)

Questions on walk time and handgrip strength were derived from various sources. First, multiple databases were searched using terms related to frailty, grip strength, and walk time. Only questionnaires in English or Dutch were included. This resulted in 11 questionnaires with potential useful questions, including the Dutch version of the 36-Item Short-Form Health Survey (SF-36) and the Disability Rating Index [1-2]. These questionnaires were screened for questions that were specifically related to walk time or handgrip strength. In addition, community-dwelling older people and experts (scientists and physical therapists, all working with frail older people) were interviewed. Based on face validity and consultation with the aforementioned experts, final sets of 11 questions for walk time and 10 questions for handgrip strength were composed (Table. The response options for all questions were 'Yes' or 'No'. afterwards, logistic regression analyses with backward stepwise elimination were performed to find the optimal set of questions as a substitute for the performance-based measures. The performance of the model was quantified as the area under the receiver operating characteristic curve (AUC). Bootstrap-validation was then performed to calculate the optimism in the estimation of the AUC. [3]

Table A: Questions

Walk time
1 When the doorbell rings, do you usually get there in time to open the door?
2 When the phone rings, do you usually get there in time to answer it?
3 Do you feel like you walk more slowly than other people your age?
4 Do you walk more slowly than you'd like?
5 When walking with other people your age, do you struggle to keep up?
6 Do other people your age regularly pass you when you're walking?
7 Do you have enough time to cross the street on foot when the traffic light turns green?
8 Do you take approximately two steps per second when walking?
9 Do you encounter problems in daily life due to walking difficulties?
10 Do you encounter problems in daily life due to poor balance?
11 Do you have enough time to cross the street at a pedestrian crossing when the light turns green?
Handgrip strength
1 Do you have trouble opening a jar that has already been opened?
2 Do you have trouble opening a jar that has not yet been opened?
3 Do you require assistance and/or a device to open the lid of a jar?
4 Do you have trouble watering plants with a spray bottle?
5 Do you have trouble wringing out a facecloth/dishrag?
6 Do you have trouble opening a drinks bottle or a carton of milk that has not yet been opened?
7 Do you have trouble turning on a tap that has been tightly closed?
8 Do you find it difficult or painful to give arm handshake?
9 Do you encounter problems in daily life due to lack of hand strength?
10 Do you feel like you have less hand strength than other people your age?

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Chapter 4

Towards a more effective strategy to detect community-dwelling frail older adults: validation of risk factors

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Abstract

Background: In the context of early detection of frail older people, prior research found several risk factors of multidimensional frailty. The current study aims to validate these risk factors.

Methods: Two data sets (BAS and D-SCOPE) in three Belgian municipalities (Ghent, Knokke-Heist and Thienen) were used and compared. The BAS data set (N = 1496) is a representative sample of community-dwelling older adults (60+), while the D-SCOPE sample (validation sample, N = 869) is based on risk factors for frailty (e.g., age, marital status, relocation in the past 10 years). Frailty was measured with the Comprehensive Frailty Assessment Instrument. The validity was examined by means of prevalence rates, distribution, and the odds rates within both data sets.

Results: The validation sample had an increase in the percentage of older adults who were mildly and highly frail for physical (men: +17.0 percent point, women: +20.7 percent point), psychological (men: +13.4 percent point, women: +13.7 percent point), social (men: +24.8 percent point, women: +4.8 percent point), and environmental frailty (men: +24.2 percent point, women: +6.8 percent point). The present results indicate that the risk of being mildly or highly frail was higher in the D-SCOPE sample compared to the BAS data.

Conclusion: The present study proved the validity of risk factors such as age, marital status and having relocated in the past 10 years. Selecting older people based on these risk factors proved to be an effective strategy for detecting frail older people.

Introduction

The world's population has aged considerably over the last few decades [1]. In line with this development, the number of older adults with a high need for care and support has continued to increase [2], though aging in place is stimulated from a policy perspective in order to reduce the high costs of institutionalization [3]. Moreover, it is also the wish of most older people to stay at home as long as possible [4]. One of the conditions that is associated with aging is frailty, which can be described as a dynamic state affecting an individual who experiences losses in one or more domains of human functioning, which increases the risk of adverse outcomes such as a higher number of admissions to long-term care facilities [5, 6]. Therewith, the possibility to age in place is threatened for frail older people [7]. To prevent frailty and its adverse negative (health) outcomes such as institutionalization, as well as to tackle their unmet needs in care and support in general, (frail) older adults are visited proactively by a nurse or a social worker in many countries [8]. However, it is often unknown which older adults are at risk of adverse outcomes and thus should be visited. Consequently, preventive home visits on a large scale can be inefficient and expensive. In some places, the decision to visit an older person proactively is based on age. However, older people are a heterogeneous group, so (merely) focusing on people of a certain age does not seem to be the most effective way to detect people in need of care and support [9, 10]. Therefore, a more targeted approach is needed to identify frail older people in need of care and support [11-13]. In the light of a more targeted approach, focusing on specific groups seems to be more promising than early detection initiatives in the general population [9].

In response to this, Dury et al. (2017) used the Belgian Ageing Studies dataset (N=28 049) to determine risk factors for four different domains of frailty (i.e., physical, social, environmental and psychological frailty), stratified by gender. Sociodemographic risk factors are age, marital status and country of birth. Socioeconomic risk factors are net household income and education [14]. A last risk factor is 'relocated the previous 10 years'. These risk factors differ depending on the frailty domain and gender (Table 1). In literature, frailty is described as a dynamic state which can deteriorate but also improve [5]. Previous research has shown that frailty in an early state is reversible. Therefore, a timely detection of frailty is important. A strategy to detect frailty is with the use of risk factors. Nonetheless, currently, it is not yet clear if selecting older people based on these risk factors is indeed an effective way of

identifying frail older people by means of preventive home visits. Therefore, the present study aimed to validate the aforementioned risk factors for frailty. The following research question is examined: can a larger number of frail older adults be detected by means of preventive home visits by using the risk factors as developed by Dury et al. (2017)?

Table 1: Risk factors per frailty domain and sex (Dury et al., 2017)

	Physical frailty		Psychological frailty		Social frailty		Environmental frailty	
	Men	Women	Men	Women	Men	Women	Men	Women
Older age	x	x	x		x	x		
Marital status			x	x	x	x	x	x
Country of birth							x	x
Relocated the previous ten years	x	x	x	x	x	x		x (not relocated)
Lower education	x	x	x	x		x	x	x
Lower income	x	x	x	x	x	x	x	x

Note: in case of environmental frailty, relocated in the past 10 years is a protective factor.

Methods

Two data sets that were collected in three Belgian municipalities (Knokke-Heist, Ghent and Thienen) were used and compared.

The first data set, using a representative sample, was the Belgian Ageing Studies (BAS). The BAS is a large-scale survey in Belgian municipalities collecting information in community-dwelling older people by means of a highly structured survey. The questionnaire contains over 80 questions regarding for example demographic information, housing, civic participation, and frailty [15]. The BAS uses a participatory peer-research methodology; older volunteers administer the survey. Data collection started in 2004 and is still ongoing in new municipalities. For the current study, BAS-data that were collected in the aforementioned municipalities were used. This sample was collected in 2011 in Ghent, in 2013 in Knokke-Heist, and in 2009 for Thienen (using a proportional sample, stratified for age and gender). The respondents were assured of their privacy and of their right to refuse to participate or answer a question. The ethical committee of the Vrije Universiteit Brussel approved the study protocol (B.U.N. 143201111521). A detailed description of the BAS and the interview-design can be found in the methodological paper of De Donder et al. [15].

The second data set, labelled as the validation sample, was gathered within the *D-SCOPE* project (Detection, Support and Care for older people: Prevention and Empowerment). D-SCOPE investigated strategies for the proactive detection of potentially frail, community-

dwelling older people in order to guide them towards the right support and/or care. The respondents were selected through the census records, based on the risk factors for frailty [14]. Consequently, the sample was not representative but overrepresented older citizens having a higher risk of being frail. Participants were free to participate in the project. The survey was administered by researchers and older volunteers. Data collection started in March 2017 and lasted until September 2017. The ethical committee of the Vrije Universiteit Brussel approved the study protocol (B.U.N. 143201630458) and written informed consent was obtained from all participants. The details of the data collection method can be found in the protocol paper [16].

Participants

In both studies, participants were community-dwelling older adults aged 60 years and over. Participants were excluded from the study in the case of hospitalization, when the participant or the informal caregiver indicated that the older adult was unable to participate, or when the interviewer noted that the older participant was unable to provide adequate answers (e.g., not being able to answer questions due to physical exhaustion or distraction).

Concerning the D-SCOPE sample (N = 869), the researchers determined that older adults had to meet at least three risk factors to be included in the analysis of the present study. The study of Dury et al. proposed several risk factors, however no clear cut-offs were suggested. Therefore, the cut-off criteria for age, marital status, education and income were determined using a ROC curve (using sensitivity and specificity rates). The cut-off inclusion groups were: 70 and older (versus 60-69) for age; living alone (versus living with a partner) for marital status; no schooling to lower secondary (versus higher secondary to university degree) for education; 500 - 1499 euro (versus 1500 euro or more) for income; relocated in the previous ten years yes (versus no); and country of birth in Belgium versus elsewhere.

In the BAS sample (N=1496), the recruitment of older adults was representative, and not based on the risk factors. Therefore, BAS was used as the gold standard for prevalence.

Measurement of frailty

Since the aim was to identify strategies for proactive detection of community-dwelling older people at risk of frailty, and to guide them towards the proper support and/or care, with a focus on empowerment and aging well in place, a multidimensional approach to frailty is

needed. Therefore, in both studies, BAS and D-SCOPE, frailty was measured using the Comprehensive Frailty Assessment Instrument (CFAI) [17]. The CFAI is a self-reported survey, which includes four domains of frailty: physical, social, psychological, and environmental frailty. The survey section on the physical domain (4 items) assesses an older adult's functionality. The psychological domain (8 items) includes questions about mood disorders (5 items) and emotional loneliness (3 items). The social domain comprises social loneliness (3 items) and the potential social support network (10 items). Finally, the environmental domain (5 items) covers the suitability of the physical housing environment. Scores on all sub scales range from 0 to 100, with higher scores indicating more severe levels of frailty. The total score (i.e., for 'overall' frailty) on the CFAI is calculated by summing the scores on each domain divided by the number of domains. The CFAI was previously validated with a second-order confirmatory factor analysis [17, 18]. Moreover, a previous study determined the presence of three natural groups within the sample: no-to-low frail, mildly frail and highly frail [19].

Statistics

The validity was tested by measuring 1) the prevalence of mildly and highly frail older adults meeting the risk factors per domain and gender in the BAS and D-SCOPE study; 2) the congruence of the distribution of frailty in older adults meeting the risk factors (D-SCOPE data) and the distribution of frailty in the 'representative sample' (i.e., the BAS data as gold standard) by means of a Mann-Whitney U test; 3) the mean differences of the frailty domains between the BAS and D-SCOPE sample using independent sample t-tests; 4) the odds' ratio between the levels of frailty per frailty domain and gender; and 5) the sensitivity, specificity, positive predicted value (PPV), negative predicted value (NPV) and accuracy. Since we were mainly interested to detect frailer older adults, only the results of the no-low group versus mildly or highly frail group were discussed in the results. All analyses were performed in SPSS 22 (IBM Corp., Armonk, NY, USA).

Results

Table 2 presents the sociodemographic and socioeconomic variables of the BAS- and the D-SCOPE sample (i.e., only older adults with the presence of at least three risk factors). In the BAS-sample, 51.5% of the men and 43.2% of the women was aged < 70 years. In the D-SCOPE sample, this ranged between 1.9% for men physical frailty and 19% for women environmental

frailty. The percentage of older adults living together was 80% for men and almost 60% for women in the BAS-sample. In the D-SCOPE sample, these percentages ranged from 1.9% for women who were psychologically frail, to 18.1% for men who were physically frail. Approximately 1 out of 5 participants in the BAS sample had relocated in the previous ten years, while in the D-SCOPE sample this number ranged between 39.2% for women with environmental frailty, to 80.4% for men with social frailty.

Table 3 presents the prevalence of frailty for each domain, and men and women separately. The D-SCOPE sample had a higher number of mildly and highly frail older adults for physical (men: +17.0 percent point, women: +20.7 percent point), psychological (men: +13.4 percent point, women: +13.7 percent point), social (men: +24.8 percent point, women: +4.8 percent point), and environmental frailty (men: +24.2 percent point, women: +6.8 percent point). Moreover, a significant difference in distribution was found for physical (men and women), psychological (men and women), social (men), and environmental frailty (men).

Table 2: Sample characteristics BAS-dataset (whole sample) and D-SCOPE (at least 3 risk factors) stratified according to domain and sex

	BAS		D-SCOPE physical 3 risk factors		D-SCOPE psychological 3 risk factors		D-SCOPE social 3 risk factors		D-SCOPE environmental 3 risk factors	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
	N= 683	N= 813	N= 105	N= 157	N= 176	N= 155	N= 153	N= 226	N= 55	N= 158
Age (years) %										
60-69	51.5	43.2	1.9	3.8	4.0	14.2	2.6	9.7	12.7	19.0
70 and above	48.5	56.8	98.1	96.2	96.0	85.8	97.4	90.3	87.3	81.0
Marital status %										
Partner	80.5	59.8	18.1	13.4	10.8	1.9	2.6	9.3	3.6	6.3
Single	19.5	40.2	81.9	86.6	89.2	98.1	97.4	90.7	96.4	93.7
Country of birth %										
Belgium	93.2	95.8	96.2	94.9	96.6	92.9	96.7	94.7	87.3	90.5
In Europe	4.6	2.8	2.9	3.8	2.8	4.5	2.6	3.5	7.3	5.7
Outside Europe	2.2	1.4	1.0	1.3	0.6	2.6	0.7	1.8	5.5	3.8
Relocated past 10 years %										
Yes	21.1	18.2	77.1	75.2	75.6	74.2	80.4	65.0	56.4	39.2
Level of education %										
< lower secondary	44.2	58.6	67.6	75.2	44.9	72.3	36.6	58.4	94.5	74.1
secondary education or more	55.8	41.4	32.4	24.8	55.1	27.7	63.4	41.6	5.5	25.9
Net Monthly household income %										
500 - 1499 €	33.1	45.4	86.7	89.8	60.8	94.2	64.7	81	98.2	93.0
> 1500 €	66.9	54.6	13.4	10.2	39.2	5.8	35.3	19	1.8	7.0

Table 3: Level of frailty

	BAS physical		D-SCOPE physical		BAS psychological		D-SCOPE psychological		BAS social		D-SCOPE social		BAS environmental		D-SCOPE environmental	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
No-low	72.2%	57.6%	55.2%	36.9%	69.1%	62.1%	55.7%	48.4%	39.8%	38.0%	15.0%	33.2%	60.6%	56.8%	36.4%	50.0%
Mild	15.5%	24.1%	29.5%	42.0%	24.5%	26.8%	30.7%	32.3%	37.8%	41.0%	54.2%	49.1%	28.1%	29.3%	36.4%	40.5%
High	12.3%	18.3%	15.2%	21.0%	6.4%	11.1%	13.6%	19.4%	22.4%	21.0%	30.7%	17.7%	11.3%	13.9%	27.3%	9.5%
Mann-Whitney			p<0.01	p<0.000			p<0.000	p<0.01			p<0.000	p>0.05			p<0.000	p>0.05

Table 4 presents the mean differences of the average frailty scores per frailty domain. For men, in the D-SCOPE sample a significant difference for each domain was found, while for women this was only the case for physical and psychological frailty, in line with the results of Table 3.

Table 4: Mean differences in Frailty score BAS versus D-SCOPE (domain and sex)

	BAS		D-SCOPE		p-value	
	Male	Female	Male	Female	Male	Female
Physical frailty	24.067 (35.4)	34.625 (38.6)	37.857 (37.9)	48.328 (37.4)	p<0.05	p<0.05
Psychological frailty	15.201 (17.3)	18.978 (20.0)	21.776 (21.6)	26.602 (24.3)	p<0.05	p<0.05
Social frailty	45.543 (21.7)	45.516 (23.1)	56.209 (53.3)	47.577 (18.6)	p<0.05	p>0.05
Environmental frailty	11.589 (18.2)	13.727 (20.9)	20.636 (21.6)	13.861 (17.6)	p<0.05	p>0.05

Note: Independent T-test

Table 5 presents the odds ratios (OR) for each domain, and for men and women separately. The risk of being mildly or highly frail was higher in the D-SCOPE sample compared to the BAS data for physical (OR men 2.103, OR women 2.315), psychological (OR men 1.780, OR women 1.749), social (OR men 3.741, OR women 1.234), and environmental frailty (OR men 2.693, OR women 1.316). These results indicate that the risk of being mildly or highly frail was higher in the D-SCOPE sample than in the BAS data.

Table 5: The risk of being more frail meeting three risk factors

	D-SCOPE physical		D-SCOPE psychological		D-SCOPE social		D-SCOPE environmental	
	Men OR (CI)	Women OR (CI)	Men OR (CI)	Women OR (CI)	Men OR (CI)	Women OR (CI)	Men OR (CI)	Women OR (CI)
No-to-low frail (ref)	0	0	0	0	0	0	0	0
Mild and high frail	2.10 (1.38-3.20)	2.32 (1.63-3.30)	1.78 (1.27-2.50)	1.75 (1.24-2.47)	3.74 (2.34-5.98)	1.23 (0.90-1.69)	2.69 (1.52-4.77)	1.32 (0.94-1.85)
No-to-low/mild frail (ref)	0	0	0	0	0	0	0	0
High frail	1.28 (0.72-2.29)	1.19 (0.78-1.81)	2.29 (1.35-3.89)	1.93 (1.22-3.04)	1.54 (1.04-2.26)	0.81 (0.55-1.18)	2.95 (1.56-5.59)	0.65 (0.37-1.15)
No-to-low frail (ref)	0	0	0	0	0	0	0	0
Mild frail	2.49 (1.53-4.03)	2.72 (1.84-4.01)	1.56 (1.07-2.27)	1.54 (1.04-2.28)	3.81 (2.33-6.22)	1.37 (0.97-1.91)	2.16 (1.13-4.10)	1.57 (1.09-2.27)
Mild frail (ref)	0	0	0	0	0	0	0	0
High frail	0.65 (0.33-1.27)	0.66 (0.41-1.05)	1.69 (0.94-3.03)	1.45 (0.87-2.43)	0.96 (0.63-1.44)	0.70 (0.47-1.05)	1.87 (0.91-3.84)	0.49 (0.27-0.90)

Note: OR = Odds ratio. CI = confidential interval

Table 6 shows that the sensitivity across the domains was varying from 0.12 to 0.27 and the specificity ranged from 0.75 to 0.95. The accuracy ranged from 44% to 84% (see table 6).

Table 6: Statistical measurements: sensitivity, specificity, PPV, NPV and accuracy

	D-SCOPE physical		D-SCOPE psychological		D-SCOPE social		D-SCOPE environmental	
	Male	Female	Male	Female	Male	Female	Male	Female
no/low-middle/high								
Sensitivity	0.20	0.22	0.27	0.21	0.24	0.23	0.12	0.18
Specificity	0.89	0.89	0.83	0.87	0.92	0.80	0.95	0.85
PPV	0.45	0.63	0.44	0.52	0.85	0.67	0.64	0.50
NPV	0.72	0.58	0.69	0.62	0.40	0.38	0.61	0.57
Accuracy	0.69	0.58	0.64	0.60	0.48	0.44	0.61	0.56
No/low/middle-high								
Sensitivity	0.16	0.18	0.35	0.25	0.24	0.19	0.16	0.12
Specificity	0.87	0.84	0.81	0.85	0.83	0.78	0.94	0.83
PPV	0.15	0.21	0.14	0.19	0.31	0.18	0.27	0.09
NPV	0.88	0.82	0.94	0.89	0.78	0.79	0.89	0.86
Accuracy	0.78	0.72	0.77	0.78	0.69	0.66	0.84	0.74
No/low-middle								
Sensitivity	0.23	0.25	0.24	0.19	0.24	0.25	0.09	0.21
Specificity	0.89	0.89	0.83	0.87	0.92	0.80	0.95	0.85
PPV	0.35	0.53	0.36	0.40	0.78	0.60	0.50	0.45
NPV	0.82	0.70	0.74	0.70	0.51	0.48	0.68	0.66
Accuracy	0.76	0.68	0.66	0.65	0.56	0.51	0.67	0.62
Middle-high								
Sensitivity	0.16	0.18	0.35	0.25	0.24	0.19	0.16	0.12
Specificity	0.77	0.75	0.76	0.81	0.76	0.75	0.91	0.79
PPV	0.34	0.33	0.31	0.38	0.36	0.26	0.43	0.19
NPV	0.56	0.57	0.79	0.71	0.63	0.66	0.71	0.68
Accuracy	0.51	0.52	0.66	0.64	0.56	0.57	0.68	0.59

Note: PPV = positive predicted value, NPV = negative predicted value

Discussion

The main goal of this study was to validate the risk factors for frailty as developed by Dury et al. [14]. The present study proved the validity of these risk factors by examining the prevalence, distribution, mean differences and the odds ratio between the BAS and the D-SCOPE sample (validation sample). The results are characterized by a low sensitivity, but a high specificity. According to the present results, selecting older people based on these risk factors

is indeed an effective strategy of identifying frail older people, which could increase efficiency of preventive home visits.

A first key finding is the proven validity of the risk factors. The average scores of the frailty domains and the prevalence of mildly and highly frail older adults is higher in older adults that meet at least three risk factors. Therewith, the odds of identifying people who are mildly or highly frail is higher if one screens people who meet at least three risk factors. The validation of these risk factors indicates that selecting older people based on these risk factors can be an effective way of detecting mildly or highly frail older adults. This affirms prior research showing that age, marital status, a lower level of education, low socioeconomic status, and ethnicity are risk factors for frailty [20-24]. However, it should be noted that the results are characterized by low specificity and high specificity, indicating that the use of these risk factors is mainly helpful for excluding a large group of people in advance. Nonetheless, the frailty status of the remaining group of people should be examined further.

A second key finding is that the identification of frail older people based on risk factors seems to be more effective in men than in women. An explanation might be that the margin to detect frailer older women is smaller. Previous research has shown that being a woman is a risk factor for frailty [25, 26], and indeed, in BAS-sample, women already had higher (i.e., more severe) frailty levels compared to men. Related hereto, the prevalence of mild and high frailty was higher in women. Another plausible explanation for this finding might be that the women within the BAS-sample already met more risk factors compared to men. For instance, only 19.5% of the men were single in BAS-sample, while 40.2% of women were single. Consequently, it should be noted that in general, the increase of older people meeting risk factors in the D-SCOPE sample (validation sample) in comparison with BAS was higher in the men group.

A third key finding is that using the risk factors especially seems to increase the detection of mildly frail older adults. Since in BAS most people are no-low frail, a general increase on the CFAI will primarily lead to the detection of a higher proportion of mildly frail older adults.

Limitations

Some limitations of the research should be highlighted. A first limitation is that only older adults who met at least three risk factors could be included for the validation sample. The lack

of older adults meeting all risk factors can be a plausible explanation why several analyses did not have significant results. However, one must be aware that using all risk factors can cause missing out (frail) older people in need of care if they not meet these risk factors.

A second limitation is the uniqueness of each municipality, implying that the risk factors and the importance of risk factors may differ in every municipality. For instance, in Thienen, the number of older adults relocated in the past 10 years was very low. Consequently, this risk factor was less applicable and assumed less relevant in the detection of frail older adults. Therefore, more in-depth research at the level of the municipality should be done (e.g., multilevel analysis) [27, 28].

A third limitation is the small number of older adults with a migration background in our samples. Due to changing societal trends, in the near future, a higher number of older adults will have a migration background [29, 30].

Implications and Future Research

Several authors define frailty as a dynamic state, and potentially reversible or modifiable by interventions [5, 31]. However, recent research has shown that the effectiveness of interventions is still inconclusive, and it is suggested that older people can become too frail to be reversible [33]. Therefore, it is believed that early detection and early intervention is important to delay or even reduce frailty [32]. The present results show that a case-finding strategy based on risk factors could be helpful in detecting frail older people. This information could be helpful for professionals in the community to detect/screen frail older people with an evidence-based strategy, which is more efficient. Since early detection is important for the dynamic state of frailty, this might also imply that the efforts made by the professionals (i.e., extra care and support) could be more effective [31, 33]. However, one must be aware that not all (frail) older people at risk of adverse outcomes fit in these risk profiles, and some people in need of more support and care will be missed using this case finding strategy. Therefore, the case finding strategy as presented in this article should be seen as a part of a larger policy. Moreover, professional health care services should be aware of changing demographics, such as increased number of older people who divorce [34], and an increased number of older adults with a country of birth outside Europe [29, 30]. These changes in demographics should be taken into account; because it might be needed to ‘update’ these risk factors. In addition, professional health care services should consider that every municipality is unique and that

risk factors may differ among municipalities. Therefore, as said before, more in-depth research at the level of the municipality should be done.

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Chapter 5

Transition to Retirement and Frailty in Later Life: A Cross-Sectional Study in Flemish Older Adults

Submitted as:

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Abstract

Background: There is evidence that the transition from working life into retirement has an impact on a person's health status at older age. However, there is hardly any research about how the conditions of retirement affect frailty in later life. Therefore, the present study aims to assess to which extent different motivations for retiring is related to frailty in later life.

Methods: A cross-sectional study was performed among community-dwelling older people In Flanders and Brussels (aged ≥60). The data of the Belgian Ageing Studies were used (N=23 387). Frailty was measured with the Comprehensive Frailty Assessment Instrument, a multidimensional frailty scale. The factors determining the choice to retire comprised 13 items. The statistical analysis was done by a General Linear Model.

Results: On average, the time spent in retirement was 11.89 years. People who retired for health-related problems, who were unemployed for some time, who were obliged to retire and who were dissatisfied with the job content or the working conditions had higher scores on the CFAI (and subdomains) in later life, meaning being frailer. When the reason to retire was the retirement of the spouse, taking up care tasks, giving young people a chance or having sufficient financial assets and the financial incentive to work longer was too low, respondents had a lower score on the CFAI (or subdomains) in later life, meaning being less frail.

Conclusion: The present study shows that the context of the transition from working life into retirement may influence the development of frailty in later life and that this process needs to be well prepared.

Introduction

Frailty is common among community-dwelling older adults. According to a systematic review, the prevalence estimates of frailty range from 4.0% to 59.1% [1]. In Flanders/Belgium, studies have estimated a prevalence of frailty ranging from 9.3% to 22.9% of the population older adults [2-4]. Transitions to states of greater frailty over time are common and any transition from the non-frail state increases health service utilization [5-7]. Many studies have shown that frailty is associated with various, adverse (health-related) outcomes such as hospitalization, institutionalization and mortality [8]. The number of older adults of retirement age (>67 years) is expected to increase from 26% (in 2017) to 39% (in 2070) [9]. Because of the aging population in Belgium (and many Western countries), an increase in the number of frail older adults with a high need for care and support is expected [5-7].

Frailty is a dynamic state affecting an individual who experiences losses in one or more domains of human functioning (physical, psychological, social), caused by the influence of a range of variables, and which increases the risk of adverse outcomes [10]. More recently, environmental indicators are also suggested as constituting a domain of frailty [11]. In the literature, early detection and intervention are regarded as important pathways to delay or prevent frailty, i.e., when it is still reversible [12]. To detect frail older adults in a timely fashion, the identification of risk factors is essential [13, 14]; therefore, current literature focuses on the importance of a life-course approach [15, 16]. A life-course approach emphasizes the temporal and social perspective, taking into account an individual's or a cohort's life experiences for clues to current patterns of health and disease, while at the same time recognizing that both past and present experiences are shaped by the wider social, economic, and cultural context [16].

In life, several events, such as marriage, birth of a child and death of beloved persons are shown to have a lasting impact on frailty [17]. One such important life event is the transition to retirement; this can be accompanied by opportunities (e.g., extra leisure, healthier lifestyle) as well as adverse events (e.g., loss of income, loss of social support) [17-21].

Several determining factors influence the decision to retire: health factors, work-related psychological factors, such as job satisfaction; physical or organizational aspects of the job such as working conditions and financial security that allow one to stop working [22, 23]. In the literature, these determining factors of retirement are usually categorized into voluntary, involuntary, and regulatory retirement [24]. Voluntary retirement can be understood as the

relative preference for leisure versus continuing work [24, 25]. Not every person retires voluntarily. Some persons are forced to retire because of corporate reorganizations, or for health-related or other reasons. This is often referred to as involuntary retirement [24, 25], while retirement at a statutory retirement age is referred to as regulatory retirement. Regulatory retirement is country-specific, given that the statutory retirement age and socially accepted retirement age differ among countries [24]. Previous research has reported that the perception of being forced into retirement (involuntary retirement) leads to lower self-reported ratings of physical and emotional health, wellbeing, and retirement satisfaction [26-28]. The negative outcomes of involuntary retirement may evince the importance of the financial or psychological readiness to retire and implies that involuntary retirement is a risk factor for health in later life [27, 29].

However, there is very little research into how the conditions of retirement affect frailty in later life [30, 31]. The goal of the present study was to assess to what extent the determining factors (reasons, motivations) leading to the decision to retire are related to frailty in later life and, if so, which motivations can be seen as risk factors and which ones as protective factors. The hypothesis in the present study is that we expect some determining factors of retirement to be related to a higher frailty score in later life, while other determining factors are related to a lower frailty score in later life.

Methods

Study Design

The data were collected in the Belgian Ageing Studies (BAS). BAS is a cross-sectional study that uses a structured questionnaire to collect information on various aspects related to quality of life. The aim of the BAS project is 1) to measure the living conditions and quality of life of older community-dwelling people, 2) to promote evidence-based policy for older people at the local level by providing input and mobilizing knowledge for planning and inclusive policy programs, 3) to support the process of creating age-friendly communities, and 4) to examine trends in particular municipalities by conducting follow-up studies. Data collection started in 2004 and is still ongoing, adding data from new municipalities. In the present study, we made use of the data collected from 2005 to 2016. Within BAS, a participatory peer-research method is used to select participants. Older volunteers who were willing to interview respondents were selected and received training. These volunteers invited randomly designated respondents to

participate in the research project by sending them a letter and subsequently contacting them face-to-face a few days later. The questionnaire was developed to be self-administered, although volunteers were allowed to clarify. The respondents were free to participate, and their anonymity was guaranteed. The ethical committee of the Vrije Universiteit Brussel approved the study protocol (B.U.N. 143201111521). The details of the data collection method can be found in a methodological paper elsewhere [32].

Participants

Respondents were community-dwelling people aged 60 years and over from the Dutch-speaking part of Belgium (Flemish region) and Brussels (in total N = 83 municipalities). The sampling fraction depended on the size of the municipality and varied between N = 109 and N = 984. In each municipality, addresses were selected randomly from the census records. The sample was stratified, using quotas for gender and age (60 – 69, 70 – 79 and 80+ years) to ensure that the sample matched the makeup of the underlying population in the community.

Frailty

The Comprehensive Frailty Assessment Instrument (CFAI) measures frailty in four domains: physical, social, psychological and environmental [11]. The scores for the subscales range from 0 to 25. The multidimensional frailty score of the CFAI (total frailty) is calculated by summing the scores for each indicator (range 0 to 100). In the present study, the CFAI was used as a continuous scale, although cut-off points exist to distinguish between no-to-low frailty, mild frailty and sever frailty [2]. The CFAI was validated by second-order confirmatory factor analysis [11].

Factors determining retirement

Questions regarding retirement were retrospective. Respondents were asked to what extent the following factors determined their decision to retire (5-point Likert scale: not important at all to very important): 1) I was obliged to retire (e.g., business closure, corporate reorganization); 2) I wanted to give young people a chance; 3) I had sufficient financial assets to retire; 4) the financial incentive to work longer was too low; 5) I had health-related problems; 6) I was dissatisfied with the job content; 7) I was dissatisfied with the working conditions; 8) I did not have enough leisure time (e.g., for traveling, hobbies); 9) my spouse

retired; 10) members of my peer group retired; 11) I needed to take up care tasks (e.g., for spouse, parents, grandchildren); 12) I had been unemployed for some time; and 13) I reached the statutory retirement age.

The determining factor 'I reached the statutory retirement age' has been assessed in the BAS questionnaire since 2014; therefore, the number of respondents who answered this question was much lower (N = 2237). A determining factor of retirement is defined as a risk factor if it is associated with a higher score on the CFAI and a protective factor if it is associated with a lower score on the CFAI.

Individual characteristics

Sociodemographic variables included age, marital status, gender, education, and relocation during the previous 10 years. Age was continuous. Marital status included six categories: married, never married, divorced, living together, widow(er), a religious worker. Level of education was divided in three classes: low (no level of secondary education), middle (a level of secondary education) and high (college or university degree).

Three socioeconomic variables were included: net household income, income (in-) sufficiency, homeownership.

Statistical methods

To explore differences in the CFAI scores between the groups, intergroup differences in the CFAI scores were examined using the Kruskal-Wallis test, due to non-normality of the data. Factors determining retirement that were not significantly ($p < 0.05$) related to frailty were not included in the subsequent step of the analysis. Predictors of frailty were studied with a univariate general linear regression analysis (GLM), whereby the final model was established through backward elimination. In order to check for problems related to intercorrelations between the independent variables, collinearity diagnostics were analyzed. The cut-off criterion was set at a variance inflation factor (VIF) of >10.0, a conventional threshold value to indicate a multicollinearity problem [33]. Non-linearity was tested and resolved by the use of a quadratic term for all frailty domains. To test for heteroscedasticity the Koenker-Basset test was used, and adjustments were made by the use of heteroscedasticity-consistent standard errors. All analyses were performed in SPSS 24 (SPSS, Inc., Chicago, IL).

Results

In total, 23 387 participants from 83 municipalities across Flanders and Brussels were included in the present study. 14 867 of the participants were men and 8520 women. The average age of the respondents was approximately 70 years. Of the men, 82.4% were married, as were 62.9% of the women. Almost 20% of the men and women were highly educated, and more than 80% were owner of a house. Table 2 presents an overview of the results. Several determining factors for retirement were found to be protective, while others were risk factors for frailty in later life. These results were based on unstandardized coefficients of the General Linear regression models (GLM). In what follows, the category 'very important' is compared to 'not important at all'. In supplementary file 1-2 the results are presented in detail.

Table 1: Descriptive statistics

		Men (N=14867)		Women (=8520)	
Age (Mean +SD)					
		70.34	7.26	70.76	7.92
Marital status (N + %)					
	Married	12244	82.4	5362	62.9
	Never married	492	3.3	415	5.1
	Divorced	425	2.9	437	5.1
	Cohabiting	292	2.0	153	1.8
	Widow(ed)	1393	9.4	2109	24.8
	Religious worker	21	0.1	44	0.5
Educational level (N + %)					
	Low	8664	58.3	5112	60.0
	Middle	3401	22.9	1789	21.0
	High	2802	18.8	1619	19.0
Relocated previous 10 years (N + %)					
	Yes	1921	12.9	1293	15.2
Homeownership (N + %)					
	Owner	13005	87.5	7120	83.6
	Rent (private)	969	6.5	707	8.3
	Rent (public)	376	2.5	288	3.4
	None	517	3.5	405	4.8
Net income (N + %)					
	500 - 999 €	1813	12.2	1684	19.8
	1000 - 1499 €	4849	32.6	2485	29.2
	1500 - 1999 €	4022	27.1	1832	21.5
	2000 - 2499 €	2122	14.3	1205	14.1
	2500 - 3999 €	1687	11.3	1098	12.9
	4000 – 4999 €	232	1.6	133	1.6
	> 5000 €	142	1.0	83	1.0
Frailty score (Mean + SD)					
	Total frailty	24.63	13.98	28.07	15.58
	Environmental frailty	3.39	4.66	3.48	4.95
	Physical frailty	5.90	8.59	8.02	9.65
	Psychological frailty	4.10	4.27	4.92	4.81
	Social frailty	11.24	5.02	11.64	5.04

Total Frailty

For men, three determining factors of retirement were associated with a higher score on the CFAI scale in later life: “I had health-related problems” ($\beta = 6.617$ CI [5.9, 7.3] $p < 0.001$), “I was dissatisfied with the job content” ($\beta = 1.662$ CI [0.105, 3.219] $p < 0.05$), and “I had been unemployed for some time” ($\beta = 2.454$ CI [0.643, 4.265] $p < 0.01$). The determining factor “I had sufficient financial assets to retire” was associated with a lower score on the total frailty scale ($\beta = –1.623$ CI [–2.695, 0.551] $p < 0.01$).

For women “I had health-related problems” (β = 7.334 CI [6.481, 8.307] p < 0.001) and “I had been unemployed for some time” (β = 1.662 CI [0.105, 3.219] p < 0.05) were associated with a higher score on the CFAI scale. The determining factors of retirement “my spouse retired” (β = –2.181 CI [–3.291, –1.071] p < 0.001), and “I needed to take up care tasks” (β = –1.328 CI [–2.416, –0.239] p < 0.05) were associated with a lower score on the CFAI.

Physical Frailty

For men, one determining factor of retirement, “I had health-related problems”, was related to a higher score on the CFAI-subdomain physical frailty in later life (β = 5.321 CI [4.890, 5.752] p < 0.001). Two determining factors were related to a lower score on the CFAI-subdomain physical frailty in later life: “the financial incentive to work longer was too low in my case” (β = –0.791 CI [–1.360, –0.222] p < 0.01) and “I was dissatisfied with the working conditions” (β = –0.918 CI [–1.534, –0.302] p < 0.01).

For women, the determining factor of retirement “I had health-related problems” was related to a higher score on the CFAI-subdomain physical frailty in later life (β = 5.090 CI [4.543, 5.637] p < 0.001). The determining factors “the financial incentive to work longer was too low in my case” (β = –0.943 CI [–1.797, –0.089] p < 0.05) and “my spouse retired” (β = –1.003 CI [–1.666, –0.339] p < 0.01) are associated with a lower score on the CFAI-subdomain of physical frailty.

Psychological Frailty

For men, three determining factors of retirement were associated with a higher score on the CFAI-subdomain of psychological frailty in later life: “I was obliged to retire” (β = 0.321 CI [0.102, 0.540] p < 0.01), “I had health-related problems” (β = 0.999 CI [0.776, 1.222] p < 0.001) and “I was dissatisfied with the job content” (β = 0.790 CI [0.228, 1.352] p < 0.01). The determining factor “I had enough financial assets to retire” was associated with a lower score on the CFAI-subdomain of psychological frailty (β = –0.461 CI [–0.792, –0.130] p < 0.01).

For women, the determining factors of retirement “I had health-related problems” (β = 1.299 CI [0.994, 1.605] p < 0.001) and “I had been unemployed for some time” (β = 0.713 CI [0.643, 4.265] p < 0.05) were associated with a higher score on the CFAI-subdomain of psychological frailty. The determining factor of retirement ‘my spouse retired’ (β = –0.442 CI [–0.791, –0.093] p < 0.05) was associated with a lower score on the CFAI-subdomain of psychological frailty.

Social Frailty

For men, “I was dissatisfied with the job content” (β = 0.771 CI [0.224, 1.318] p < 0.01) was associated with a higher score on the CFAI domain of social frailty, while “I wanted to give young people a chance” (β = –0.644 CI [–0.996, –0.293] p < 0.001) was associated with a lower score on the CFAI-subdomain of social frailty.

For women, two determining factors were associated with a higher score on the CFAI-subdomain of social frailty in later life: “I had health-related problems” (β = 0.521 CI [0.205, 0.837] p < 0.01) and “I was dissatisfied with the working conditions” (β = 0.710 CI [0.124, 1.295] p < 0.05). Two determining factors of retirement were related with a lower score in the CFAI-subdomain of social frailty: “the financial incentive to work longer was too low in my case” (β = –0.746 CI [–1.272, –0.220] p < 0.01) and “I needed to take up care tasks” (β = –0.528 CI [–0.909, –0.146] p < 0.01).

Environmental Frailty

For men, four determining factors of retirement were associated with a higher score on the CFAI-subdomain of environmental frailty in later life: “I was obliged to retire” (β = 0.273 CI [0.042, 0.503] p < 0.05), “I had health-related problems” (β = 0.333 CI [0.105, 0.560] p < 0.01), “I was dissatisfied with the job content” (β = 0.559 CI [0.034, 1.083] p < 0.05), and “I had been unemployed for some time” (β = 1.121 CI [0.496, 1.746] p < 0.001), while one was related with a lower score: “my spouse retired” (β = –0.734 CI [–1.199, –0.268] p < 0.01).

For women, “I had health-related problems” (β = 0.427 CI [0.134, 0.720] p < 0.01) was associated with a higher score on the CFAI-subdomain of environmental frailty.

Differences between gender and across frailty domains

Differences were found between men and women. The results indicate that ‘I needed to take up care tasks’ was a protective factor for women, but not for men. For men, having sufficient financial assets was an important protective factor, but not for women. Dissatisfaction with the job content was a risk factor for men, but not for women.

Across the various frailty domains some differences are found: 1) the number of significant risk and protective factors differed for each frailty domain; 2) the significance of the determining factors of retirement differed across frailty domains. For instance, when retiring

because “I needed to take up care tasks” was statistically significant for the social frailty domain, but not for the physical, psychological, or environmental frailty domains; 3) the factor “I had health-related problems” was the only determining factor of retirement appearing as a risk factor for all frailty domains and the total frailty scale except the subdomain of social frailty in men.

Table 2: Summary protective and risk factors of frailty

	Total frailty		Physical frailty		Psychological frailty		Social frailty		Environmental frailty	
	Protective factor	Risk factor	Protective factor	Risk factor	Protective factor	Risk factor	Protective factor	Risk factor	protective factor	Risk factor
Men	1) I had sufficient financial assets to retire	1) health-related problems 2) I was dissatisfied with the job content 3) I had been unemployed for some time	1) the financial incentive to work longer was too low 2) I was dissatisfied with the working conditions	1) health-related problems	1) I had sufficient financial assets to retire	1) obliged to retire 2) health-related problems 3) I was dissatisfied with the job content	1) in order to give young people a chance	1) I was dissatisfied with the job content	1) my spouse retired'	1) obliged to retire 2) health-related problems 3) I was dissatisfied with the job content 4) I had been unemployed for some time
Women	1) my spouse retired 2) I needed to take up care tasks	1) health-related problems 2) I had been unemployed for some time	1) the financial incentive to work longer was too low 2) my spouse retired	1) health-related problems	1) my spouse retired	1) health-related problems 2) I had been unemployed for some time	1) the financial incentive to work longer was too low 2) to take up care tasks	1) health-related problems 2) I was dissatisfied with the working conditions		1) health-related problems

Note: This table is based on a univariate general linear regression analysis (GLM), whereby the final model was established through backward elimination. The data are presented in supplementary file 2. The protective factors are related with being less frail in later life (lower score CFAI), while the risk factors are related with being more frail in later life (higher score on CFAI). Only the significant factors (p-value < 0.05) are included; all others are not mentioned. The models were adjusted for age, gender, marital status, education, relocated the past 10 years, income, income sufficiency, homeownership and time spent in retirement

Discussion

According to the present results, several determining factors of retirement were related to multidimensional frailty and its subdomains (physical, psychological, social and environmental) of frailty. The protective factors were: “I wanted to give young people a chance”, “I had sufficient financial assets to retire”, “the financial incentive to work longer was too low in my case”, “I was dissatisfied with the working conditions”, “my spouse retired” and “I needed to take up care tasks”. Five factors determining retirement were identified as a risk factor: “I was obliged to retire”, “I had health-related problems”, “I was dissatisfied with the job content”, “I was dissatisfied with the working conditions”, and “I had been unemployed for some time”.

In previous research, the focus was mainly on voluntary versus involuntary retirement [24], whereby involuntary retirement was associated with negative (health) outcomes such as lower wellbeing, self-reported physical and emotional health [27, 28]. The results for the determining factors “I was obliged to retire” and “I had health-related problems” consequently confirm the idea that involuntary retirement is related with negative outcomes [34]. Conversely, determining factors based on voluntary retirement such as “I had sufficient financial assets to retire” and “my spouse retired” are associated with a lower score on the CFAI (being less frail). However, the present results show that voluntary retirement also can be associated with a higher score on the CFAI (being more frail). To illustrate, the determining factor “I was dissatisfied with the job content” can be classified as voluntary retirement, but is associated with a higher score on the CFAI [34]. In the literature, a second type of classification makes use of ‘push’ and ‘pull’ factors. Push factors have been defined as negative considerations, such as poor health or dislike of one’s job, that induce older workers to retire. Pull factors are typically positive considerations, such as the desire to pursue leisure interests or volunteering activities, that attract older employees toward retirement. It is suggested that, after the time of retirement, push and pull factors will almost certainly continue to influence the retiree’s life in either a positive or a negative way [28, 35]. Push factors will assumedly be a risk factor for health outcomes, while pull factors will be a protective factor. The determining factor “I was dissatisfied with the job content” can be classified as a push factor, which according to the push-pull framework, will continue to influence the retiree’s life in a negative way. Consequently, the present results indicate that if a determining factor of retirement is

voluntary but at the same time also a push factor (e.g., I was dissatisfied with the job content), it can be associated with negative (health) outcomes.

It is not always clear whether a determining factor of retirement is voluntary or involuntary, or a push or pull factor. Therefore, the authors (MVDE, JDL and JL) discussed as to whether these determining factors of retirement are voluntary or involuntary and push or pull factors. The results of this discussion can be found in supplementary file 3 [28, 34, 36]. It is likely that a determining factor of retirement can be a push factor for some persons, but a pull factor for others (the same applies to voluntary versus involuntary) [34]. To illustrate this, "I needed to take up care tasks" was classified in several ways during this meeting (see supplementary file 3). Previous research showed that partners caring for injured/ill military personnel appear to be at risk of experiencing personal distress caused by impaired relationship functioning, which may lead to diminished physical and mental wellbeing [37]. However, there is emerging evidence that supporting others also has beneficial health effects for the informal caregiver depending on the level of caregiving [38]. Therefore, it is likely that some persons will perceive this motivation for retirement as voluntary; for others it is involuntary retirement. For some this will be a pull factor but a push factor for others. Probably this is the reason why "I was dissatisfied with the working conditions" is found to be protective and as a risk factor depending on the frailty subdomain. Consequently, one can assume that pull and push factors (or voluntary and involuntary retirement) neutralize each other, leading to no significant results (ecological fallacy) [39]. More research is needed to gain a better understanding of how some factors should be classified and whether this depends on specific situations such as the level of caregiving or coping.

The present study demonstrates the need for a life-course approach to have a better understanding of the development of frailty. The respondents in the present study had been retired on average for 11.89 years and still association between the determining factors of retirement and frailty is still found. This confirms the statement by Kuh: "We need to harness the power of the life course approach and study design with the biomedical and social research on frailty and undertake comparative studies using different cohorts" [15]. More focus on a life-course approach may be necessary to acquire a better understanding of the development of frailty and to give insights into strategies to prevent frailty [40].

Strengths and Limitations

A strength of the present study is the use of a large dataset that includes 23 387 participants. A first limitation in the present study is the absence of variables related to work burden, for example, the role of physical job demands, psychological job stress, work histories, or occupation. Previous research found evidence that psychological job stress is damaging to health [41]. A second limitation is the absence of variables related to frailty such as comorbidity and disability [42]. Thirdly, the result of the determining factor of health-related problems should be interpreted with caution since frailty may be the trigger to retire as suggested by previous research [23, 43]. Fourthly, one must take into account that most people had retired long before this study took place. Therefore, memory bias could occur. Fifthly, the proportion of the variance in the dependent variable that is predictable from the independent variables, is low (see adjusted R-square). A final limitation, based on the present results one can state the existence of a relationship between frailty in later life and the determining factor of retiring (e.g., health-related reasons); however, one cannot make any statements about how the frailty trajectory evolved between time of retirement and the time of the survey. Therefore, there is a need for longitudinal studies.

Future research and policy implications

Future research should focus more on a life-course approach to acquire a better understanding of the development of frailty. This may give insight into strategies to prevent frailty [40]. The present results suggest that the transition from working life into retirement can be a trigger in the development of frailty in later life. However, longitudinal studies are needed to get a better understanding of the development of frailty over time. Future studies should not focus solely on voluntary versus involuntary retirement to explain the association between the motivation for retirement and negative (health) outcomes. Adding extra factors, such as push and pull factors, offers a more convenient framework. Although more research is necessary and perhaps a more elaborated framework including factors such as planned/unplanned retirement, and physical demands, may provide even a better framework to explain the results [44, 45].

The present results show that some groups of people score higher on a frailty scale in later life (e.g., persons who retire because of health-related problems). Hence, instead of screening the total population on frailty, a more targeted screening (case-finding) based on the factors

determining retirement could be more efficient and effective [14]. Thereby, the results may also indicate that it could be beneficial to start interventions to prevent or delay frailty around the retirement phase (e.g., a home visit by a community worker, intervention with regard to physical activities), while frailty is probably still reversible [21, 46]. With regard to the external validity of the present results, one should take into account the social, cultural, and economic context across populations. Risk and/or protective factors cannot be considered in the same way for developed, developing or underdeveloped countries. Also, within countries, the context evolves: e.g., the evolvement of traditional gender roles. In the present study, differences are found between men and women, which may not be surprising since the labor trajectories/histories are different for both [47]. However, this might change if traditional gender roles continue to evolve. Lastly, the relation between frailty and health-related problems may indicate that an increase in the statutory retirement age may not be feasible for everyone.

Conclusion

The present study shows evidence that several determining factors of retirement are associated with frailty and the subdomains of frailty in later life: some as a risk factor such as “I had health-related problems”, “I was obliged to retire”, “I was dissatisfied with the job content”, and others as a protective factor like “I had sufficient financial assets”, “my spouse retired”, “I needed to take up care tasks”. Based on these risk factors, a more targeted and effective screening (case-finding) to detect frail older adults can be carried out instead of screening the whole population. To get a better insight into the development of frailty, more research is needed, focusing on a life-course approach. Previous research focuses mainly on voluntary versus involuntary retirement, while present research shows that this classification is too limited and that a more comprehensive framework will be more suitable.

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Supplementary File 1: Characteristics baseline and comparison within groups

Table A: Characteristics baseline and comparison within groups (Men)

	TF	FF	PF	SF	EF
1. Obliged to retire	34.838***	16.098**	89.283***	6.674	68.558***
2. Young people	17.277**	17.999***	79.817***	33.915***	55.419***
3. Sufficient financial assets	83.338***	89.719***	65.093***	16.337***	68.171***
4. Financial incentive too low	9.136*	47.831***	45.993***	26.434***	46.807***
5. Health-related problems	625.037***	804.005***	335.225***	22.658***	125.635***
6. Dissatisfaction job content	69.112***	9.527*	229.746***	29.137***	148.147***
7. Dissatisfaction working conditions	53.891***	21.482***	191.649***	18.510***	116.633***
8. Lack of free time	49.030***	56.350***	148.694***	2.883	93.961***
9. Retirement of spouse	58.225***	12.189*	129.308***	1.548	76.032***
10. Retirement of peer group	30.304***	14.353**	164.363***	7.231	96.232***
11. Care tasks	37.599***	2.540	156.615***	3.949	66.299***
12. Unemployed	104.042***	17.889***	131.800***	10.416*	119.530***
13. Statutory retirement age	7.395	6.714	18.891***	0.480	8.797

Note: Kruskal-Wallis; Dependent variables: TF= total frailty; FF = Physical frailty; PF = psychological frailty and SF = Social frailty; EF=environmental frailty; * = p < .05; ** = p < .01 and *** = p < .001

Table B: Characteristics baseline and comparison within groups (Women)

	TF	FF	PF	SF	EF
1. Obliged to retire	18.069***	2.992	32.106***	6.678	38.311***
2. Young people	13.591**	15.393**	7.714	6.686	23.154***
3. Sufficient financial assets	40.461***	45.000***	23.725***	21.735***	21.031***
4. Financial incentive too low	10.582*	28.354***	9.715*	9.067*	17.590***
5. Health-related problems	259.567***	300.397***	143.119***	17.241**	46.191***
6. Dissatisfaction job content	13.129*	4.014	68.424***	5.511	30.035***
7. Dissatisfaction working conditions	12.871*	8.843	66.360***	15.985**	33.606***
8. Lack of free time	46.374***	58.543***	37.368***	9.287	23.266***
9. Retirement of spouse	36.568***	15.945**	44.057***	16.322**	25.521***
10. Retirement of peer group	8.919	15.636**	33.782***	10.130*	18.803***
11. Care tasks	44.913***	19.981***	30.629***	33.904***	30.935***
12. Unemployed	25.316***	7.431	49.196***	2.123	36.201***
13. Statutory retirement age	1.121	3.845	1.911	3.787	2.363

Note: Kruskal-Wallis; Dependent variables: TF= total frailty; FF = Physical frailty; PF = psychological frailty and SF = Social frailty; EF=environmental frailty; * = p < .05; ** = p < .01 and *** = p < .001

Supplementary File 2: Results statistical analysis

Table A: Determinant factors of retirement and Total frailty

		Men				Women			
		Estimate	CI		p-value	Estimate	CI		p-value
1. Obliged to retire									
2. Young people									
	very important	-1.623	-2.695	-0.551	<0.01				
	rather important	-0.903	-1.584	-0.222	<0.01				
3. Sufficient financial assets	neither important/ neither not important	-0.337	-0.990	0.315	NS				
	rather not important	-0.554	-1.400	0.292	NS				
	not at all important (ref.)	0a							
	very important	-0.702	-1.713	0.309	NS				
	rather important	-0.762	-1.478	-0.045	<0.05				
4. Financial incentive too low	neither important/ neither not important	-1.904	-2.577	-1.231	<0.001				
	rather not important	-0.989	-1.828	-0.151	<0.05				
	not at all important (ref.)	0a							
	very important	6.617	5.935	7.300	<0.001	7.394	6.481	8.307	<0.001
	rather important	4.847	4.133	5.560	<0.001	4.511	3.589	5.433	<0.001
5.Health-related problems	neither important/ neither not important	2.478	1.650	3.306	<0.001	2.644	1.464	3.825	<0.001
	rather not important	1.854	0.897	2.811	<0.001	1.286	-0.061	2.632	NS
	not at all important (ref.)	0a				0a			
	very important	1.662	0.105	3.219	<0.05				
	rather important	2.027	1.046	3.008	<0.001				
6. Dissatisfaction job content	neither important/ neither not important	0.927	0.082	1.772	<0.05				
	rather not important	1.040	0.096	1.983	<0.05				
	not at all important (ref.)	0a							
7. Dissatisfaction working conditions									
8. Lack of free time									
	very important					-2.181	-3.291	-1.071	<0.001
	rather important					-0.973	-1.962	0.015	NS
9. Retirement of spouse	neither important/ neither not important					0.068	-1.119	1.256	NS
	rather not important					0.777	-0.894	2.447	NS
	not at all important (ref.)					0a			
	very important	-0.482	-1.896	0.932	NS				
	rather important	0.818	0.001	1.634	<0.05				
10. Retirement of peer group	neither important/ neither not important	0.989	0.216	1.763	<0.05				
	rather not important	0.760	-0.196	1.715	NS				
	not at all important (ref.)	0a							
	very important					-1.328	-2.416	-0.239	<0.05
	rather important					-1.368	-2.439	-0.298	<0.05
11. Care tasks	neither important/ neither not important					-0.374	-1.693	0.944	NS
	rather not important					0.122	-1.437	1.682	NS
	not at all important (ref.)					0a			
	very important	2.454	0.643	4.265	<0.01	2.216	0.189	4.243	<0.05
	rather important	0.977	-1.088	3.043	NS	1.950	-0.192	4.092	NS
12. Unemployed	neither important/ neither not important	0.641	-0.313	1.595	NS	-0.749	-2.024	0.525	NS
	rather not important	0.339	-1.082	1.760	NS	0.696	-1.230	2.623	NS
	not at all important (ref.)	0a				0a			
13. Statutory retirement age									

Note: General linear regression, unstandardized coefficients. Dependent variable: CFAI (rang 0-100). SD = standard deviation, CI = Confidential Interval.

The final model was established through backward elimination, the determinant factors without results were not included in the final model**.** The models were adjusted for age, marital status, education, relocated the past 10 years, income, income sufficiency, homeownership and time spent in retirement.

Table B: Determinant factors of retirement and Physical Frailty

		Men				Women			
		Estimate	CI		p-value	Estimate	CI		p-value
1. Obliged to retire									
2. Young people									
3. Sufficient financial assets									
4. Financial incentive too low	very important	-0.791	-1.360	-0.222	<0.01	-0.943	-1.797	-0.089	<0.05
	rather important	-0.496	-0.897	-0.096	<0.05	-0.103	-0.733	0.528	NS
	neither important/ neither not important	-0.961	-1.314	-0.609	<0.001	-0.745	-1.311	-0.179	<0.01
	rather not important	-0.396	-0.875	0.082	NS	-0.026	-0.79	0.738	NS
	not at all important (ref.)	0[a]				0[a]			
5.Health-related problems	very important	5.321	4.890	5.752	<0.001	5.09	4.543	5.637	<0.001
	rather important	3.272	2.833	3.712	<0.001	2.738	2.169	3.307	<0.001
	neither important/ neither not important	1.211	0.747	1.674	<0.001	1.269	0.545	1.992	<0.001
	rather not important	0.833	0.272	1.394	<0.01	1.195	0.318	2.072	<0.01
	not at all important (ref.)	0[a]				0[a]			
6. Dissatisfaction job content									
7. Dissatisfaction working conditions	very important	-0.918	-1.534	-0.302	<0.01				
	rather important	-0.747	-1.258	-0.235	<0.01				
	neither important/ neither not important	0.089	-0.377	0.555	NS				
	rather not important	-0.234	-0.769	0.301	NS				
	not at all important (ref.)	0[a]							
8. Lack of free time	very important					-0.530	-1.578	0.519	NS
	rather important					-1.000	-1.656	-0.344	<0.01
	neither important/ neither not important					-0.739	-1.441	-0.037	<0.05
	rather not important					0.347	-0.483	1.176	NS
	not at all important (ref.)					0[a]			
9. Retirement of spouse	very important					-1.003	-1.666	-0.339	<0.01
	rather important					-0.521	-1.131	0.088	NS
	neither important/ neither not important					0.118	-0.611	0.846	NS
	rather not important					-0.474	-1.462	0.514	NS
	not at all important (ref.)					0[a]			
10. Retirement of peer group									
11. Care tasks									
12. Unemployed									
13. Statutory retirement age									

Note: General linear regression, unstandardized coefficients. Dependent variable: CFAI subdomain physical frailty (rang 0-25). SD = standard deviation, CI = Confidential Interval. The final model was established through backward elimination, the determinant factors without results were not included in the final model. The models were adjusted for age, marital status, education, relocated the past 10 years, income, income sufficiency, homeownership and time spent in retirement.

Table C: Determinant factors of retirement and Psychological Frailty

		Men				Women			
		Estimate	CI		p-value	Estimate	CI		p-value
1. Obliged to retire	very important	0.321	0.102	0.540	<0.01				
	rather important	0.266	-0.004	0.537	NS				
	neither important/ neither not important	0.129	-0.094	0.352	NS				
	rather not important	0.299	-0.074	0.673	NS				
	not at all important (ref.)	0[a]							
2. Young people									
3. Sufficient financial assets	very important	-0.461	-0.792	-0.130	<0.01				
	rather important	-0.282	-0.490	-0.073	<0.01				
	neither important/ neither not important	-0.175	-0.365	0.015	NS				
	rather not important	-0.154	-0.418	0.110	NS				
	not at all important (ref.)	0[a]							
4. Financial incentive too low									
5.Health-related problems	very important	0.999	0.776	1.222	<0.001	1.299	0.994	1.605	<0.001
	rather important	0.956	0.731	1.181	<0.001	0.847	0.527	1.166	<0.001
	neither important/ neither not important	0.603	0.337	0.868	<0.001	0.782	0.356	1.208	<0.001
	rather not important	0.462	0.148	0.776	<0.01	0.073	-0.412	0.557	NS
	not at all important (ref.)	0[a]				0[a]			
6. Dissatisfaction job content	very important	0.790	0.228	1.352	<0.01	0.643	-0.162	1.448	NS
	rather important	0.794	0.425	1.164	<0.001	0.587	0.035	1.139	<0.05
	neither important/ neither not important	0.359	0.045	0.673	<0.05	0.196	-0.232	0.625	NS
	rather not important	0.441	0.090	0.793	<0.05	0.751	0.280	1.223	<0.01
	not at all important (ref.)	0[a]				0[a]			
7. Dissatisfaction working conditions	very important	0.285	-0.105	0.676	NS				
	rather important	0.469	0.141	0.797	<0.01				
	neither important/ neither not important	0.109	-0.211	0.428	NS				
	rather not important	-0.061	-0.425	0.303	NS				
	not at all important (ref.)	0[a]							
8. Lack of free time									
9. Retirement of spouse	very important					-0.442	-0.791	-0.093	<0.05
	rather important					-0.171	-0.504	0.162	NS
	neither important/ neither not important					0.015	-0.397	0.428	NS
	rather not important					0.608	0.022	1.194	<0.05
	not at all important (ref.)					0[a]			
10. Retirement of peer group	very important	0.055	-0.415	0.524	NS				
	rather important	0.614	0.330	0.898	<0.001				
	neither important/ neither not important	0.296	0.055	0.536	<0.05				
	rather not important	0.387	0.083	0.691	<0.05				
	not at all important (ref.)	0[a]							
11. Care tasks									
12. Unemployed	very important					0.713	0.028	1.398	<0.05
	rather important					0.666	-0.078	1.409	NS
	neither important/ neither not important					-0.044	-0.462	0.374	NS
	rather not important					0.123	-0.501	0.746	NS
	not at all important (ref.)					0[a]			
13. Statutory retirement age									

Note: General linear regression, unstandardized coefficients. Dependent variable: CFAI subdomain psychological frailty (rang 0-25). SD = standard deviation, CI = Confidential Interval. The final model was established through backward elimination, the determinant factors without results were not included in the final model. The models were adjusted for age, marital status, education, relocated the past 10 years, income, income sufficiency, homeownership and time spent in retirement.

Table D: Determinant factors of retirement and Social Frailty

		Men				Women			
		Estimate	CI		p-value	Estimate	CI		p-value
1. Obliged to retire									
	very important	-0.644	-0.996	-0.293	<0.001				
	rather important	-0.524	-0.779	-0.270	<0.001				
2. Young people	neither important/ neither not important	-0.041	-0.299	0.217	NS				
	rather not important	0.03	-0.300	0.359	NS				
	not at all important (ref.)	0[a]							
3. Sufficient financial assets									
	very important	-0.331	-0.706	0.043	NS	-0.746	-1.272	-0.220	<0.01
	rather important	-0.404	-0.677	-0.131	<0.01	-0.151	-0.525	0.223	NS
4. Financial incentive too low	neither important/ neither not important	-0.645	-0.889	-0.401	<0.001	-0.264	-0.600	0.072	NS
	rather not important	-0.686	-0.997	-0.376	<0.001	0.062	-0.404	0.528	NS
	not at all important (ref.)	0[a]				0[a]			
	very important	0.082	-0.160	0.324	NS	0.521	0.205	0.837	<0.01
	rather important	0.411	0.149	0.674	<0.001	0.309	-0.025	0.643	NS
5.Health-related problems	neither important/ neither not important	0.539	0.231	0.846	<0.01	0.197	-0.217	0.610	NS
	rather not important	0.339	-0.026	0.705	NS	-0.132	-0.664	0.400	NS
	not at all important (ref.)	0[a]				0[a]			
	very important	0.771	0.224	1.318	<0.01				
	rather important	0.847	0.468	1.225	<0.001				
6. Dissatisfaction job content	neither important/ neither not important	0.247	-0.047	0.541	NS				
	rather not important	-0.063	-0.411	0.285	NS				
	not at all important (ref.)	0[a]							
	very important					0.710	0.124	1.295	<0.05
	rather important					0.662	0.183	1.141	<0.01
7. Dissatisfaction working conditions	neither important/ neither not important					0.546	0.116	0.976	<0.05
	rather not important					0.246	-0.274	0.767	NS
	not at all important (ref.)					0[a]			
8. Lack of free time									
9. Retirement of spouse									
10. Retirement of peer group									
	very important					-0.528	-0.909	-0.146	<0.01
	rather important					-1.003	-1.387	-0.619	<0.001
11. Care tasks	neither important/ neither not important					-0.735	-1.177	-0.293	<0.01
	rather not important					-0.538	-1.069	-0.008	<0.05
	not at all important (ref.)					0[a]			
12. Unemployed									
13. Statutory retirement age									

Note: General linear regression, unstandardized coefficients. Dependent variable: CFAI subdomain social frailty (rang 0-25). SD = standard deviation. The final model was established through backward elimination, the determinant factors without results were not included in the final model. The models were adjusted for age, marital status, education, relocated the past 10 years, income, income sufficiency, homeownership and time spent in retirement.

Table E: Determinant factors of retirement and Environmental Frailty

		Men				Women			
		Estimate	CI		p-value	Estimate	CI		p-value
	very important	0.273	0.042	0.503	<0.05	0.152	-0.194	0.499	NS
	rather important	0.27	-0.031	0.571	NS	0.51	0.062	0.958	<0.05
1. Obliged to retire	neither important/ neither not important	0.348	0.069	0.626	<0.05	0.504	0.140	0.868	<0.01
	rather not important	0.124	-0.323	0.571	NS	0.192	-0.401	0.785	NS
	not at all important (ref.)	0[a]				0[a]			
	very important	0.313	-0.012	0.639	NS				
	rather important	0.126	-0.120	0.371	NS				
2. Young people	neither important/ neither not important	-0.201	-0.455	0.053	NS				
	rather not important	0.176	-0.147	0.500	NS				
	not at all important (ref.)	0[a]							
3. Sufficient financial assets									
	very important	0.305	-0.048	0.658	NS				
	rather important	0.099	-0.149	0.348	NS				
4. Financial incentive too low	neither important/ neither not important	-0.178	-0.395	0.040	NS				
	rather not important	0.233	-0.062	0.527	NS				
	not at all important (ref.)	0[a]							
	very important	0.333	0.105	0.560	<0.01	0.427	0.134	0.720	<0.01
	rather important	0.26	0.018	0.501	<0.05	0.566	0.250	0.882	<0.001
5.Health-related problems	neither important/ neither not important	0.197	-0.104	0.498	NS	0.589	0.206	0.971	<0.01
	rather not important	0.353	-0.008	0.714	NS	0.135	-0.294	0.563	NS
	not at all important (ref.)	0[a]				0[a]			
	very important	0.559	0.034	1.083	<0.05				
	rather important	0.971	0.617	1.326	<0.001				
6. Dissatisfaction job content	neither important/ neither not important	0.581	0.281	0.88	<0.001				
	rather not important	0.348	0.011	0.684	<0.05				
	not at all important (ref.)	0[a]							
7. Dissatisfaction working conditions									
8. Lack of free time									
	very important	-0.734	-1.199	-0.268	<0.01				
	rather important	-0.132	-0.477	0.213	NS				
9. Retirement of spouse	neither important/ neither not important	0.097	-0.238	0.431	NS				
	rather not important	0.324	-0.075	0.723	NS				
	not at all important (ref.)	0[a]							
10. Retirement of peer group									
11. Care tasks									
	very important	1.121	0.496	1.746	<0.001				
	rather important	0.622	-0.088	1.332	NS				
12. Unemployed	neither important/ neither not important	0.245	-0.139	0.628	NS				
	rather not important	0.132	-0.414	0.679	NS				
	not at all important (ref.)	0[a]							
13. Statutory retirement age									

Note: General linear regression, unstandardized coefficients. Dependent variable: CFAI subdomain environmental frailty (rang 0-25). SD = standard deviation. The final model was established through backward elimination, the determinant factors without results were not included in the final model. The models were adjusted for age, marital status, education, relocated the past 10 years, income, income sufficiency, homeownership and time spent in retirement.

Supplementary File 3: Classification of the determining factors and motivation

Table A**:** Classification of the determining factors and motivation

	Involuntary		Voluntary	
	Push	Pull	Push	Pull
1. Obliged to retire	Retirement is forced, unexpected and unplanned, the person can't control the situation. They may retire before they are financially or psychologically ready, which could lead to a lower well-being.			
2. Young people	Social pressure can be the reason why the person retires, this social pressure can be perceived as a forced (involuntary) and negative retirement.			The person retired because of the desire to give the young generation a chance. The retirement can be perceived as voluntary (own, decision, under own control) and positive.
3. Sufficient financial assets				Retirement is not forced, the person examined his financial resources (pre-retirement planning), the retirement is planned, the person controls the situation.
4. Financial incentive too low			Retirement is not forced, although a negative perception arises: why should I continue to work? The work itself is not motivating enough to continue working. The person controls the situation.	
5. Health-related Reasons	A decline in health of a health shock can force a person into retirement, retirement is unexpected, the person can't control the situation.			
6. Dissatisfaction job Content			Retirement is not forced, although a negative perception raised. The person controls the situation.	
7. Dissatisfaction working conditions			Retirement is not forced, although a negative perception arises. The person controls the situation.	
8. Lack of free time			Retirement is not forced. A negative perception arises (the person wants to have more time, this can be due to the burden of a job). The person controls the situation.	Retirement is not forced. A positive perception arises: the person makes a pre-retirement plan, retirement gives him the opportunity to enjoy life while still young and fit enough. The retirement is planned, the person controls the situation.

Table A: Classification of the determining factors and motivation (continue)

	Involuntary		Voluntary	
	Push	Pull	Push	Pull
9. Retirement of Spouse				Retirement is not forced. A positive perception arises: the person makes a pre-retirement plan, retirement gives him the opportunity to spend more time with his/her spouse. The retirement is planned, the person controls the situation.
10. Retirement of peer group			Retirement is not forced. However, a negative perception arises: why should I continue to work if all others are not? This could decrease to motivation to continue working. A certain peer pressure or cultural pressure can arise. Therefore, the retirement happens earlier than initially planned.	Retirement is not forced. A positive perception arises: the person makes a pre-retirement plan, retirement gives him the opportunity to spend more time with for instance family or friends. The retirement is planned, the person controls the situation.
11. Care tasks	The person retires because of the obligation to care for instance for a spouse or a parent. The retirement can be perceived as forced (involuntary) and negative. The negative perceptions can also be linked to the burden of the care giving.	The person retires because of the obligation to care for instance for a spouse or a parent. The retirement can be perceived as forced (involuntary) and positive. The positive perception can be linked to the sense of being useful.		The person retires because of the desire to give care to grandchildren for instance. The retirement can be perceived as voluntary (own, decision, under own control) and positive.
12. Unemployed	Nonworking older workers face more constraints reentering the labor market, meaning that some of them become 'discouraged workers', people willing to work, but who dropped out of the labor force involuntarily. The retirement can be perceived as forced, unplanned and negative.			The person perceives being unemployed as negative, social stigma for example: one doesn't want to work. Retirement causes the social stigma to disappear. The person wants to retire, retirement is not forced and perceived as positive.
13. Statutory retirement age	Generous social security benefits can act as a form of unemployment insurance, effectively subsidizing workforce reductions by lowering the cost to the firm of shedding older workers. The retirement can therefore be perceived as forced, unexpected and negative. The person is financially or psychologically not ready to retire.			Eligibility for state occupational/private pension. Retirement is not forced (voluntary). The retirement is planned, the person was financially and psychologically ready for retirement.

Chapter 6

The relation between age of retirement and frailty in later life: A cross-sectional study in Flemish older adults

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Abstract

Background: Policymakers in several European countries, concerned about the sustainability of their pension system, have raised the statutory retirement age. While several studies investigated the effect of retirement on health, the relationship between retirement and frailty is neglected. Notwithstanding, frailty is associated with adverse outcomes. The aim of this study was to examine the relationship between age of retirement and frailty in later life.

Methods: Data of the Belgian Ageing Studies, a cross-sectional research project were used. The present study includes N = 12 659 participants (>60y) in 83 Flemish municipalities. To address reverse causality, only participants not retired because of health-related reasons were included. The Comprehensive Frailty Assessment Instrument, a multidimensional frailty scale with four domains (physical, psychological, social and environmental), was used to operationalize frailty. Univariate general linear regression analyses (GLM) were performed for scores on the total frailty scale and the four subdomains separately. The analysis was done for men and women separately, since both groups have different labor trajectories.

Results: The present study found a negative association between age of retirement and physical frailty for both men and women in later life, and total frailty for men, although the differences were small. No evidence was found for a relation between age of retirement and the other subdomains of frailty.

Conclusions: The results suggest that age of retirement is not a clinically relevant predictor for frailty in later life. Differences within and between subpopulations (e.g., profession) can shed a new light on this relation.

Introduction

Demographic changes such as increased longevity have led to widespread public concerns in many countries about the sustainability of their pension systems. Therefore, policymakers in several European countries have redetermined the statutory retirement age. In Belgium, the current statutory retirement age is 65. However, the government agreed to raise the statutory age of retirement by 2030 by two years to the age of 67 [1]. Critics of these reforms express the concern that workers in strenuous occupations might not be able to continue working until they officially reach the retirement age and that unemployment and disability benefits will increase [2, 3]. In previous research, the effect of (the age of) retirement on health has been investigated, although the results still are inconclusive [4-6]. Rijs et al. found some evidence that age at retirement affects self-perceived health, but the effect is disparate depending on age group (e.g., retirees at age 59 – 60 were more likely to attain excellent or good self-perceived health, while early [55–58] and late [61–64] retirees were unaffected by retirement compared to people who continued working) [7]. Another study suggests that early retirement is associated with a reduction in both mortality and in inpatient care [8]. Therefore, increasing the mandatory retirement age may generate government revenues but also negatively affect health care expenditures. Heller-Sahlgren reports that spending a longer time in retirement has a negative impact on self-assessed, general, mental and physical health [9]. According to Haapanen et al., continuing to be occupationally active until the age of 70 years and older is associated with increased risk of frailty among men. However, the lowest prevalence of frailty was observed in former business executives who retired at ages 66 – 67 years [5]. These contradictory results can partly be explained by the different impact of retirement on a person. For example, one's health can be negatively affected by a decrease in physical activity or social relationships (e.g., loss of interactions with former colleagues) after retirement [10, 11]. However, retirement might also bring new opportunities such as new social contacts along with more leisure time and the opportunity to live a healthier lifestyle [3, 12-19]. In other studies, evidence was found that the effect of retirement on (mental) health depends on how the transition from work to retirement took place. Forced retirement (or involuntary retirement) leads to lower self-reported ratings of physical and emotional health and retirement satisfaction, while voluntary retirement comes with higher levels of well-being [20, 21].

While previous research mainly examined the relationship between retirement and health, the present study focuses on frailty. Frailty cannot be considered as a synonym of health. According to the definition of Huber et al., health is the ability to adapt and self-manage social, physical, and emotional challenges [22]. Frailty is a dynamic state affecting an individual who experiences losses in one or more domains of functioning (physical, psychological, social, and environmental) [23-25]. Consequently, an older adult can be healthy, but at the same time frail, and vice versa. Therefore, the association between age of retirement and frailty can be different in comparison with health. Frailty in older adults is a very common condition and associated with adverse (health) outcomes, like hospitalization, institutionalization, and death [26, 27]. Several risk factors for frailty have been found such as age, marital status, level of education, and income [28]. Some authors suggest that early detection and intervention are very important for preventing or delaying frailty and the associated adverse outcomes [29-32]. This approach of early detection and intervention is inherently related to the life course perspective that emphasizes a temporal and social perspective, looking back across an individual's or a cohort's life experiences or across generations for clues to current patterns of health and disease, whilst recognizing that both past and present experiences are shaped by the wider social, economic, and cultural context [33]. Early identification of those who may become frail and timely interventions may be able to modify such a trajectory and delay the emergence of frailty [34-37].

So far, we are aware of one study assessing the relationship between age of retirement and frailty. In this study, frailty was operationalized with the Fried Phenotype, a unidimensional, medical approach of frailty including exhaustion, weakness (grip strength), slow walking speed, and low physical activity [5]. Consequently, we do not know whether there is a relationship between age of retirement and a multidimensional approach to frailty. Therefore, the aim of the present study is to assess to what extent the decision to retire at a given age is associated with the level of frailty in later life, and the relevance of a life course perspective in frailty research. Since risk factors can change per subdomain, a sub analysis is done for each frailty domain [28]. Two research questions were examined: What is the relationship between age of retirement and total frailty? What is the relationship between age of retirement and the subdomains of frailty (physical, psychological, social, and environmental)?

Methods

Study design

For this cross-sectional study, data from the Belgian Ageing Studies (BAS) was used. BAS is a large-scale cross-sectional survey that uses a structured questionnaire to collect information on various aspects related to the quality of life. Data collection started in 2004 and is still ongoing, adding data from new municipalities. In the present study, data collected from 2005 to 2016 were used. To maximize the response, respondents were surveyed through a participatory peer research method. Through an intensive recruitment campaign, older volunteers were selected and trained to interview older respondents. These volunteers invited respondents to participate in the research project by sending them a letter and subsequently contacting them face-to-face a few days later. The questionnaire was developed to be self-administered, although volunteers were allowed to clarify questions. The respondents were free to participate, and their anonymity was guaranteed. The respondents were guaranteed the right to withdraw answering, and their right to privacy. When respondents refused to complete the questionnaire, the volunteers received alternative addresses. The ethical committee of the Vrije Universiteit Brussel approved the study protocol (B.U.N. 143201111521). The details of the data collection method can be found in a methodological paper [38].

Participants

The respondents were community-dwelling people aged 60 and over from the Dutch-speaking part of Belgium (Flemish Region) and Brussels (N = 12 659). The current study was carried out in N = 83 Flemish municipalities. In each municipality, addresses were randomly selected from population registries. The sample was stratified, using quotas for gender and age (60 - 69, 70 - 79 and 80+ years) to ensure that the sample matched the makeup of the underlying population in the municipality. The sampling fraction depended on the size of the municipality and varied between N = 109 and N = 984.

Variables and measurements

The selection of variables for this study from the basic questionnaire was made by three researchers (MVDE, JDL and BS). Out of 83 questions in total, 18 were selected.

Frailty

The Comprehensive Frailty Assessment Instrument (CFAI) was used to assess frailty. It measures frailty in four domains: physical, social, psychological, and environmental [24]. The physical domain has 4 items: (1) less demanding activities like carrying shopping bags, (2) walking up a hill or some stairs, (3) bending or lifting, (4) going for a walk. The social domain of frailty measures older people's social support networks (10 items, e.g., spouse) and social loneliness (3 items): (1) there are enough people whom I can rely on when I am in trouble, (2) I know many people whom I can trust totally, (3) there are enough people with whom I feel a bond. The psychological domain is captured by 8 items measuring mood disorders and emotional loneliness: (1) I feel unhappy and depressed, (2) I feel like I am losing my self-confidence, (3) I feel like I cannot cope with problems, (4) I feel like I am under constant pressure, (5) I feel like I am not worth anything anymore, (6) I experience a general sense of emptiness, (7) I miss having people around me, (8) I often feel rejected. The environmental aspect contains 5 items: (1) my house is in a bad condition/poorly kept, (2) my house is not very comfortable, (3) it is difficult to heat my house, (4) there is insufficient comfort in my house, (5) I do not like my neighborhood. The scores for the subscales were calculated by adding the scores of the specific items. All subscales ranged from 0 to 25. The total score of the CFAI was calculated by summing the scores on each indicator (ranging 0 to 100). The CFAI was previously validated, using a second-order confirmatory factor analysis and cross-validated against The Tilburg Frailty Indicator [24, 39].

Age of retirement and time spent in retirement

Respondents were asked at what age they retired (retirement or early retirement) retrospectively. Time spent since retirement was calculated by calculating age at data collection minus age of retirement.

Determining factors of retirement

The survey was performed retrospectively. Respondents were asked to what extent the following factors determined their decision to retire (using a five-point Likert scale: from not important at all to very important): (1) it was mandatory to retire (e.g., business closure, corporate reorganizations), (2) in order to give young people a chance, (3) I had sufficient financial assets to retire, (4) the financial incentive to work was too small, (5) health-related

reasons, (6) I was dissatisfied with the job content, (7) I was dissatisfied with the working conditions, (8) lack of free time (e.g., travelling, hobbies), (9) my partner retired, (10) members of my peer group retired, (11) to take up care tasks (e.g., spouse, parents, grandchildren), (12) I was unemployed for some time.

Sociodemographic and socioeconomic variables

The sociodemographic variables were age, marital status, gender, level of education, and whether the person had relocated during the past 10 years. Three socioeconomic variables were included: net household income, income (in)sufficiency, and homeownership. Data of the sociodemographic and socioeconomic variables were assessed at the time of the survey and not at the time of retirement.

Statistical methods

The statistical model contains the following elements: the dependent variable was frailty (total frailty) or a subdomain of frailty (physical, psychological, social, and environmental). For each dependent variable, a separate univariate general linear regression (GLM) was drawn. The statistical model contained the following independent variables: (1) age of retirement was necessary to answer the research question; (2) time spent in retirement was necessary to control for non-linearity over time; (3) determining factors of retirement, solely the significant determining factors of retirement were included for every subdomain (Van der Elst et al., in submission); (4) sociodemographic variables and (5) socioeconomic variables were included as control variables.

In the literature, methodological issues are discussed as affecting this type of study. The following issues are reported in particular: unobserved heterogeneity, non-linearity, and reverse causality [3, 40-46]. To address the issue of reversed causality a restricted sample was used, using only the data of the subpopulation that explicitly declined health issues (Likert score = 1) as a determining factor for retirement, a strategy also applied by Dave et al [40]. The analysis was done for men and women separately, since labor histories are different in both groups. Age of retirement has been used as a continuous variable. To determine differences between participants retiring pre- or post-statutory retirement age, the age of retirement has been divided into 4 categories (< 56, 56 - 60, 61 - 65, and > 65). To address the other methodological issues the following assumptions were analyzed and adjusted if

necessary: multicollinearity (VIF > 10), heteroscedasticity (Koenker-Bassett test), linearity (quadratic specification), and specification errors (Ramsey reset test). In the analyses, we excluded cases with missing responses. In supplementary file 1, the results with regard to the testing of assumptions can be found. Some problems with linearity, heteroscedasticity, and specification errors arose. To resolve non-linearity an age square was added and time spent in retirement was deleted because of multicollinearity. All analyses were performed in SPSS 24 (SPSS, Inc., Chicago, IL).

Results

Table 1 presents the characteristics of the sample for men and women separately. In total 12 659 participants (8093 men, 4566 women) in 83 municipalities across Flanders (and Brussels) were included in the analysis. The average age of the respondents was 70.7y. The majority of the included participants were male (63.6%), since many of the women were housewives in the past. 84.4% of the men lived together with a partner or spouse and 15.5% were living alone; for women 64.4% were living together. 88.3% of the male respondents were homeowners, and 83.5% of the women. 20.7% of the men and 18.3% of the women reported completing higher education. The mean retirement age was 58.87y (SD 4.11) for men and 57.92 (5.47) for women. The average time spent in retirement was 11.7 years for men and 13 years for women.

Table 1: Descriptive statistics

		Men (N=8093)		Women (=4566)	
Age (Mean +SD)					
		70.6	7.26	70.9	7.83
Age of retirement (Mean+SD)					
		58.9	4.11	57.9	5.47
Marital status (N + %)					
	Married	6677	82.5	2869	62.8
	Never married	262	3.2	241	5.3
	Divorced	220	2.7	216	4.7
	Cohabiting	156	1.9	74	1.6
	Widow(ed)	772	9.5	1144	25.1
	Religious worker	6	0.1	22	0.5
Educational level (N + %)					
	Low	4478	55.3	2737	59.9
	Middle	1942	24	995	21.8
	High	1673	20.7	834	18.3
Relocated previous 10 years (N + %)					
	Yes	995	12.3	672	14.7
Homeownership (N + %)					
	Owner	7133	88.1	3812	83.5
	Rent (private)	519	6.4	375	8.2
	Rent (public)	169	2.1	149	3.3
	None	272	3.4	230	5
Net income (N + %)					
	500 - 999 €	823	10.2	850	18.6
	1000 - 1499 €	2488	30.7	1330	29.1
	1500 - 1999 €	2241	27.7	989	21.7
	2000 - 2499 €	1250	15.4	667	14.6
	2500 - 3999 €	1030	12.7	598	13.1
	4000 - 4999€	160	2	72	1.6
	> 5000 €	101	1.2	60	1.3
Frailty score (Mean + SD)					
	Total frailty	22.3	12.9	25.9	14.7
	Environmental frailty	3.1	4.5	3.2	4.8
	Physical frailty	4.6	7.7	6.8	9.2
	Psychological frailty	3.6	4.0	4.4	4.6
	Social frailty	11.1	5.0	11.5	5.1

Continuous model (table 2)

For men, a statistically significant negative association was found between age of retirement and total frailty (β = −0.076, p < 0.05 CI: [−0.143, −0.008]), and between age of retirement and physical frailty (β = −0.046, p < 0.05 CI: [−0.086, −0.005]). This indicates that the older a person retires the lower the total and physically frailty score in later life will be. For all other domains, no statistically significant association was found. For women, a statistically significant negative association was found between age of retirement and physical frailty (β = −0.069, p < 0.05 CI: [−0.113, −0.024]). For all other frailty domains, no statistically significant association was found.

Table 2: Age of retirement and frailty (continuous model)

	Men (N=8093)				Women (N=4566)			
	Beta	CI	p-value	Adj. R-square	Beta	CI	p-value	Adj. R-square
Total frailty	-0.076	-0.143; -0.008	0.029	0.146	-0.049	-0.123; 0.025	0.191	0.174
Environmental frailty	0.014	-0.012; 0.039	0.293	0.055	0.000	-0.025; 0.026	0.987	0.037
Physical frailty	-0.046	-0.086, -0.005	0.027	0.149	-0.069	-0.113; -0.024	0.003	0.211
Psychological frailty	0.001	-0.021; 0.024	0.913	0.075	-0.005	-0.029; 0.019	0.708	0.069
Social frailty	-0.028	-0.056; -0.000	0.054	0.029	0.024	-0.003; 0.052	0.079	0.027

Note: General linear regression: parameters. The relationship between age of retirement and frailty (and subdomains). Beta: Unstandardized coefficients. Covariates: age, marital status, level of education and whether the person had relocated during the past 10 years, net household income, income (in-)sufficiency, homeownership, motivation for retirement, and time spent in retirement. Because of non-linearity, age-square was added to the model. Time spent in retirement was excluded from the model because of multicollinearity.

Categorical model (table 3)

The present results indicate that men retiring at age 55 or younger had a significant higher score on total frailty (β = 2.141, p < 0.05 CI: [0.124, 4.158]) and physical frailty (β = 1.354, p < 0.05 CI: [0.151, 2.558]) in comparison with men retiring after the statutory retirement age of > 65. For women a statistically significant difference was found in physical frailty. Women retiring after the statutory retirement age > 65 scored less physical frail in comparison with those retiring at age 60 or younger (β = 1.929, p < 0.05 CI: [0.191, 3.667]) or 55 and younger (β = 2.262, p < 0.05 CI: [0.502, 4.021]). No other statistically significant differences were found.

Table 3: Age of retirement and frailty (categorical model)

		Men (N=8093)			Women (N=4566)		
		Beta	CI	p-value	Beta	CI	p-value
Total Frailty	<56 year	2.141	0.124; 4.158	0.037	1.780	-1.110; 4.671	0.227
	56-60 year	0.940	-1.015; 2.895	0.346	1.859	-0.996; 4.713	0.202
	61-65 year	1.371	-0.605; 3.346	0.174	0.748	-2.166; 3.662	0.615
	>65 year		Ref.			Ref.	
	Adj. R-square		0.146			0.175	
Environmental Frailty	<56 year	0.307	-0.432; 1.046	0.416	-0.598	-1.618; 0.423	0.251
	56-60 year	0.228	-0.484; 0.941	0.531	-0.480	-1.489; 0.528	0.351
	61-65 year	0.524	-0.197; 1.244	0.154	-0.596	-1.626; 0.434	0.256
	>65 year		Ref.			Ref.	
	Adj. R-square		0.055			0.037	
Physical Frailty	<56 year	1.354	0.151; 2.558	0.027	2.262	0.502; 4.021	0.012
	56-60 year	0.643	-0.524; 1.809	0.280	1.929	0.191; 3.667	0.030
	61-65 year	0.799	-0.380; 1.978	0.184	1.136	-0.638; 2.911	0.209
	>65 year		Ref.			Ref.	
	Adj. R-square		0.150			0.212	
Psycholgical Frailty	<56 year	0.154	-0.499; 0.807	0.644	0.201	-0.749; 1.152	0.678
	56-60 year	0.026	-0.605; 0.656	0.936	0.339	-0.600; 1.278	0.479
	61-65 year	0.191	-0.446; 0.828	0.557	0.220	-0.738; 1.179	0.652
	>65 year		Ref.			Ref.	
	Adj. R-square		0.075			0.069	
Social Frailty	<56 year	0.220	-0.614. 1.055	0.605	-0.191	-1.268; 0.887	0.728
	56-60 year	0.021	-0.787; 0.830	0.959	-0.034	-1.098; 1.030	0.950
	61-65 year	-0.091	-0.908; 0.727	0.827	-0.167	-1.253; 0.920	0.763
	>65 year		Ref.			Ref.	
	Adj. R-square		0.029			0.026	

Note: General linear regression: parameters. The relationship between age of retirement and frailty (and subdomains). Beta: Unstandardized coefficients. Covariates: age, marital status, level of education and whether the person had relocated during the past 10 years, net household income, income (in-)sufficiency, homeownership, motivation for retirement and time spent in retirement. Because of non-linearity, age-square was added to the model. Time spent in retirement was excluded from the model because of multicollinearity.

Discussion

The aim of this study was to investigate the relationship between age of retirement and frailty (domains) in later life. An association between age of retirement and total respectively physical frailty was found for men. For women, an association was found between age of retirement and physical frailty, indicating that the later in life one retired, the lower one scored on the physical frailty measurement later in life. However, the differences in frailty scores were small. The present results indicate that early retirement before the age of 56 is related to a higher physical frailty score for both men and women, and a higher total frailty

score for men. No significant association was found between age of retirement and the other subdomains of frailty.

The results in the present study with regard to early retirement (< 56y) is in line with previous research. Haapanen et al. do find a relation between age of retirement and frailty [5]. Their estimates showed that persons retired at age 55 or younger have a higher risk of becoming frail in comparison to persons retired at age 58 - 67 [5]. Rijs et al. also reported that the effect of retirement is disparate depending on age group. Their study indicated that retiring at age 59 - 60 was beneficial for attaining excellent perceived health in comparison with people who continued working; for other age groups no differences were found [7]. Heller-Sahlgren reports that spending a longer time in retirement has a negative impact on self-assessed, general, mental, and physical health. The various studies seem to agree that retirement before the age of 55 is not beneficial for health/frailty (in later life) [9].

Throughout life, men and women often have a different employment trajectory, whereby women more often work part-time or take a short beak for family care [47]. Consequently, one could expect different results for men and women in the present study. However, only small differences were found between age of retirement and frailty (subdomains) for men and women. This may indicate that work history is not a relevant factor for frailty in later life. However, Wu et al. concluded that for women a career with short-term breaks for family care may be advantageous for lessening frailty risk in later life [47].

The present results reveal only small differences (e.g., physical frailty) or no association (e.g., social frailty). As stated in the introduction retirement can be accompanied by opportunities (e.g., extra leisure time, healthier lifestyle) as well as by adverse events (e.g., loss of income, loss of social support). A plausible explanation for these results is that these different mechanisms (opportunities and adverse outcomes) neutralize each other. For instance, Chung et al. describe that the effect of retirement on physical activity differed across subgroups. Physical activity decreased with retirement from a physically demanding job but increased with retirement from a sedentary job (Chung et al., 2009)). Barnett et al. report that retirement may lead to a decrease of total physical activity, but an increase in physical activity related to leisure time [12]. Börsch-Supan and Schultz report that retirement in general, and early retirement in particular, reduces the size of a social network. In particular, the number of friends and other non-family contacts in the interpersonal environment decreased post retirement [17]. However, Bogaard et al. emphasize that the number of contacts or contact

frequency is a markedly different concept than social support [19]. Seeing each other often or having many friends does not necessarily mean an exchange of support. Their study showed that retirees start giving more instrumental support to family and friends. This 'instrumentalization' of the relationship can perhaps also lead to stronger ties, and better relationships or social connectedness [19, 48]. A retired person could also choose to invest in activities within the comfort zone. These different mechanisms, positive and negative, could neutralize each other and explain why in the present study only small differences were obtained.

Strengths and limitations

A primary strength is the large sample size of the present study. Secondly, previous studies mostly examined the effect of retirement on health. However, age of retirement is a more relevant predictor for determining the desirability of the increase in statutory retirement age. Lastly, this study adjusted reverse causality and addressed other methodological issues like non-linearity and heteroscedasticity specification errors. When necessary or possible, adjustments were made.

This study also has some limitations. A first limitation is the cross-sectional nature of the study. Although several strategies were applied, it is difficult to point out the direction of the relationship. Instead, a longitudinal study could give more insights, especially in the evolution of frailty over time. Secondly, frailty cannot be considered as a synonym of health. A longitudinal study would also clarify how health status affects their motivation to retire, a group that has been excluded in the present study. Consequently, one must be cautious when comparing the present results with the results of previous research. Thirdly, no adjustment is made for white/blue-collar jobs or the stress level of a job or work trajectories before retirement, while previous research emphasizes the importance of these variables [47, 49]. Fourthly, no adjustment is made for comorbidity. Previous research has untangled the concept of frailty from other concepts like comorbidity and disability and provides support for frailty as an independent concept, distinct from comorbidity and disability [50]. Although frailty is an independent concept, it is related to comorbidity. One last limitation is the low R-square of environmental frailty and social frailty. This suggests that the model does not explain the variance of the outcome well and indicates that age of retirement is not that relevant.

Conclusion

A better understanding of the relationship between age of retirement and frailty could be a valuable argument in discussions to determine an increase of the statutory retirement age. This understanding would help identifying age of retirement as a predictor for frailty so effective strategies to detect frail older adults may be developed. To avoid a problem with reverse causality, a restricted sample was used including people who did not retire because of health-related problems. The present study found negative associations between age of retirement and physical frailty and total frailty (for men), although the differences in frailty score remain very small. No relationship between age of retirement and the other subdomains of frailty was found. These results suggest that age of retirement is not a clinically relevant predictor for frailty in later life and no evidence was found that to continue working after the statutory retirement age is associated with a higher frailty score in later life. On the contrary, retirement before the age of 55 seems to be related to a higher score on physical frailty and total frailty (for men). However, this study sample does not include participants who did retire because of health-related reasons and can therefore not be generalized to the total population. Future research should take into account that underlying mechanisms and incentives influence retirement. We assume that retirement can be a positive but also a negative experience, depending on various factors such as the transition to retirement and personal traits.

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Supplementary File 1*:* Testing assumptions GLM: heteroscedasticity and specification error

Table A: Testing assumptions GLM: heteroscedasticity and specification error

	Men					Women				
	TF	EF	FF	PF	SF	TF	EF	FF	PF	SF
R-square	0.029	0.017	0.053	0.028	0.0004	0.020	0.009	0.036	0.024	0.024
N	8093	8093	8093	8093	8093	4566	4566	4566	4566	4566
N*R-square	234.7	137.6	428,9	226.6	3.2	91.3	41.1	164.3	109.6	109.6
Heteroscedasticity	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
Specification error	Yes	Yes	Yes	Yes	No	No	No	Yes	No	No

Note: statistical models were tested on the assumption's heteroscedasticity and specification error. Heteroscedasticity = Koenker-Bassett test; critical value =3,84. Specification error: Ramsey reset test. TF= total frailty; EF= environmental frailty; FF = physical frailty; PF= psychological frailty and SF = social frailty.

Chapter 7

Interventions for frail community-dwelling older adults have no significant effect on adverse outcomes: a systematic review and meta-analysis

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Abstract

Background: According to some studies, interventions can prevent or delay frailty, but their effect in preventing adverse outcomes in frail community-dwelling older people is unclear. The aim is to investigate the effect of an intervention on adverse outcomes in frail older adults.

Methods: A systematic review and meta-analysis of Medline, Embase, the Cochrane Library, and Social Sciences Citation Index. Randomized controlled studies that aimed to treat frail community-dwelling older adults were included. The outcomes were mortality, hospitalization, formal health costs, accidental falls, and institutionalization. Several sub-analyses were performed (duration of intervention, average age, dimension, recruitment).

Results: Twenty-five articles (16 original studies) were included. Six types of interventions were found. The pooled odds ratios (OR) for mortality when allocated in the experimental group were 0.99 [95% CI: 0.79, 1.25] for case management and 0.78 [95% CI: 0.41, 1.45] for provision information intervention. For institutionalization, the pooled OR with case management was 0.92 [95% CI: 0.63, 1.32], and the pooled OR for information provision intervention was 1.53 [95% CI: 0.64, 3.65]. The pooled OR for hospitalization when allocated in the experimental group was 1.13 [95% CI: 0.95, 1.35] for case management. Further sub-analyses did not yield any significant findings.

Conclusion: This systematic review and meta-analysis does not provide sufficient scientific evidence that interventions in frail older adults can be protective against the included adverse outcomes. A sub-analysis for some variables yielded no significant effects, although some findings suggested a decrease in adverse outcomes.

Registration: Prospero registration CRD42016035429

Introduction

The population in the European Union is aging rapidly [1], and studies show that 30% of this population will be over age 65 by 2060 [1]. Therefore, the number of frail older adults with a high need for care and support will increase, and resource optimization is necessary [2, 3]. The literature describes two approaches to frailty [4-6]. The first, often designated as physical frailty, emphasizes frailty as a biological/medical concept, defined as "A medical syndrome with multiple causes and contributors that is characterized by diminished strength, endurance, and reduced physiologic function that increases an individual's vulnerability for developing increased dependency and/or death" [7]. The second approach investigates frailty in a multidimensional way. In addition to strength or endurance, this perspective emphasizes cognitive, social, and psychological factors as defined by Gobbens et al.: "Frailty is a dynamic state affecting an individual who experiences losses in one or more domains of human functioning (physical, psychological, social), which is caused by the influence of a range of variables and which increases the risk of adverse outcomes" [8].

Many studies suggest that frailty is associated with adverse outcomes including mortality, institutionalization, hospitalization, and accidental falls [7, 9-12]. Some authors assume that early detection and intervention are important to prevent or delay frailty, improve quality of life, and reduce costs of care [7, 13]. Nevertheless, it is unclear if interventions in frail community-dwelling older adults can be protective against adverse frailty outcomes [14-18].

This systematic literature review and meta-analysis examines the following three questions: Which interventions are applied to protect frail community-dwelling older adults against adverse outcomes? What effect do interventions have on frail community-dwelling older adults in terms of mortality, hospitalization, formal health costs, accidental falls, and institutionalization? Finally, how do age, study duration, and the multi- versus unidimensional approaches of frailty and recruitment influence the effect of an intervention?

Methods

A systematic review and meta-analysis was performed. Four electronic databases were consulted: Medline, Embase, The Cochrane Library (CL), and Social Sciences Citation Index (SSCI). The SSCI was consulted to assure that articles with a multidimensional approach to frailty would be found. The recommendations of the Cochrane Handbook for Systematic

Reviews for Interventions 5.1.0 were used [19], and the protocol was registered (Prospero registration CRD42016035429).

Search strategy

The search strategy used four key terms: aged, frail elderly, independent living, and randomized controlled trial (RCT). The final search strategy was developed with the help of a librarian (supplementary file 1: Search strategy). The search for articles was carried out for the first time in September 2015 and the second time on June 17, 2016. The references for the selected articles were screened for other potentially relevant publications.

Inclusion and exclusion criteria

Within the scope of this study, the population in the included articles had to be 60 years or older, diagnosed as frail, and community-dwelling. Concerning the intervention and methodology, all studies had to be RCTs, frailty had to have been operationalized (regardless of the frailty operationalization), all types of intervention were allowed, there was no recruitment after hospital discharge (inpatient and outpatient), and the intervention must have been compared with care as usual. The studies needed to have one or more of the following outcomes: mortality, institutionalization, hospitalization, formal health costs, and accidental falls. Pilot studies and studies not written in English, French, German, or Dutch were excluded.

Selection of studies

Retrieval and selection of studies were performed in a stepwise way. After duplicate records were removed, titles and abstracts were screened. Two reviewers assessed a sample of 12% (MVDE and DD). If their agreement reached 95%, the first author continued the inclusion process alone. In the next step, two researchers (MVDE and DD) independently read the full text of the selected articles for the inclusion and exclusion criteria. In cases of doubt or disagreement, a third researcher (BV) was asked to judge.

Critical appraisal

Two independent researchers (DL and BF) assessed the quality of each article with the Cochrane risk of bias tool [19]. An evaluation was made in seven areas (sequence generation,

allocation concealment, blinding participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other bias). If an article met two or fewer criteria, it was defined as low quality; meeting three or four criteria was defined as medium quality; and if it met more than four criteria, it was considered a high-quality paper.

Data extraction

The first author preformed the data-extraction by preparing an Excel sheet including all the necessary data to answer the research questions like average age of a study, number of participants. Subsequently two researchers (DL and BF) controlled the accuracy of the data-extraction. Information concerning average age, percentage of male participants, type of intervention, operationalization of frailty, and method of recruitment of participants (e.g., participants could be recruited through census records, a service center or a care center) were subsequently collected and categorized (supplementary file 2: Extra information operationalization and categorization of Variables). Frailty was defined unidimensionally if it included solely biological aspects (i.e., nutritional status, physical activity, mobility, strength, and energy). Frailty was defined multidimensionally if it also included variables such as cognition, mood, and social relations/social support [20].

Statistics

The statistical analysis was performed with SPSS 23.0 (IBM Corp., Armonk, NY, USA) and Review Manager 5.3 [21]. For the outcomes of mortality, institutionalization (residential home/nursing home/long-term care facility), and hospitalization (inpatients), the odds ratio (OR) was calculated for every intervention; for the outcome of accidental falls, the incidence rate ratio (IRR) was presented; for formal health costs a percentage was calculated, the sum of all the presented formal health costs in the intervention group (IG) was divided by the sum of all the presented formal health costs in the control group (CG). Raw data were used for the variables mortality, institutionalization and hospitalization, for accidental falls the IRR scores were used reported in the articles. If data were unclear the first author was contacted If possible, a pooled meta-analysis was executed to measure the odds ratio. A random effect model was applied because one can assume no common effect size exists, the study population may differ from each other in ways that could affect the treatment effect (e.g., differences in the average age of the study population). Differences among included studies

were assessed and described in terms of heterogeneity. A sub-analysis was performed for duration of intervention, a multi- versus unidimensional approach to frailty, average age, recruitment method of the participants, and studies with a moderate or high quality. A sub-analysis also was performed for studies that used the Fried criteria or the Frailty Index. Funnel plots were inspected, and studies with multiple research arms were analyzed separately.

Results

The details of the search process are presented (supplementary file 3: Flow chart). After the databases were searched, 25 articles were included for review representing 16 original studies. Duplicate data were excluded. All included papers are listed in Table 1 with study characteristics. The 16 original studies involved the following: nine with a case management intervention [2, 22-37], three with information provision interventions [38-41], one with physical intervention [42], one with psychosocial intervention [43], one with a pharmaceutical intervention [44], and one with a technological intervention [45]. Six articles approached frailty in a unidimensional way [2, 22-26, 37, 42, 44, 45], nine articles approached frailty in a multidimensional way [27, 29-36, 38-41, 43], and in one article the approach of frailty was unclear [28]. Two papers were of low quality (≤2) [39, 45]. For the interventions of case management and information provision, pooled meta-analyses were performed. For case management, sub-analyses also were performed.

Table 1. Descriptive information included articles (N=16 original studies, 25 articles) continued

OS. Author	arms	N	Frailty	Dim	Intervention	Duration	Age	QA
1. Aggar (2012), Cameron (2013), Fairhall (2012, 2014 & 2015)		237	Fried	1	Case management	12	83.3	4
2. De Vriendt (2016)		168	BEL-profile scale	1	Case management	2,5	80.4	4
3. Dorrestein (2016)		359	Poor self-perceived general health, concerns about falls and related activity avoidance	2	Psychosocial intervention	4	78.3	6
4. Favela (2013)	4.1	89	Rockwood	2	Case management	9	76	3
	4.2	88	Rockwood	2	Case management	9	76	3
5. Hall (1992)		167	≥65 and admitted by the Long Term Care program to personal care at home	-	Case management	36	77.9	4
6. Kehusmaa (2010), Ollonqvist (2008)		708	Meet the criteria for entitlement to the SII Pensioners' Care Allowance	2	Case management	8	78.4	4
7. Kim (2015)		66	Fried	1	Pharmaceutical intervention	3	80.7	5
8. Kono (2012 & 2013)		323	Being classified into the two lowest care need levels in the LTCI system: Support Levels 1 and 2 (out of 7)	2	Information provision intervention	24	79.9	2
9. Kono (2016)		360	Being classified into the two lowest care need levels in the LTCI system: Support Levels 1 and 2 (out of 7)	2	Information provision intervention	24	79.2	5
10. Metzelthin (2013, 2014 & 2015)		346	GFI	2	Case management	24	77.2	3
11. Monteserin (2010)		285	Meet 2 of following criteria:≥85y, >=9 the Gijon Social Scale, ≥2 the Pfeiffer test, ≥2 the Charlson comorbidity index, ≥1 the Yesavage Depression Scale, ≥91 the Barthel index, ≥12 the Mini-Nutritional Assessment Short Form, polymedication, >1 fall in the last 6 months and daily urinary incontinence in the last 6 months.	2	Information provision intervention	0	81.2	3
12. Perttila (2016)		83	Fried	1	Physical intervention	12	78.8	3
13. Upatising (2013)		32	Fried	1	Technological interention	12	-	2
14. Van Hout (2010)		651	Self-reported score in the worst quartile of at least two of six COOP–WONCA charts	2	Case management	18	81.4	4
15. Van Leeuwen (2015), Hoogendijk (2016)	15.1	683	Identified by primary care physician as frail	2	Case management	6	80.6	3
	15.2	694	Identified by primary care physician as frail	2	Case management	12	80.4	3
	15.3	682	Identified by primary care physician as frail	2	Case management	18	80.8	3
16. Williams (1987)		117	No medical evaluation during the preceding year, significant decline in functional ability, unstable medical problem, unmet needs in the performance of ADL, taking three or more medications who had not had a medical evaluation within the past year, dissatisfied with current medical care, seeking a second opinion	1	Case management	8	76.5	6

Note: Dim = dimension of frailty: 1 = unidimensional physical/medical; 2 = multidimensional (social, cognitive, psychological) - =missing. Duration in months, age in years. Van Leeuwen et al. and Favela et al. are studies with several arms. Ref. = reference. QA = Quality assessment, OS = original study.

The effects of an intervention

The effects of an intervention in the original studies are listed in Table 2. Two results were significantly better in the IG in comparison with the CG. In Hall et al. (29), the intervention of case management resulted in a lower institutionalization, with an OR of 0.32 [95% confidence interval (CI): 0.12, 0.87]. Perttila et al. performed a study with a physical intervention, which resulted in a lower number of accidental falls with an IRR of 0.43 [42]. Four articles also offered an economic evaluation of the intervention, with one involving an information provision intervention showing a decrease in formal health costs in the IG of 11.84% in comparison with the CG [39].

Table 2: Results intervention on adverse outcomes

OS. Author	Mortality [CI]	Institutionalization [CI]	Health costs [CI]	Accidental falls [CI]	Hospitalization [CI]
01.Cameron et al.	1.28 [0.53, 3.09]	-	-	-	-
01.Fairhall et al.	-	-	-	1.12 [0.78, 1.63]	-
01.Fairhall et al.	-	0.83 [0.46, 1.53]	4.8%	-	1.47 [0.87, 2.47]
02.De Vriendt et al.	2.89 [0.12, 72.08]	-	-	-	-
03.Dorrestein et al.	1.20 [0.41, 3.49]	-	-	0.86 [0.65, 1.13]	-
04.Favela et al.	0.98 [0.13, 7.26]	-	-	-	-
Favela et al.	0.49 [0.04, 5.59]	-	-	-	-
05.Hall et al.	0.79 [0.36, 1.71]	0.32 [0.12, 0.87]	-	-	-
06.Kehusmaa et al.	0.85 [0.39, 1.83]	1.28 [0.79, 2.06]	30%	-	1.03 [0.77, 1.39]
07.Kim et al.	3.19 [0.13, 81.25]	-	-	-	-
08.Kono et al.	0.52 [0.24, 1.13]	1.70 [0.40, 7.23]	-11.8%	-	-
09.Kono et al.	1.35 [0.69, 2.64]	2.41 [0.61, 9.49]		-	-
10.Metzelthin et al.	1.21 [0.53, 2.76]	-	-	-	-
10.Metzelthin et al.	-	0.65 [0.20, 2.18]	29%	-	0.92 [0.55, 1.55]
11.Monteserin et al.	0.59 [0.24, 1.43]	0.59 [0.10, 3.56]	-	-	-
12.Perttila et al.	-	-	-	0.43 [0.33, 0.57]	-
13.Upatising et al.	7.48 [0.35, 157.7]	-	-	-	-
14.Van Hout et al.	0.86 [0.54, 1.37]	1.12 [0.60, 2.08]	-	-	1.23 [0.90, 1.68]
15.Van Leeuwen et al.	1.11 [0.50, 2.48]	-	-	-	-
Van Leeuwen et al.	0.88 [0.49, 1.56]	-	-	-	-
Van Leeuwen et al.	1.37 [0.75, 2.48]	-	-	-	-
16.Williams et al.	-	1.30 [0.33, 5.09]	-	-	1.11 [0.51, 2.42]

Note: mortality, institutionalization, and hospitalization as odds ratio [Confidence Interval]; formal health costs as ratio intervention group relative to control group; accidental falls as IRR; double data are not reported. OS=original study. -=missing. Van Leeuwen et al. and Favela et al. are studies with several arms.

For case management and information provision intervention, a pooled meta-analysis was performed (Table 3). The pooled ORs for mortality when allocated in the experimental group

were 0.99 [95% CI: 0.79, 1.25] for case management, and 0.78 [95% CI: 0.41, 1.45] for provision information intervention. The mortality ORs for the other interventions (pharmaceutical, 3.19 [95% CI: 0.13, 81.25]; psychosocial, 1.20 [95% CI: 0.41, 3.49]; technological, 7.48 [95% CI: 0.35, 157.76]) were greater than one.

For institutionalization, the pooled OR with case management was 0.92 [95% CI: 0.63, 1.32], and the pooled OR for information provision was 1.53 [95% CI: 0.64, 3.65]; they were not significant. The pooled OR for hospitalization when allocated in the experimental group was 1.13 [95% CI: 0.95, 1.35] for case management. The funnel plots, statistical heterogeneity and forest plots can be found in the appendix [supplementary file 4: Funnel plot and Forest plot].

Table 3: Odds ratio and meta-analysis of case management and information intervention provision

	Mortality [CI]	Institutionalization [CI]	Hospitalization [CI]
Case management			
Cameron et al. (2013)	1.28 [0.53, 3.09]	-	-
De Vriendt et al. (2016)	2.89 [0.12, 72.08]	-	-
Fairhall et al. (2015)	-	0.83 [0.46, 1.53]	1.47 [0.87, 2.47]
Favela et al. (2013)	0.98 [0.13, 7.26]	-	-
Favela et al. (2013)	0.49 [0.04, 5.59]	-	-
Hall et al. (1992)	0.79 [0.36, 1.71]	0.32 [0.12, 0.87]	-
Kehusmaa et al. (2014)	0.85 [0.39, 1.83]	1.28 [0.79, 2.06]	1.03 [0.77, 1.39]
Metzelthin et al. (2015)	1.21 [0.53, 2.76]	0.65 [0.20, 2.18]	0.92 [0.55, 1.55]
Van Hout et al. (2010)	0.86 [0.54, 1.37]	1.12 [0.60, 2.08]	1.23 [0.90, 1.68]
Van Leeuwen et al. (2015)	1.11 [0.50, 2.48]	-	-
Van Leeuwen et al. (2015a)	0.88 [0.49, 1.56]	-	-
Van Leeuwen et al. (2015b)	1.37 [0.75, 2.48]	-	-
Williams et al. (1987)	-	1.30 [0.33, 5.09]	1.11 [0.51, 2.42]
Total (95% CI)	0.99 [0.79, 1.25]	0.92 [0.63, 1.32]	1.13 [0.95, 1.35]
Information provision intervention			
Kono et al. (2013)	0.52 [0.24, 1.13]	1.70 [0.40, 7.23]	-
Kono et al. (2016)	1.35 [0.69, 2.64]	2.41 [0.61, 9.49]	-
Monteserin et al. (2010)	0.59 [0.24, 1.43]	0.59 [0.10, 3.56]	-
Total (95% CI)	0.78 [0.41, 1.45]	1.53 [0.64, 3.65]	-

Note: Total = meta-analysis. -=missing. [CI] = confidence interval.

Sub-analysis

The influence of duration of intervention, average age, multi- versus unidimensional approach to frailty, and recruitment on the effect of an intervention was explored. Various sub-analyses were performed but with no significant results (Table 4). For the variable of age in the category ≤80, the risk for an adverse outcome was lower. Several methods to operationalize frailty were allowed, and a sub-analysis was performed. When frailty was operationalized with the Fried criteria [5] or the Frailty Index [6], the OR for mortality was 1.12 [95% CI: 0.52, 2.41].

Table 4: Odds ratio or pooled odds ratio of the sub-analyses for a case management intervention for the outcomes of mortality, institutionalization, and hospitalization

	Mortality [CI]	Institutionalization [CI]	Hospitalization [CI]
Duration (months)			
≤ 6	1.18 [0.54, 2.56]	-	-
> 6 & ≤ 12	0.93 [0.62, 1.38]	1.10 [0.77, 1.58]	1.12 [0.88, 1.43]
> 12	1.00 [0.74, 1.37]	0.75 [0.47, 1.19]	1.14 [0.88, 1.49]
Dimension			
Unidimensional	1.37 [0.59, 3.18]	0.90 [0.52, 1.56]	1.35 [0.87, 2.08]
Multidimensional	0.99 [0.77, 1.27]	1.15 [0.80, 1.65]	1.09 [0.90, 1.33]
Age (years)			
≤ 80	0.90 [0.58, 1.40]	0.94 [0.65, 1.38]	1.01 [0.79, 1.29]
> 80	1.03 [0.78, 1.35]	0.96 [0.63, 1.48]	1.29 [0.99, 1.68]
Recruitment			
Primary health care center	1.03 [0.79, 1.36]	1.00 [0.58, 1.73]	1.14 [0.88, 1.49]
Health services	0.85 [0.50, 1.46]	0.96 [0.63, 1.45]	1.03 [0.77, 1.39]
Register	0.73 [0.16, 3.37]	-	-
Rehabilitation	1.28 [0.53, 3.09]	0.83 [0.46, 1.53]	1.47 [0.87, 2.47]
Combination	-	1.30 [0.33, 5.09]	1.11 [0.51, 2.42]

Note: A sub-analysis was made for duration intervention, dimensional approach frailty, average population, and recruitment of the older adults. - = missing. [CI] = confidence interval.

Two papers had a low quality (≤2) (supplementary 5: Critical appraisal) [39, 45]. For information provision, a sub-analysis was performed, and the pooled OR for mortality increased from 0.76 to 0.94 [95% CI: 0.42, 2.11]. For institutionalization, the pooled OR decreased from 1.53 to 1.35 [95% CI: 0.34, 5.29] [supplementary 4: Funnel plot and Forest Plot].

Discussion

The aim of this study was to investigate the effect of interventions to prevent adverse outcomes in frail community-dwelling older people. This systematic review and meta-analysis

does not provide sufficient scientific evidence that interventions can be protective against the included adverse outcomes. A sub-analysis for some variables (duration of intervention, average age, dimension, recruitment) yielded no significant effects, although some findings suggested a decrease in adverse outcomes.

The results of this systematic review are in line with previous studies: the effect is unclear and inconsistent. In a systematic review, You et al. examined the effect of case management on mortality/survival days, and two out of seven articles reported a significant result [16]. Also, Hallberg and Kristerisson found in their systematic review that the effect of an intervention differed among studies: some found no effect on hospital admission, length of stay, or number of hospital days whereas others reported fewer hospital admissions and/or shorter lengths of stay [46]. Mayo-Wilson et al. concluded in their systematic review that home visiting is not consistently associated with a higher risk of mortality [47].

A pooled meta-analysis should lead to more significant and consistent results, yet this analysis did not. However, the literature provides evidence that a pooled meta-analysis could produce significant findings. For example, Elkan et al. reported that mortality and institutionalization are significantly lower after a home-based support intervention for frail older adults in comparison with a control group [48]. Thomas et al. concluded that a physical intervention reduces mortality in older community-dwelling adults, but the inclusion criteria did vary among the included studies in these two analyses, which may explain the differences in outcome. Elkan et al. included non-randomized studies and studies with older adults recently discharged from the hospital [48] whereas the older adults in Thomas et al. are not defined as frail [49].

Remarkably, the data in the current work show that the odds of being hospitalized are higher in the intervention group than in the control group (Table 2). Berglund et al. reported in their RCT that after the intervention, participants in the experimental group were much more aware of whom to contact with questions about care and services [50]. This effect could explain why the odds of being hospitalized were higher in the intervention group than in the control group and is a likely reason why the results for the outcome of formal health cost in the experimental group were not significantly lower than in the control group.

The studies in the current analysis showed heterogeneity for average age, duration, etc., which could explain the inconsistency in the results [51]. A sub-analysis should lead to significant and consistent results. For example, Stuck et al. concluded that a preventive

program reduces mortality in a younger study population (mean age < 80 years) but not in older populations [52]. However, in this study, a sub-analysis for the variable average age ≤ 80 years (Table 3) was not significant, and neither were the results of other sub-analyses. Our findings confirm Elkan et al.: population type, duration, and age have no significant effect on mortality and institutionalization [48].

Considerations for future research

A plausible reason for the lack of evidence is the heterogeneity within studies. Within studies, the contextual factors of the population in the experimental group was heterogeneous, with differences in age, educational level, morbidities, and context, etc. If frailty is operationalized with a multidimensional approach, however, the question that arises is: 'which dimensions were problematic?' Also, the local setting within studies was heterogeneous; Van Leeuwen et al. used two regions, and Kono et al. and Perttila et al. used three regions [36, 39, 40, 42]. It is plausible that an intervention within a subgroup is effective. Analyzing the results of an experiment on an aggregated level might lead to an ecological fallacy [53].

Future research should not solely focus on the effect of an intervention but also address the question: why did interventions work when they did or why not, for whom did they work and what contextual factors triggered the mechanisms required to make them work. This is described by Pawson and Tilley in 'realistic evaluation' (1997). They suggest that a realistic evaluation approach might provide a better understanding of the effect of an intervention [54]. This approach is a theory-driven method that not only addresses the outcome of an intervention, but also why interventions worked, when they worked or for whom they worked [54].

A consensus about the concept of frailty is necessary for future research and would enable comparison, evaluation, and replication of interventional studies. Some authors have made valuable efforts toward reaching a consensus [7]; for example, 'The White Book on Frailty' has delivered an important contribution to this understanding [13].

Several other explanations are possible for the current results. The selected population may have been detected too late and already have been too frail [13, 15]. In addition, societal trends, such as changes in structure and function of families, might have aggravated the incidence or severity of frailty and complicated its effective management [13]. A lack of mindfulness for these societal trends also may be an explanation for the non-significant

results. Several authors have discussed the difficulties of implementing the intervention [32, 34]. As a last consideration, future research making an economic evaluation must consider the extra awareness of services that older adults gain through an intervention [50].

Strengths and limitations

Previous systematic reviews have focused on the effect of one intervention in comparison with care as usual [55-58]. A strength of the current analysis is the overview of interventions for frail community-dwelling older adults in the context of several adverse outcomes. A second strength is that only RCTs were included whereas several other systematic reviews have also included non-RCTs [46, 51]. In this analysis, differences among studies were assessed (heterogeneity) in terms of duration of the intervention, average participant age, dimensional approach to frailty, recruitment of participants, and frailty operationalization, constituting a third strength. A fourth strength is that three of the five outcome measures – mortality, institutionalization, and hospitalization – are collected primarily through registers and can be seen as objective data, which decreases the risk for bias [2].

The analysis also has some weaknesses, so that the results should be interpreted with caution. A first weakness is the small number of original studies, which led to meta-analyses only for case management and information provision and reduced the reliability of the results. One reason for the small numbers of included publications is the lack of operationalization of 'frailty' in studies. An absence of an operationalization of frailty is also a feature in other studies [15, 17]. Other reasons for exclusion were a lack of usual care, no relevant outcomes, and the recruitment of non-community-dwelling participants. A second weakness is the concept of frailty. Several methods are used to operationalize frailty, and some may not be accurate enough to recruit frail older adults, making study comparison and evaluation difficult [56]. A third weakness is that several concepts, such as case management, information provision, institutionalization, and formal health costs, have different operationalizations, leading to heterogeneity among studies. In the current analysis, mortality, institutionalization, accidental falls, formal health costs, and hospitalization were used because they are often cited as adverse outcomes. Other outcomes not included in this systematic review include functional status, physical performances, quality of life, mastery, disability, etc. [14], which can be seen as a weakness. These outcomes are not included because of the different methods to operationalize these concepts.

Conclusion

The number of frail older adults with a high need of care and support is increasing. According to some studies, interventions can prevent or delay frailty, but their effect in preventing adverse outcomes in frail community-dwelling older people is unclear. The aim of this article was to investigate if interventions for frail community-dwelling older adults can be protective against adverse outcomes. This systematic review (and meta-analysis) does not provide sufficient scientific evidence that supports this assumption, even though some results suggest a decrease in adverse outcomes.

Future research must consider that the research population of older adults is very heterogeneous, also within studies. A good breakdown of all of these characteristics is necessary, and sub-analyses might avoid ecological fallacies. Each patient's specific needs, and how to deliver the services to meet these needs, are probably essential for the effectiveness of an intervention. New methods/approaches, for example the realist approach, might provide a better understanding of the effect of an intervention. Future research must also consider new societal trends, implementation problems, and heightened awareness about services that may influence the results.

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Supplementary File 1: Search strategy

Medline

((("Frail Elderly"[MeSH] OR (("Aged"[Mesh:noexp] OR aged[tiab] OR aging[tiab] OR ageing[tiab] AND elder*[tiab] AND "Aged, 80 and over"[MeSH] OR oldest old[tiab] OR old*[tiab] OR senior*[tiab] OR geriatric*[tiab] OR "Veterans"[MeSH] OR veteran*[tiab]) AND (frail*[tiab] OR weakness[tiab] OR weak[tiab] OR fragil*[tiab] OR vulnerab*[tiab] OR unhealth*[tiab] OR debil*[tiab] OR "functional impairment"[tiab])))) AND ("home care service"[Mesh] OR Domiciliary Care[tiab] OR home care*[tiab] OR home[tiab] OR "homecare"[tiab] OR "home based care"[tiab] OR "community dwelling"[tiab] OR "Independent Living"[MeSH] OR independent*[tiab] OR "Intermediate Care Facilities"[Mesh] OR "aging in place"[tiab] OR "congregate living facilities"[tiab] OR "congregate living facility"[tiab])) AND ((((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR drug therapy[sh] OR randomly[tiab] OR trial[tiab] OR groups[tiab]))) NOT (animals[mh] NOT humans[mh]))

Embase

frail elderly'/exp OR ('aged'/de OR 'veteran'/exp OR 'very elderly'/exp OR 'aged':ab,ti OR 'aging':ab,ti OR 'ageing':ab,ti OR elder*:ab,ti OR 'oldest old':ab,ti OR old*:ab,ti OR senior*:ab,ti OR geriatric*:ab,ti OR veteran*:ab,ti AND (frail*:ab,ti OR weak:ab,ti OR weakness:ab,ti OR fragil*:ab,ti OR vulnerab*:ab,ti OR unhealth*:ab,ti OR debil*:ab,ti OR 'functional impairment':ab,ti)) AND ('home care'/exp OR 'domiciliary care':ab,ti OR home:ab,ti OR 'home care':ab,ti OR 'homecare':ab,ti OR 'home based care':ab,ti OR 'community dwelling':ab,ti OR 'independent living'/exp OR 'independent':ab,ti OR 'intermediate care facilities':ab,ti OR 'aging in place':ab,ti OR 'congregate living facilities':ab,ti OR 'congregate living facility':ab,ti) AND ('randomized controlled trial (topic)' OR 'controlled clinical trial (topic)' OR 'randomized':ab,ti OR 'placebo':ab,ti OR 'drug therapy':ab,ti OR randomly:ab,ti OR trial:ab,ti OR groups:ab,ti) NOT ('animals':ab,ti NOT 'human':ab,ti) AND 'article'/it

SSCI

1. ("aged" OR "aging" OR "ageing" OR "very elderly" OR elder* OR "oldest old" OR old* OR senior* OR geriatric* OR veteran*)
2. ("frail elderly" OR frail* OR "weak" OR "weakness" OR fragil* OR vulnerab* OR unhealth* OR debil* OR "functional impairment")
3. ("randomized" OR "controlled clinical trial" OR "randomly" OR "randomized controlled trial" OR "groups" OR "trial" OR "drug therapy" OR "placebo")
4. ("home care service" OR "domiciliary care" OR "home care" OR "homecare" OR "home" OR "home based care" OR "community dwelling" OR "independent living" OR "intermediate care facilities" OR "congregate living facilities" OR "aging in place")

#4 AND #3 AND #2 AND #1

The Cochrane Library

1) Frail Elderly[MeSH]
2) Aged[MeSH:noexp]
3) aged[tiab]
4) aging[tiab]
5) ageing[tiab]
6) elder*[tiab]
7) Aged, 80 and over[MeSH]
8) oldest old[tiab]
9) old*[tiab]
10) senior*[tiab]
11) geriatric*[tiab]
12) Veterans[MeSH]
13) veteran*[tiab]
14) 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13
15) frail*[tiab]
16) weakness[tiab]
17) weak[tiab]
18) fragil*[tiab]
19) vulnerab*[tiab]
20) unhealth*[tiab]
21) debil*[tiab]

22) functional impairment[tiab]

23) 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR22

24) home care service[MeSH]

25) Domiciliary Care[tiab]

26) home care*[tiab] OR home[tiab]

27) homecare[tiab]

28) home based care[tiab]

29) community dwelling[tiab]

30) Independent Living[MeSH]

31) independent*[tiab]

32) Intermediate Care Facilities[MeSH]

33) aging in place[tiab]

34) congregate living facilities[tiab]

35) congregate living facility[tiab]

36) 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35

37) 14 AND 23 AND 36

38) randomized controlled trial[pt]

39) controlled clinical trial[pt]

40) randomized[tiab]

41) placebo[tiab]

42) drug therapy[sh]

43) randomly[tiab]

44) trial[tiab]

45) groups[tiab]

46) 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45

47) 37 AND 46

48) animals[mh]

49) humans[mh]

50) 49 NOT 48

51) 47 AND 50

Supplementary File 2: Extra information operationalization and categorization of Variables.

Age: The mean age of the total study population. The mean age of the total study population was calculated if the data for the experimental and control groups were given. A weighted method was used. If the data were given as a categorical variable, the mean age was calculated by a proxy. ∑(Lower age + upper age)/2*N.

Intervention

The development of the interventions started with a search in PubMed in August 2015. The search strategy was frailty*RCT*last 5 years. This resulted in 102 articles. The 102 articles were categorized into six types of interventions.

Definitions

Case management –a collaborative process of assessment, planning, facilitation, care coordination, evaluation, and advocacy for options and services to meet an individual's and family's comprehensive health needs through communication and available resources to promote quality, cost-effective outcomes [1].

According to Van Durme et al. [2], case management interventions include four of the six elements of the definition of the Case Management Society of America (CMSA). In this study, an intervention was categorized as case management if it included four of the six elements of the definition.

No distinction between case management and integrated care was made. There were overlaps between the different models of care. Integrated care models usually included case management.

Information provision intervention (MeSH) – information intended for potential users of medical and healthcare services. There is an emphasis on self-care and preventive approaches as well as information for community-wide dissemination and use.

Psychosocial intervention – includes the broad spectrum of treatments of complaints that are not strictly medical or somatic. On the one hand, these interventions deal with various psychological problems such as anxiousness, nervousness, tenseness (posttraumatic or acute) stress, depression and feeling depressed, burn out, loneliness, and irritability. On the other hand, these interventions concern various social problems such as poverty/financial problems,

housing problems, problems with social security or health care, adjustment problems, and loss/death of family/partner [3].

Pharmaceutical intervention – an intervention that uses drugs or supplements, etc., and that prospectively assigns human participants or groups of humans to a health-related intervention with drugs/supplements to evaluate the effects on health outcomes [4].

Technological intervention – (1) an intervention with devices, not affixed to the body, designed to help persons having musculoskeletal or neuromuscular disabilities to perform activities involving movement (MeSH); or (2) an intervention with telemedicine, the use of electronic information and communications technologies to provide and support health care when distance separates the participants [5].

Physical intervention – any bodily movement produced by skeletal muscles that requires energy expenditure [6].

Primary health care center – first-contact, accessible, continued, comprehensive, and coordinated care. First-contact care is accessible at the time of need; ongoing care focuses on the long-term health of a person rather than on the short duration of the disease; comprehensive care is a range of services appropriate to the common problems in the respective population, and coordination is the role by which primary care acts to coordinate other specialists that the patient may need [7].

Home services – (1) home care services (MeSH): community health and nursing services providing coordinated multiple services to the patient at the patient's home, provided by a visiting nurse, home health agencies, hospitals, or organized community groups using professional staff for care delivery; or (2) homemaker services (MeSH): non-medical support services, such as food preparation and bathing, given by trained personnel to disabled, sick, or convalescent individuals in their home.

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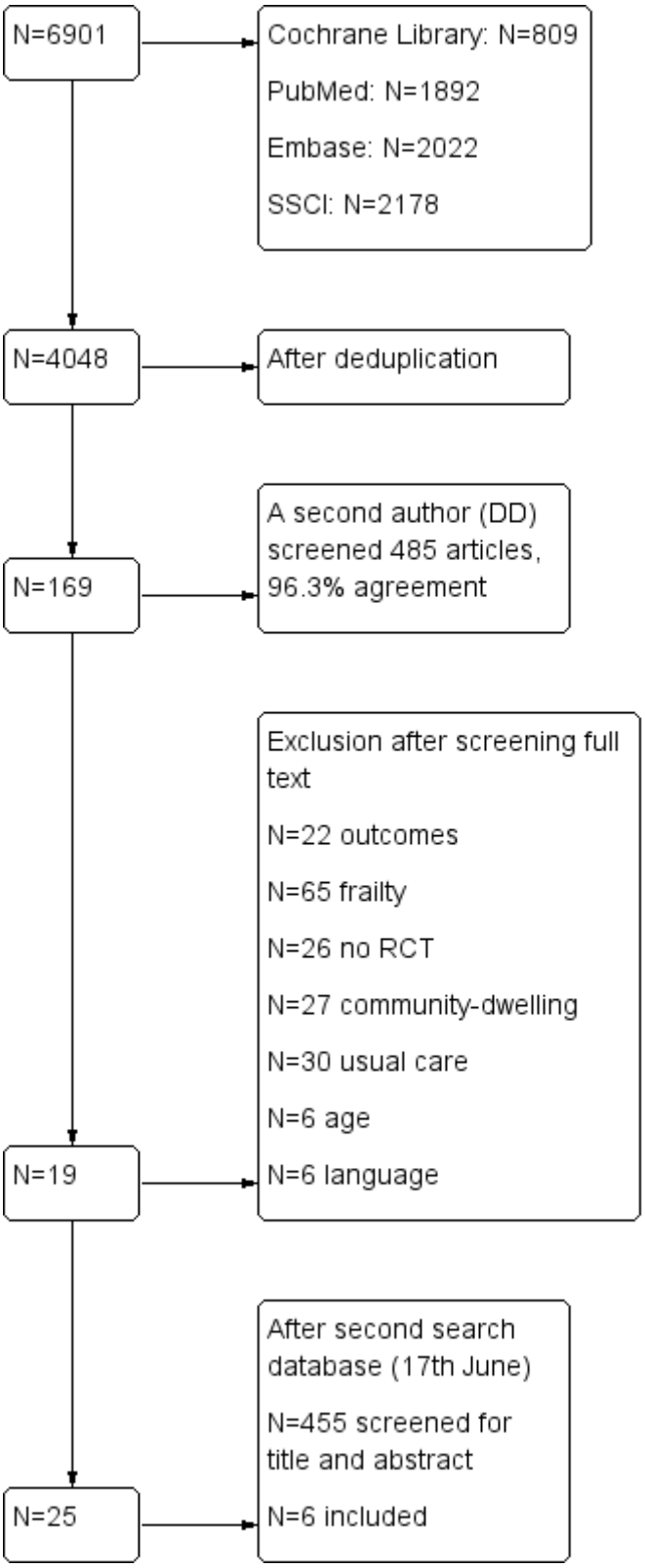
Supplementary File 3: Flow chart



Supplementary File 4: Funnel plot and Forest plot

Figure A: Forest plot: intervention case management, outcome mortality

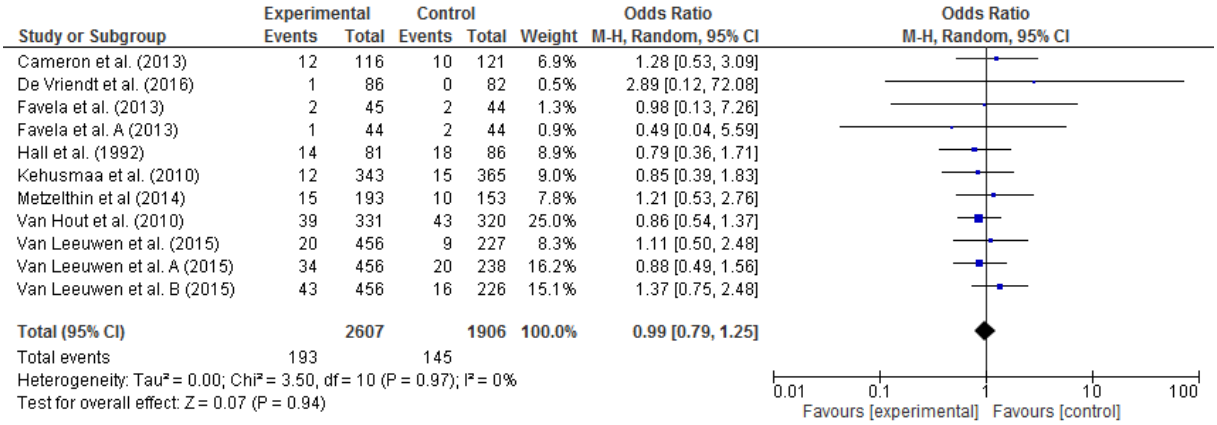


Figure B: Funnel plot: intervention case management, outcome mortality

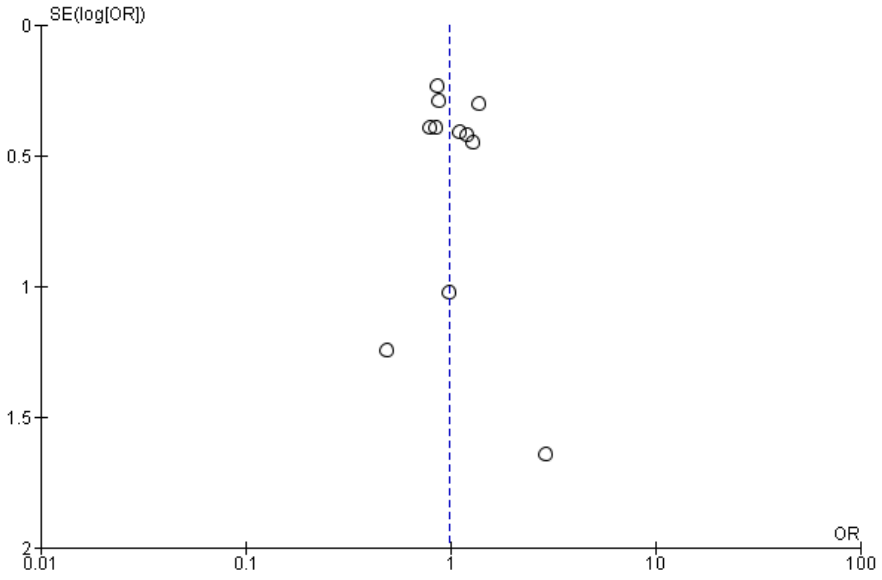


Figure C: Forest plot: intervention case management, outcome institutionalization

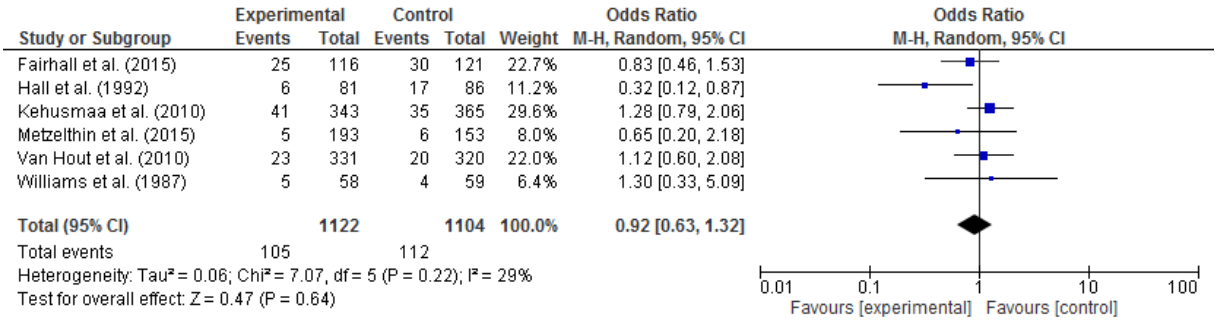


Figure D: Funnel plot: intervention case management, outcome institutionalization

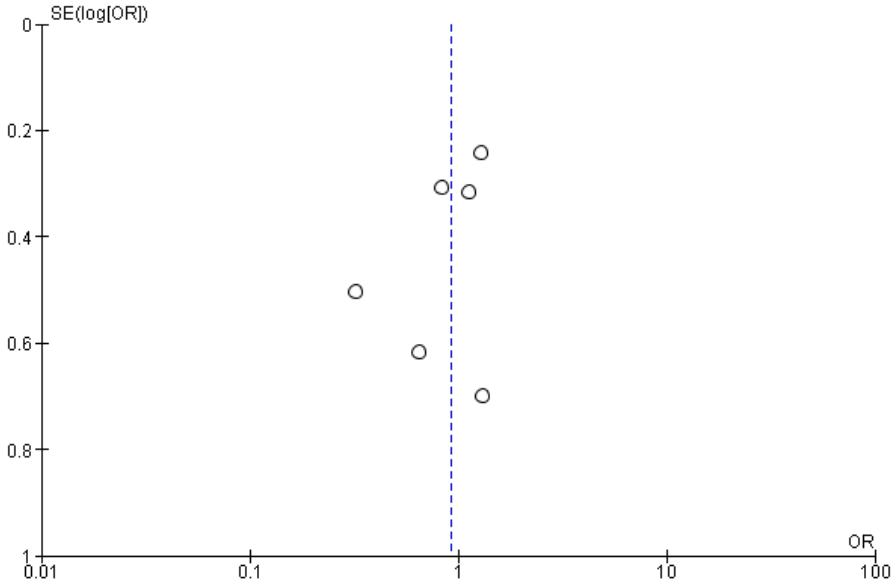


Figure E: Forest plot: intervention case management, outcome hospitalization

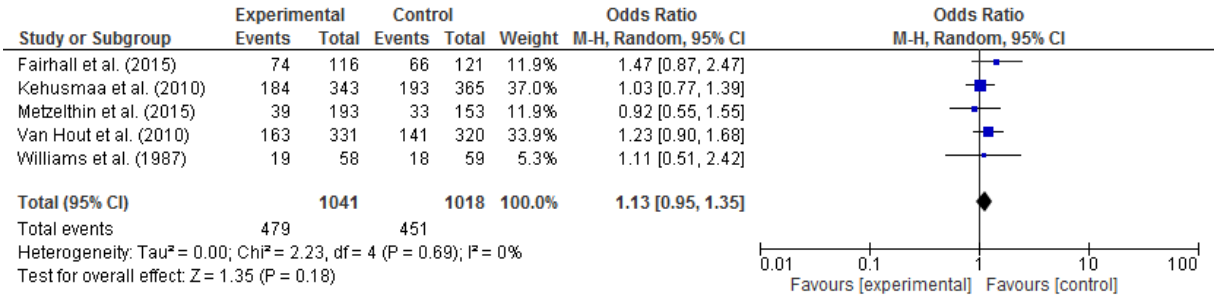


Figure F: Funnel plot: intervention case management, outcome hospitalization

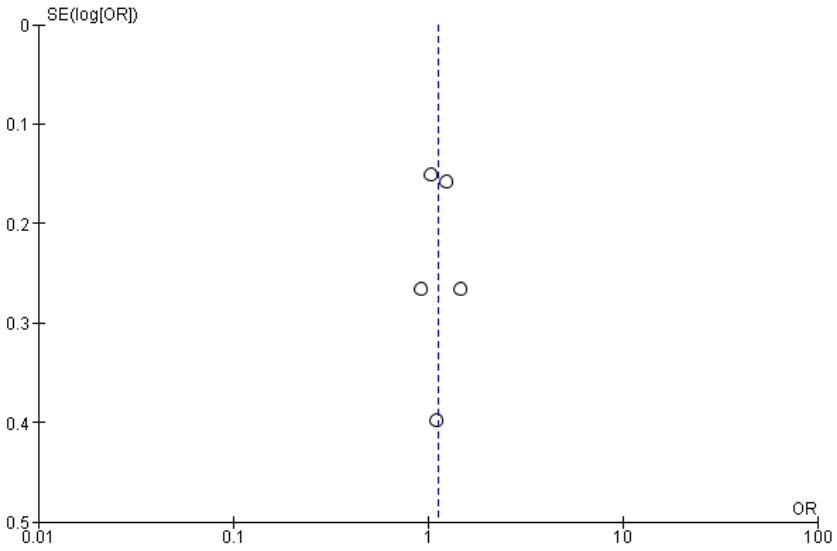


Figure G: Forest plot: intervention information provision, outcome mortality

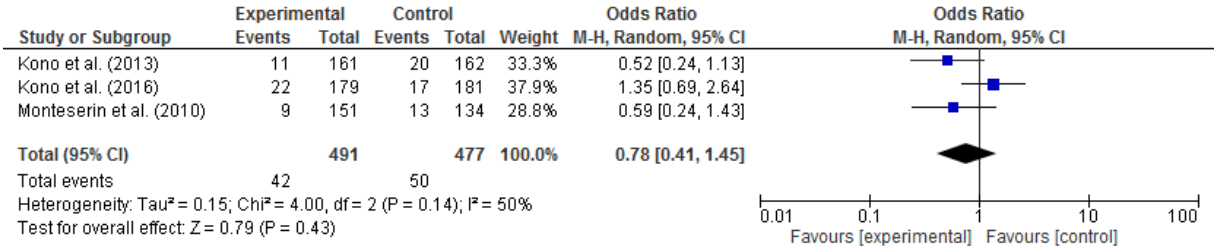


Figure H: Funnel plot: intervention information provision, outcome mortality

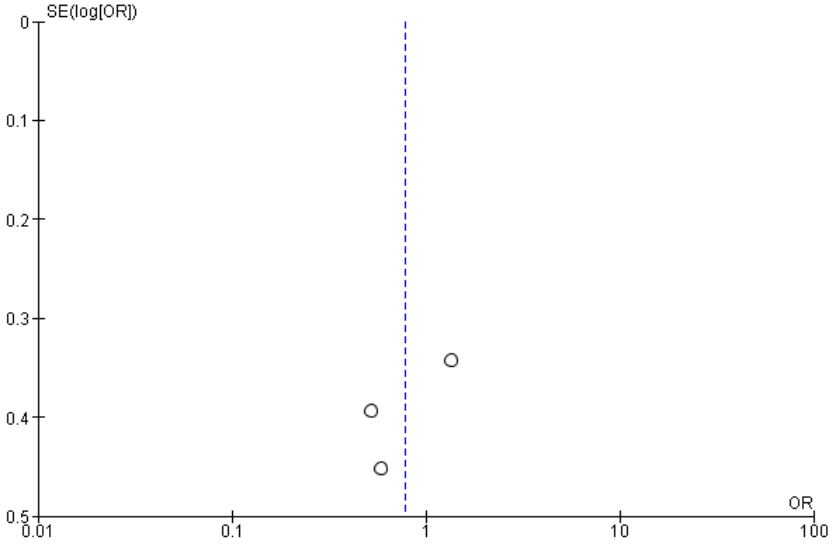


Figure I: Forest plot: intervention information provision, outcome institutionalization

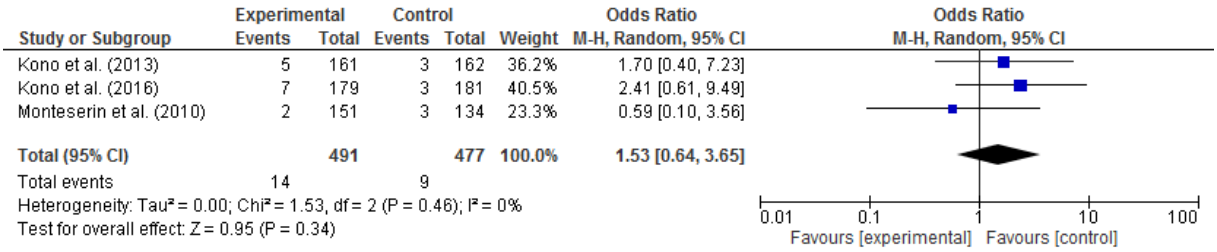
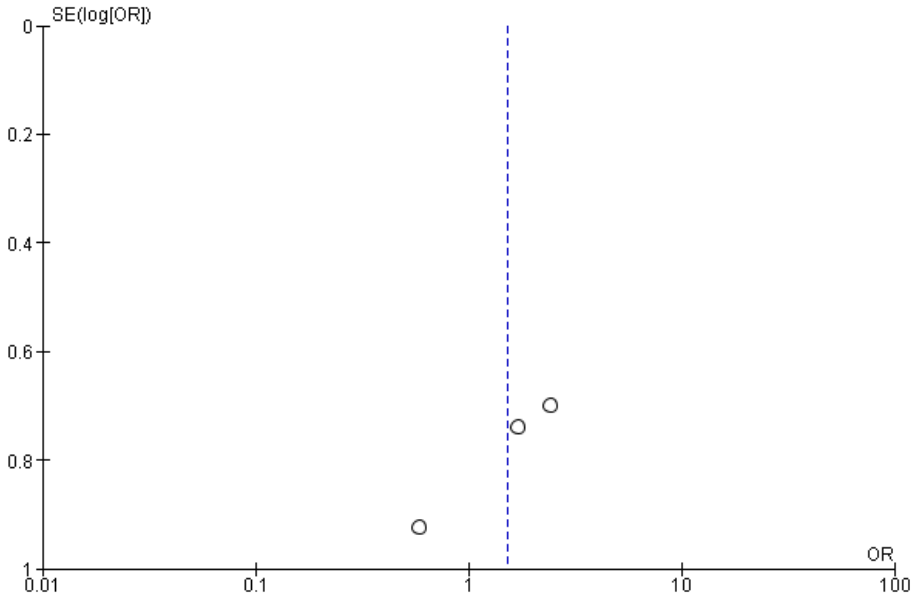
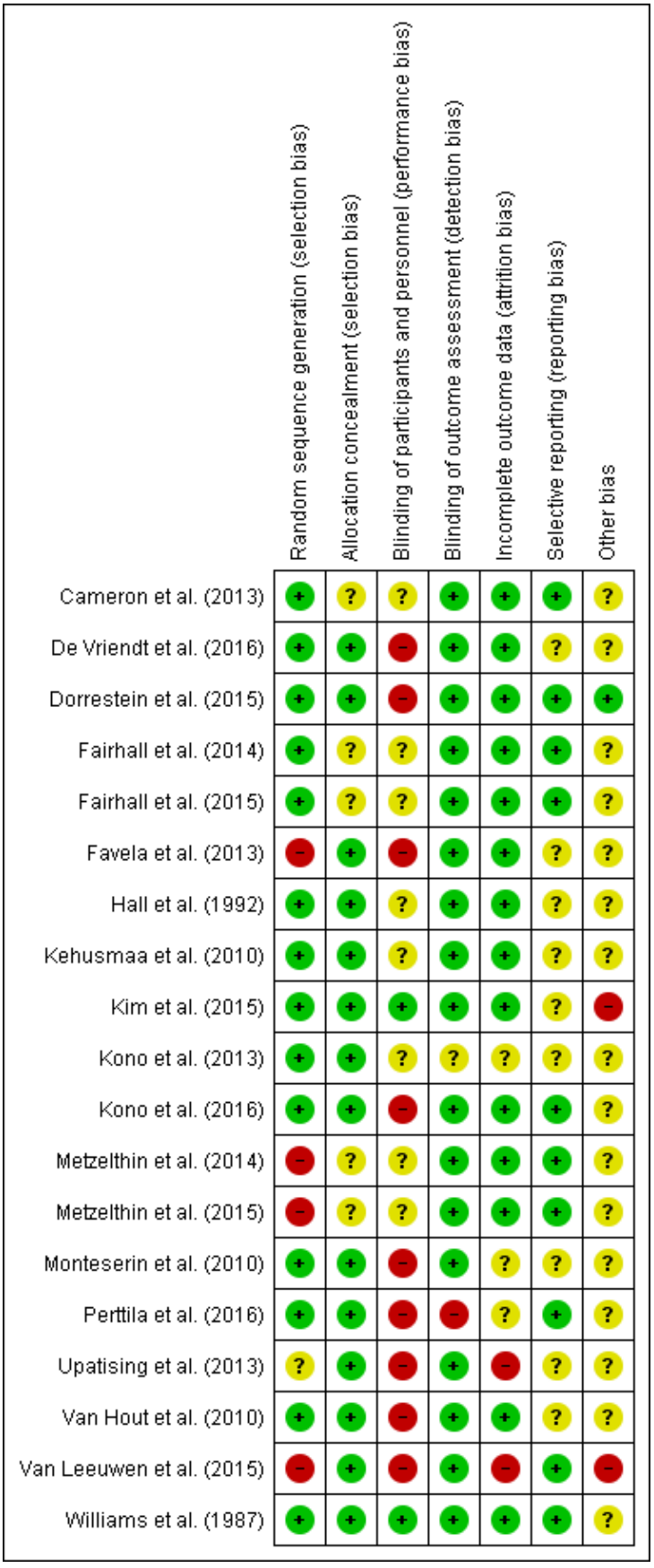


Figure J: Funnel plot: intervention information provision, outcome institutionalization



Supplementary File 5: Critical appraisal



Chapter 8

A Search for relevant Contextual Factors in Intervention Studies: A Stepwise Approach with Online Information

Submitted as:

Van der Elst, M., Schoenmakers, B., Dierickx, E., De Roeck, E. E., Duppen, D., Fret, B., Schols, J. M. G. A., Kempen, G. I. J. M., De Lepeleire, J., & D-SCOPE Consortium, A Search for relevant Contextual Factors in Intervention Studies: A Stepwise Approach with Online Information

Abstract

The role of the context within intervention studies is often ignored. To consider the context in future research, one needs to know whether enough contextual information is available, and a uniform methodology to study the local context in a standardized way is desirable. Through the World Wide Web, a lot of relevant information is nowadays available. The aim of the present study is to describe a stepwise approach to study which contextual factors might moderate the effect of healthcare interventions and to test the feasibility of this approach within the D-SCOPE project. In the D-SCOPE project a complex intervention by means of home visits was set up to improve the access to tailored care in 3 municipalities (Ghent, Knokke-Heist and Thienen). A five-step approach was designed and tested: (1) a theoretical/conceptual discussion of relevant contextual factor domains was held; (2) a search was done to find appropriate web-based public datasets which covered these topics with standardized information; (3) a list of all identified contextual factors was made (inventory); (4) to reduce the long list of contextual factors, a concise list of the most relevant contextual factors was developed based on the opinion of two independent reviewers; and (5) a Nominal Grouping Technique was applied. The present study shows that the five-step approach is feasible to determine relevant contextual factors that might affect the results of an intervention study. Such information may be used to correct for in the statistical analyses and for interpretation of the outcomes of intervention studies.

Introduction

Randomized controlled trials (RCTs) are widely regarded as the gold standard to identify causal relations between interventions and their predetermined outcomes. Some critics argue that, with respect to randomized trials of complex public health interventions, researchers fail to address the interaction of intervention components with each other and with the local context [1-3]. In the literature, the concept 'context' refers to the spatial and institutional locations of social situations, with the inherent norms, values, and interrelationships and describes those features of the conditions in which programs are introduced [1, 3]. The key features of complex interventions are: 1) the number of interacting components (the number and complexity of behaviors required by those delivering or receiving the intervention), 2) the number of groups or organizational levels targeted by the intervention, 3) the number and variability of outcomes, and 4) the degree of flexibility or tailoring of the intervention permitted [4]. As interventions are almost always introduced into diverse contexts (e.g., municipalities, neighborhoods, clinics), the mechanisms activated by the intervention will vary according to the saliently different context conditions. Because of the relevant variations in context and mechanisms activated by an intervention, its result is liable to have mixed outcome patterns [1]. In RCTs of complex interventions, the role of implementers, the local context, and other factors, that may moderate the effect of an intervention, often are ignored [2, 5]. Some authors argue that certain contexts are supportive to the intervention and some are not [1]. The need for including contextually relevant factors was also highlighted in 'The National Care For Elderly Programme' (2008 - 2016), a countrywide government-funded program in the Netherlands. Its goal was to develop a more proactive, integrated health-care system for older adults. More than 70 scientific projects were conducted, including nine large-scale trials. None of these nine proactive primary-care programs demonstrated clinically relevant effects on daily functioning. After the evaluation of these trials, one of the conclusions was the need to pay more attention to the in-depth analysis of the context and to develop a uniform methodology to study the local context in a standardized way [6]. Currently, more attention is given to the importance of context and the understanding of the context in complex interventions [7-8]. Several guidances have been developed to support researchers during the design of a complex intervention and to take the context into account [7-10]. One can use a wide range of research methods to gain a better understanding of the context in

which the intervention will operate, although the focus is on qualitative methods and less on quantitative methods [7-8]. Nowadays, a significant amount of information can be found online, which was not available or difficult to find in the past. The World Wide Web could offer an opportunity for researchers to study the setting of an intervention. However, it is unknown whether the information available online is useful to study and compare the local contexts.

The present study is framed within the Detection, Support and Care for Older People: Prevention and Empowerment (D-SCOPE) project and features an organized trial that was aimed to enable older adults to age well in place. After the baseline assessment, older participants assigned to the experimental group were contacted for a home visit by a professional from the social service of the municipality. During the home visit, the professional from the social service of the municipality explored the older adult's competences, needs and preferences. The professional from the social service of the municipality proposed a type of intervention based on the results of the baseline assessment and the home visit. In consultation with the participant and social network, decisions with regard to tailored care and support were made. The intervention depended on the availability of the care and support services in the municipality, and could be formal (e.g., home care) or informal (e.g., activities of an older adult's association). A professional from the social service of the municipality monitored which care the participant received, whether the older person canceled the care and support and if the care recipient was satisfied with the supplied care. This was assessed monthly by telephone. The trial was performed in three municipalities [11]. As a part of the D-SCOPE project, we wanted to know which contextual factors might interact/moderate the effect of a home visit and its related tailored care and support. This information can be useful in explaining the results of the D-SCOPE intervention study and provide insight regarding which context might be supportive for a home visit and which might not.

The aim of the present study is to describe an approach to study which contextual factors might moderate the effect of healthcare interventions, and to test this approach for the D-SCOPE intervention. As web-based public data are generally easily obtainable, we focus on context data from such resources. To determine the feasibility of an in-depth study of the local context, the following research questions are answered: 1) are there relevant standardized web-based public data available in these three municipalities? and 2) how can the contextual factors most likely to interact with the intervention and moderate its outcomes be determined?

Methods

Design

To test the feasibility of determining relevant contextual factors in an RCT, an explorative case study was conducted within the D-SCOPE project [11]. This D-SCOPE trial was performed in three municipalities in the Flemish region in Belgium (Ghent, Knokke-Heist and Thienen, see supplementary file 1: Map of Flanders). Therefore, only the contextual factors of these three municipalities were considered. The different steps of the approach to determine the relevant contextual factors that might moderate the effects of health care interventions are hereby described.

Five-step approach:

Because of the complex nature of its intervention and depending on the availability of the care and support services in the municipality, the effect may be context-sensitive [12-14]. To determine the relevant contextual factors within the D-SCOPE project, five steps were taken (see Figure 1).

In the first step, a theoretical/conceptual discussion of the relevant contextual factor domains was held. A meeting (by the first, second and last author) was organized to discuss the topics that should be covered with regard to the D-SCOPE intervention; which features the data must fulfill to be included. The meeting was organized based on the results of the meta-analysis of Van der Elst et al. [5] and the professional experience of the two co-authors (the second and last author). Several inclusion and exclusion criteria, such as the exclusion of factors only related to children, such as childcare or crèches, were formulated [5].

In step two, after determining which topics should be covered, an explorative online search was performed (by the first author) to find appropriate and relevant public web-based datasets, which included the general contextual factors discussed in step one (e.g., datasets including official statistics).

In step three, after determining the appropriate public web-based datasets, an inventory of the contextual factors retrieved from the public datasets was made (by the first author).

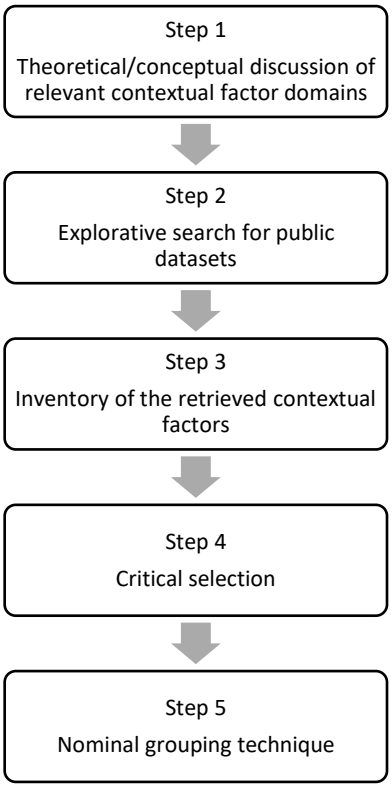
Regarding the availability of services, the inventory was based on the frameworks of official organizations. Microsoft Excel and the technique of mind mapping was used to construct the inventory. Mind mapping was used to structure and compare the available services in the three municipalities.

In step four, to reduce the number of contextual factors, a (critical) selection of the collected contextual factors was made by two experienced clinicians in primary care (the second and last author). Both received the inventory with the contextual factors and its distributions and were asked to assign each contextual factor a green, orange or red score, independently of each other. A green score indicated that the contextual factor might moderate the effect of the D-SCOPE intervention. An orange score reflected the opinion that one was not sure if the contextual factor might moderate the effect of the D-SCOPE intervention. A red score indicated that the contextual factor was not considered able to moderate the effect of the D-SCOPE intervention. The contextual factors assigned a green score by both reviewers were included in the fifth step; those factors with only red scores were automatically excluded. Regarding the status of all other contextual factors, and in the case of discrepancies, a meeting was held (between the first, second and last author) to reach consensus.

In the fifth and last step, in order to determine the most relevant contextual factors a Nominal Grouping Technique (NGT) was applied [15]. The NGT included seven researchers, all familiar with the D-SCOPE intervention, with various educational backgrounds and expertise (e.g., nurse, psychologist, educational scientist) and lasted approximately one hour. NGT is a highly structured method in decision-making and contains five parts: 1) generating ideas: the participants received the inventory of the contextual factors and its distributions. Each participant was asked to write down the contextual factors that might influence the outcome of a home visit (to keep it concise a maximum of ten), and had to motivate why these factors were chosen. The participants registered them without discussion; 2) recording ideas: the participants then shared their ideas and motivations with the group, without discussion; 3) discussing/clarifying ideas: in this phase, the participants discussed the contextual factors and the motivations of choosing them; 4) voting/rating ideas: after discussion, every participant was asked to register those contextual factors (maximum of 10) that might influence the results of a home visit and rank them; and lastly, 5) summing the ratings: a list of the ten

highest ranked contextual factors was made. The NGT method overcomes the problem of reluctance in participants who might be less willing to suggest ideas because of concerns of being criticized or creating conflict in groups [16-18].

Figure 1: Flow chart of the five-step approach to determine assumedly the most relevant contextual factors



Results

Below, the results of the five-step approach applied within the D-SCOPE project are presented.

Step 1: Theoretical/conceptual discussion of relevant contextual factor domains

The aim of the intervention was to detect frail older people, improve their access to tailored care and support, and facilitate aging well in place. Therefore, the research team decided that the retrieved information should cover sociodemographic, socioeconomic contextual factors, factors related to care supply/availability or care use, and factors related to the local government. Moreover, it was determined that these contextual factors should focus on older adults (aged 60 years and older) and that the public web-based dataset should use standardized data (e.g., official statistics) of the three municipalities of the D-SCOPE trial.

Step 2: Explorative search for public datasets

Three suitable online public web-based datasets were identified in the selected municipalities: (1) the 'InterMutualistic Agency' database, (2) the 'Local Statistics' database, and (3) the 'Social Map' database. In the 'InterMutualistic Agency' database the data of seven Belgian health insurance institutions were collected and stored. The 'Local Statistics' database is a portal site in which all types of statistics regarding the local and provincial administrations have been collected. The 'Social Map database collects data from health care organizations (broad interpretation) in a structured database. additional information regarding the databases can be found in supplementary file 2: Databases.

Step 3: Inventory of the retrieved contextual factors

In total, 157 contextual factors were retrieved from the aforementioned datasets: 70 contextual factors were derived from the 'InterMutualistic Agency' database, 36 contextual factors were derived from the 'Local Statistics' database and 51 contextual factors were derived from the 'Social Map' database. These contextual factors covered a broad range of information regarding the municipalities, including sociodemographic, socioeconomic, local governmental information, and data on care supply/availability. Microsoft Excel was used to list the contextual factors and its distributions. Since the 'Social Map' lists all organizations and describes the services they offer, the technique of mind mapping was used to structure and

compare the available services in the municipalities (supplementary 3: Mind Mapping). To categorize the availability of care and support in the municipality, the framework of the agency 'Zorg en Gezondheid' (Care and Health) was used. This framework includes 12 domains, such as home care, geriatric care, and hospitals, as well as several subdomains of each domain. The agency 'Zorg en Gezondheid' was founded by the Flemish authorities and its main task is the organization of care and support [19].

Step 4: Critical selection

In total, two reviewers (the second and last author) independently selected 41 of the 157 contextual factors, that were presented during the NGT. Eighty-five contextual factors received a red score (do not moderate the effect of the intervention) by both reviewers, while 28 were assigned a green score (might moderate the effect of the intervention) by the reviewers. All other factors were discussed (between the first, second and last author) until consensus was reached. The final inventory of contextual factors included nine factors of the 'InterMutualistic Agency' database, seven contextual factors were derived from the 'Local Statistics' database, and 25 of the 'Social Map' database.

Step 5: Nominal Grouping Technique

During the NGT, the list of the remaining contextual factors (see step 4) was presented. First, all participants were given 10 minutes to go through the list of contextual factors and their distribution. The participants were then asked to register the most relevant factors according to their opinions including motivating why. Secondly, the participants were asked to share their most relevant factors and motivation, without any discussion. This task required 15 minutes. Thirdly, a discussion of approximately 30 minutes was held. Fourthly, a voting was organized and the results were counted (step 5). In total, 20 of the 41 contextual factors presented in the NGT received votes. Within the D-SCOPE project, the aim was to retrieve a concise list of contextual factors. Therefore, table 1 presents those contextual factors with the highest scores (10) after voting in the NGT, together with the data of the three municipalities (derived from the three aforementioned databases). According to the participants of the NGT, those ten contextual factors were likely the most important moderators of the D-SCOPE intervention. The number of contextual factors on the list is purely meant to illustrate the approach; further research should determine whether the selected contextual factors are

moderating the D-SCOPE trial. The dependency ratio (age 65+/20-64) had the highest score of all the contextual factors.

Table 1. Ten contextual factors and their distribution after Nominal Grouping Technique†

	Contextual factors	Ghent	Knokke-Heist	Thienen	Rank	Score
Sociodemographic contextual factors	1) Age 80+/total population 2015	5.0%	9.6%	6.6%	3	38
	2) Dependency ratio (65+/20-64 years) 2015	27.0%	63.1%	36.2%	1	64
	3) % age 65+ and living alone 2014	29.9%	30.7%	27.7%	6	30
Socioeconomic contextual factors	4) Percentage of beneficiaries aged 65 + and entitled to a guaranteed income	6.9%	5.5%	4.1%	3	38
	5) Underprivileged index (=% of births in underprivileged families in year 2014)	22.6%	13.6%	11.9%	5	32
	6) Percentage of beneficiaries entitled to additional compensation in Public health insurance	18.5%	12.9%	14.6%	9	20
Community resources	7) Total resources of the community social security in euros per inhabitant 2013 (in euro)	304	151	229	10	8
Availability of community health care centers	8) Community center	Yes	No	Yes	2	46
	9) 24/24 care	Yes	No	Yes	8	25
	10) Center for mental health care	Yes	No	Yes	7	24

Note: †The ten highest scoring contextual factors determined in the Nominal Grouping Technique, rank and score.

Discussion

In RCTs of complex interventions, the role of the local context which may moderate the effect of an intervention, is often ignored. Therefore, an in-depth analysis of the context is needed. However, it was unknown whether it is feasible to construct an in-depth study of the local context with online information. The present research has shown that based, on a five-step approach an in-depth study of context using online data(bases) is feasible. The results have shown that a large amount of standardized data (contextual factors) is accessible on public web-based datasets. The five-step approach seems useful to collect and select the relevant contextual factors that might influence the outcome of such intervention.

A first key finding is the large amount of standardized public information/data currently available online (e.g., official statistics) which offers an opportunity for researchers. These web-based datasets cover a broad range of domains, including sociodemographic, and socioeconomic data, and data related to care supply and availability of care, which were considered important in the context of the D-SCOPE program that was the point of departure in the present study. The approach that was adopted in the current study makes it possible for future research to have a comprehensive understanding of the setting in which a healthcare intervention is implemented. However, the amount and type of information identified may differ depending on country/region and topic of study. For instance, in the D-SCOPE project the inventory contextual factors consisted of 157 factors.

Since a large amount of online information is available, one can assume that not all of this information is useful. Therefore, a systematic approach is essential to construct a concise list of contextual factors. A second result of the present study therefore, is the five-step approach as described in the methods that was used to identify relevant contextual factors. The discussion section within the NGT (step 5) can be used to formulate hypotheses and may help to explain the final results of the intervention. For instance, during the discussion in the NGT it was argued that the availability of a community center would have a moderating effect in the D-SCOPE intervention because it is important for social participation and organizing activities, but it also provides information, educational activities, meals and helps people to refer to other care and support services (‘snowball-effect’). The lack of a community center in Knokke-Heist made it impossible for the professional of the social service center to refer participants towards other care and support services.

Thirdly, as a result of the five-step approach, it was revealed that in the D-SCOPE program, large differences were found between the three municipalities (Ghent, Knokke-Heist and Thienen). Socio-demographically, Knokke-Heist had the oldest population, with a dependency ratio (65+/20-64y) of 63.1% compared to 27.03% in Ghent and 36.21% in Thienen. In Knokke-Heist, the percentage of adults older than 80 years of age was almost twice as high compared to Ghent, while the total resources of community social security in euros per inhabitant in the year 2013 was only half of the budget in Ghent. These differences in contextual settings between the three municipalities may moderate the effect of the D-SCOPE intervention on its outcomes and emphasizes the relevance of the context. For instance, a previous systematic review by Stuck et al. concluded that preventive home visits reduce mortality in a younger study population (mean age < 80 years) but not in older populations [20].

Strengths and limitations

The present study has several strengths. First, the present study gives a systematic approach to investigate the local context in an easy-to-apply way. Second, previous studies have shown that the NGT is a valid method in decision-making, based on the expertise of experienced researchers [16-17]. The NGT made it feasible to reduce a long inventory of contextual factors to a short and concise list with the assumedly most relevant ones.

Our study also has some limitations. First, according to the socioecological model, context can be divided into various layers: microsystem, mesosystem, exosystem and macrosystem. The present study solely focuses on the level of the municipality and not on the individual or the cultural level. For example, no information is found regarding the relevant contextual factors, such as the level of coordination between and within services/institutions, or the norms and values within/between municipalities [21]. Secondly, the present information was retrieved from three public web-based datasets. The correctness of the analysis depends on the correctness and accuracy of those datasets (e.g., for many contextual factors the latest update was in 2014 - 2015, although the intervention study started in 2017). Thirdly, regardless of the large amount of information that can be found online, it is plausible that a significant amount of relevant information is still missing. For instance, we are aware that Knokke-Heist does not have a community center; however, no information is available regarding the activities organized by local organizations or other initiatives organized by the municipality that could function as an alternative for a community center. Fourthly, several aspects of the 5-step

approach are based on experts' opinions (e.g., part four and five). This indicates the assumption that the D-SCOPE trial can interact with the selected contextual factors. However, further evidence-based research is needed.

Implications and future research

New innovations and technologies offer opportunities for contemporary and future scientists. Before the existence of the World Wide Web, constructing an inventory of contextual factors in different communities would be a considerable and time-consuming challenge. Today, a substantial amount of information can be found in online-standardized datasets. This enables future intervention studies to take the local context into account. For instance, the present results can be useful to explain differences in the effects of the D-SCOPE intervention in the three municipalities and provide insight regarding the contexts that might be supportive for a home visit and those that are not. For instance, older adults in need of extra social contact and participation could not be referred to a community center in Knokke-Heist, when this is possible in Ghent and Thienen, where a community center is available. The lack of a community center in Knokke-Heist could impact how the D-SCOPE intervention affected its outcomes. Based on these insights of the present study, new (theory-driven) hypotheses can be formulated that can be tested, giving a better understanding of the mechanisms related to an intervention. Therefore, we would advise researchers to perform an in-depth analysis of the context before the start of an intervention to avoid post-hoc data-driven analysis in the urge to explain the results. In case an intervention study includes many municipalities, a contextual factor can also be used as moderator in the statistical model. For instance, the availability of a community center could be an independent dummy variable in the statistical analysis.

Because of the proposed five-step approach, future RCTs could meet the criticism of lack of attention to the context when evaluating an intervention [1]. This five-step approach can also be used for interventions with other topics (e.g., economic research, criminology) or research for other purposes; for instance, the risk stratification of areas whereby the characteristics (e.g., sociodemographic, socioeconomic, care supply) of a village, municipality or city are assessed and compared to macro-level data to determine the local (health) needs and challenges [22, 23].

Conclusion

Some authors argue that certain contexts are supportive for the implementation of an intervention and some are not, although the role of the context is often ignored in RCTs [1]. The present study shows that it is feasible to perform an in-depth analysis of a local context. A significant amount of information is available online and an easy-to-apply five-step approach can determine the assumedly most relevant contextual factors. With this five-step approach, future intervention studies can consider the local context when examining the effect of an intervention and formulate theory-driven hypotheses in RCTs. This should give us a better understanding of the effect of an intervention and the mechanisms related to the intervention.

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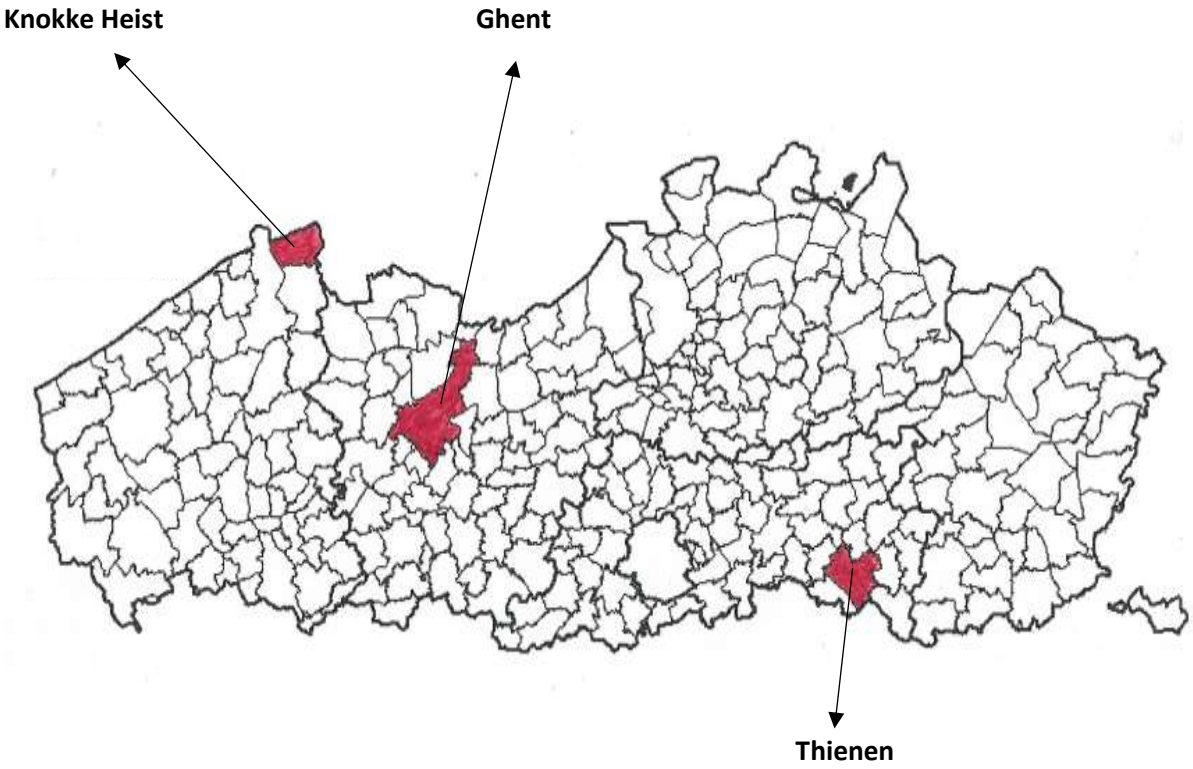
Supplementary file 1: Map of Flanders in Belgium

The three municipalities participating in the D-SCOPE programme are Knokke-Heist, Ghent and Thienen.



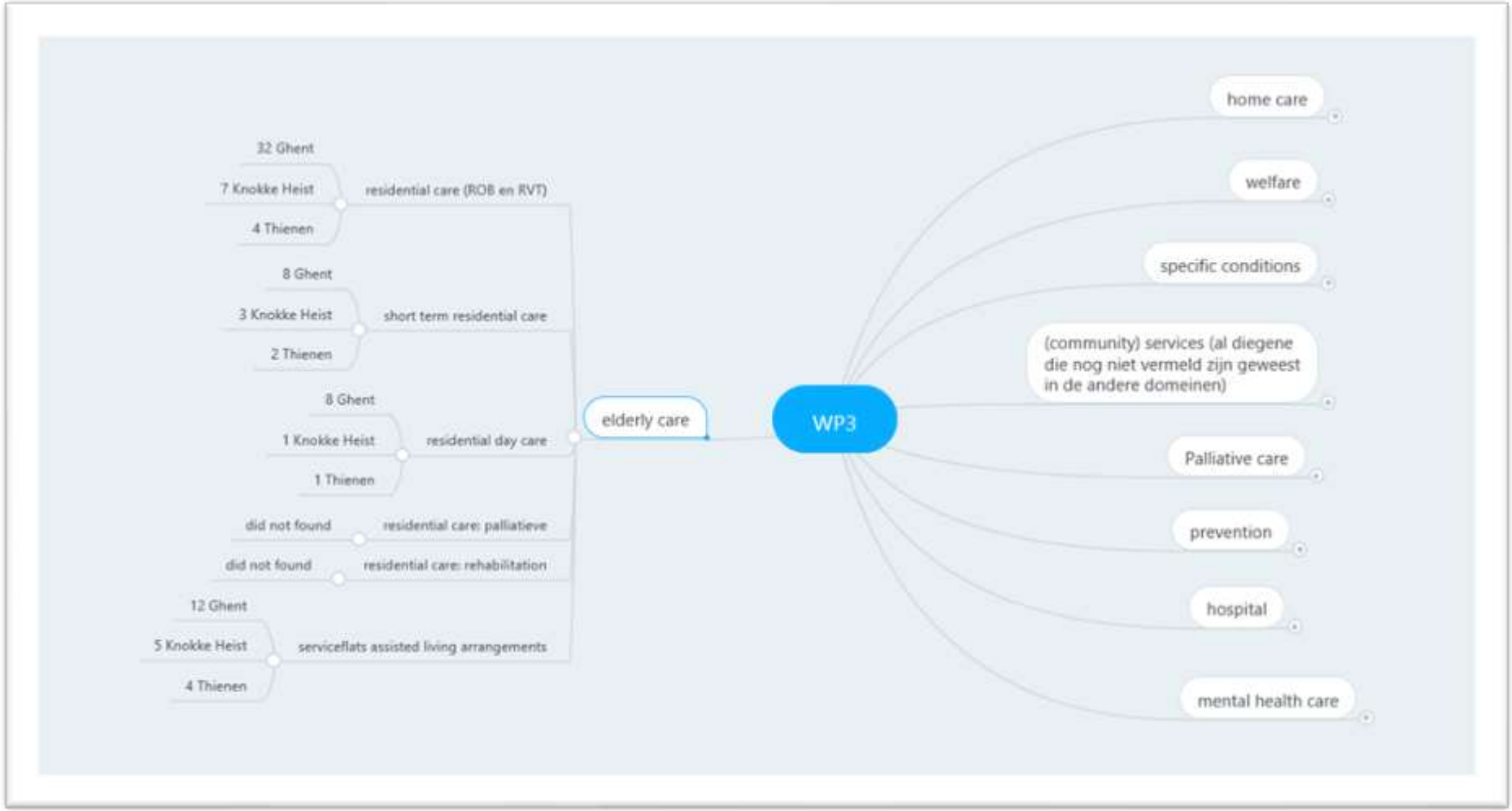
Supplementary file 2: Databases

InterMutualistic Agency (IMA): The IMA collects, manages, and stores the data of the seven Belgian health insurance institutions. Examples of data are percentages of people age 75 or more with chronical illnesses, and percentages of people aged 65 or more which make use of day care. The IMA Atlas (website) is an open-source database with health contextual factors. IMA analyzes the data on its own initiative or at the request of other partners. Its aim is to preserve or to improve the performance, the quality, and the accessibility of the Belgian health care system and health insurance.

Local Statistics: The Local Statistics website is a joint venture between the Study Center of the Flemish Government, the Agency for Local Government, the Association of Flemish Cities and Municipalities, the Association of Flemish Provinces and the Flemish Community Commission of Brussels. It is a portal site where all types of statistics about local and provincial administrations, such as number of people aged 65 and more, and total resources of the community social security in euros per inhabitant in 2013 have been collected. Databases from various policy domains of the Flemish government are brought together.

Social Map: The Social Map database collects data from health care organizations (broad interpretation) in a structured database. It contains contact details, qualitative information such as target groups, and opening hours. Social Map aims to guide people in need of specific care to the appropriate organization.

Supplementary file 3: Mind mapping



Chapter 9

General discussion

Current policies are focusing on facilitating 'healthy aging' and 'aging (well) in place' more and more. However, a better understanding of how to facilitate 'healthy aging' and 'aging (well) in place' is needed. In this respect, attention for phenomena such as frailty and its conceptualization and operationalization, the life course of older adults, and the effect of supporting interventions in frail older adults is also important. Therefore, the objectives of this dissertation are threefold: (1) to study the relatedness of frailty conceptualizations and operationalizations; (2) to study strategies that enable early detection and a proactive approach of frailty in older persons; and (3) to expand our knowledge with regard to the aspects that should be taken into account when conducting a complex intervention study. This chapter summarizes the main findings, reflects on theoretical considerations, and discusses several methodological issues. In the end, implications for clinical practice, future research, and policy are discussed.

Main findings

Approach and measurement of frailty: unidimensional versus multidimensional frailty assessment (RQ 1-2)

Many frailty scales have been developed in previous years [1], although it is unknown how these frailty scales are related to each other. Comparative studies about these frailty scales are scarce and mainly focus on the predictability for adverse outcomes (e.g., mortality, hospitalization) [2, 3]. The aim of chapter 2 was twofold: first, to compare a unidimensional approach of frailty by means of the Fried Phenotype Criteria with a multidimensional approach of frailty by means of the Comprehensive Frailty Assessment Instrument (CFAI), and second, to compare the characteristics of the 'frail participants' according to both scales. This was done in community-dwelling older adults (N = 196) in three Belgian municipalities (Ghent, Knokke-Heist, and Thienen). The results of the study showed that the Fried Phenotype Criteria and CFAI do measure partly the same 'frailty concept'. The moderate association between both measurements was mainly attributed to the physical domain of the CFAI and, to a lesser extent, the psychological domain. The social domain and environmental domain of the CFAI were not related to the Fried Phenotype. The results also indicated that 23 participants were frail according to both scales, 12 participants were frail according to the CFAI but not according to the Fried Phenotype, and 15 participants were frail according to the Fried Phenotype but

not according to the CFAI. Therefore, we observed some significant differences in the characteristics of the 'frail sample' depending on the used frailty measurement. For instance, participants who were solely frail according to the CFAI had a lower level of life satisfaction and net income but were physically more active. Also, some differences were found for other characteristics, such as age, sense of mastery, and aging well in place; however, they were not statistically significant. Based on the present results, one can conclude that the use of a frailty scale as an inclusion instrument in scientific studies may have an important impact on the selected group of participants.

Operationalization of physical frailty: psychometric properties of replacement questions (RQ 3)

When screening large populations, an easy to apply frailty measurement is necessary [4]. Therefore, performance-based tests are often replaced by self-report questions. Little is known about which questions (or set of questions) are most valid to substitute the performance-based measures. These modifications have an important impact on classifying older adults as frail or not frail and its predictive ability on adverse outcomes. To have a better understanding of which replacement questions are valid, the psychometric properties should be tested. However, this is rarely done. Therefore, the aim of chapter 3 was to validate a set of questions replacing the slowness and weakness of performance-based measures as part of the Fried Phenotype in community-dwelling older adults (N = 196). We observed that the concordance between the Fried Phenotype including the 6 replacement questions and the Fried Phenotype including the 2 performance-based measures is substantial. The results were characterized by a high specificity but a moderate sensitivity. This indicates that the replacement questions have the ability to correctly identify those without physical frailty, whereas their ability to correctly identify those with physical frailty seems to be less adequate. The concordance between the Fried Phenotype performance-based measures (slowness and weakness) and the set of replacement questions at item level was fair. Therefore, one might consider the scale with the replacement questions as a step in a sequential process to detect frailty in large populations.

Early detection of frailty and a proactive frailty approach (RQ 4-6)

Risk factors

In the literature, frailty is seen as a dynamic state that can deteriorate but also improve. Previous research has shown that physical frailty at an early state is reversible [5-7]. However, the evidence for reversibility of frailty at a later stage is rather limited [8]. To enable early detection, determining risk factors for frailty in general and its different domains in particular (physical, psychological, social, and environmental) is essential for targeting those older individuals at risk for adverse outcomes and to undertake specific and or tailored preventive actions. Previously, Dury et al. determined several risk factors: age, marital status, level of education, country of birth, relocation in the previous 10 years, and income [9]. The aim of chapter 4 was to validate these risk factors and to assess whether these risk factors are, indeed, an effective way for identifying frail older people. The average scores of the frailty domains and the prevalence of mildly and highly frail older adults were higher in older adults that met at least three risk factors. The results indicated an increase in the percentage of older adults who were mildly and highly frail for physical, psychological, social, and environmental frailty. Therefore, the odds of identifying people who were mildly or highly frail were higher if one screens people who met at least three risk factors. According to the results in chapter 4, selecting older people based on these risk factors can be an effective strategy for identifying frail older people (RQ4).

Life course approach: retirement and frailty in later life

In chapter 5 and chapter 6, we focused on the transition into retirement (Belgian Ageing Studies-dataset) [10]. Retirement can be accompanied by positive (e.g., extra leisure time, healthier lifestyle) as well as by negative aspects (e.g., loss of income, loss of social support) [11-15]. A better understanding of whether the transition into retirement is related to frailty in later life and of the specific circumstances can be insightful to develop a proactive approach of frailty. Since the transition into retirement occurs at an earlier phase in life while most people are not frail yet, so far, only a few studies have focused on retirement and its relation to frailty [16, 17].

The aim of chapter 5 was to assess to what extent different motivations for retiring are related to frailty in later life. On average, the time spent in retirement of the group under study was

11 years. People who retired for health-related problems, who were unemployed for some time before retirement, who were obliged to retire (e.g., business closure), and who were dissatisfied with the job content had higher scores on the CFAI (and subdomains) in later life, meaning that they were more frail. When the reason to retire was the retirement of the spouse, taking up care tasks, giving young people a chance, or having sufficient financial assets and the financial incentive to work longer was too low, respondents had a lower score on the CFAI (or subdomains) in later life, meaning that they were less frail. Being dissatisfied with the working conditions was related to a higher score (social domain, women) as well as with a lower score (physical domain, men) on the CFAI. The results were different for men and women, indicating that 'I needed to take up care tasks' and 'my spouse retired' are protective factors mainly for women. For men, having sufficient financial assets is an important protective factor. Dissatisfaction with the job content is a risk factor for multidimensional frailty (and the subdomains, except physical frailty) for men but not for women. The difference in gender may not be surprising since the labor trajectories/histories are different between both groups [18].

In chapter 6, the aim was to examine the relationship between age of retirement and frailty in later life. The results suggested a negative association between age of retirement and physical and multidimensional frailty in later life, although the differences were small. No evidence was found for a relationship between age of retirement and the other subdomains of frailty. The results suggest that age of retirement is not clinically relevant for frailty in later life, and no evidence was found that increasing the statutory retirement age would cause an increase in the number of frail older adults in later life (RQ6). The results in men and women were rather similar. Based on chapters 5 and 6, one can conclude that the motivation for retiring is important for frailty in later life, whereas the timing is not.

The effect of (complex) interventions in frail older persons (RQ 7-10)

Previous studies have shown that frailty is associated with adverse outcomes, including mortality, institutionalization, hospitalization, and accidental falls [19]. Since frailty is considered to be dynamic, some authors assume that early detection and intervention are important to prevent or delay frailty [20]. In chapter 7, the aim of the systematic review and meta-analysis was threefold: (1) Which interventions are applied to protect frail community-dwelling older adults from adverse outcomes? (2) What effect do interventions have on frail

community-dwelling older adults in terms of mortality, hospitalization, formal health costs, accidental falls, and institutionalization? (3) How do age, study duration, and the multi- versus unidimensional approaches of frailty and recruitment influence the effect of an intervention? In total, 16 studies were included in the systematic review and meta-analysis. The following types of interventions were found: a case management intervention, an information provision intervention, a physical intervention, a psychosocial intervention, a pharmaceutical intervention, and a technological intervention. We focused on the following outcome measures: mortality, hospitalization, formal health costs, accidental falls, and institutionalization. Based on the results of the systematic review, two included studies described a significant effect. In Hall et al., the intervention of case management resulted in a lower institutionalization [21]. Perttila et al. performed a study with a physical intervention, which resulted in a lower number of accidental falls [22]. However, based on the results of the meta-analysis, no significant results were found for the observed adverse outcomes (RQ7). A sub-analysis for some variables yielded no significant effects, although some findings suggested a decrease in adverse outcomes (e.g., an average age of the participants of 80 or less) (RQ8). In the present study, no evidence was found that interventions might be protective against the included adverse outcomes of frailty.

Based on the interpretation of the literature review, we recognized the need for more emphasis on the context and setting in which an intervention is implemented. In the literature, it is argued that some contexts are supportive for an intervention while others are not [23, 24]. Since the D-SCOPE project (introduced in the general introduction) aimed to apply an intervention study in three municipalities, the aim of chapter 8 was to assess whether it is feasible to make an in-depth study of the local context. The following questions were examined: 1) Are there relevant standardized web-based public data about the local context available in these three municipalities? and 2) How can the contextual factors that are most likely to interact with the intervention and moderate its outcomes be determined? We designed an approach on how to do a search for relevant contextual factors with online information. This resulted in a 5-step approach: (1) to hold a theoretical/conceptual discussion of relevant contextual factor domains; (2) to search and find appropriate web-based public datasets that cover the domains with standardized information; (3) to inventory all identified contextual factors; (4) to reduce the long list of contextual factors towards a concise list based

on the opinions of independent reviewers; and (5) to hold a Nominal Grouping Technique to determine the most important contextual factors. Therefore, we applied this approach on the D-SCOPE trial, which included three municipalities (Ghent, Knokke-Heist, and Thienen). Based on the explorative case study, one can conclude that: 1) a large amount of standardized data (contextual factors) is accessible on public web-based datasets (RQ9); 2) it is very feasible to get an in-depth analysis of a local setting in order to get a better understanding of the effect of an intervention and the mechanisms related to the intervention (RQ10).

Theoretical considerations

In this section, the theoretical considerations regarding the conceptualization of frailty instruments and ecological fallacies are discussed.

The conceptualization of frailty

As mentioned before, numerous frailty measurements exist [1]. Therefore, each measurement has its own specificities [1]. In general, two approaches of frailty can be distinguished: 1) frailty as a physical construct (unidimensional approach); for example, the frailty phenotype, which includes the following criteria: unintentional weight loss ≥5 kg in the past year, self-reported exhaustion in the past week, low levels of physical activity, low grip strength, and/or slow walking speed [25], 2) frailty as an integrative construct (multidimensional approach); for example, the CFAI including four domains: physical, psychological, social, and environmental frailty. In the current dissertation, we do not assume that one approach is better than the other. Several operationalizations have proven their reliability, internal and external validity [25-30]. However, the use of a frailty measurement can have an impact on the composition of the sample and its characteristics (as shown in chapter 2) [31, 32]. Consequently, one can assume this might have an impact on the outcomes of a study. Therefore, the risk factors or the CFAI (chapter 4) can be different for the Fried Phenotype. Ntanasi et al. reported that the risk factors for the Fried Phenotype are age, level of education, occurrence of dementia, and occurrence of depression [33]. In chapters 5 and 6, we could only do the analysis for the CFAI since the Fried Phenotype was not a part of the Belgian Ageing Studies. However, the results in chapter 6 with regard to early retirement (< 56 years) are in line with a study by Haapanen et al. using the Fried Phenotype. This study showed that persons that retired at the age of 55 or younger have a higher risk of becoming

frail in comparison to persons that retired at the age of 58 – 67 [16]. In addition, Theou et al. reported that the modifications within the Fried Phenotype have an important impact on its classification and predictive ability [34].

Within the measurements with a multidimensional approach, different operationalizations exist as well, such as the CFAI, the Groningen Frailty Indicator (GFI), and the Tilburg Frailty Indicator (TFI) [26-28]. The TFI includes physical, psychological, and social domains, while the GFI and CFAI also respectively include a cognitive and environmental domain. More recently, a cognitive domain has been added to the CFAI (CFAI-Plus) [35]. Roppolo et al. compared the Fried Phenotype and the TFI [32]; the number of frail older adults was much larger according to the TFI in comparison with the Fried Phenotype [32]. In chapter 2, the CFAI and the Fried Phenotype had a similar number of frail older adults. This may indicate that large differences also occur between multidimensional frailty measurements (e.g., in frailty prevalence). These differences may have a large impact on the relationship between measurements, specific characteristics of the frail sample, and study outcomes [32]. Consequently, one needs to be very cautious to assign specific characteristics to a unidimensional approach or a multidimensional approach (see chapter 2). In addition, more research is needed to get a better understanding of the different modes to operationalize frailty.

Ecological fallacy

One of the most discussed manuscripts with regard to an ecological fallacy is Durkheim's work 'Suicide'. Durkheim found an association between suicide and religion (Catholic versus Protestant) [36]. However, this relationship could be biased because of confounding variables [37]. In the interpretation of the results, one must be aware of the ecological fallacies, meaning making an inference about an individual based on aggregate data for a group [38]. Robinson showed that ecological correlations cannot validly be used as substitutes for individual correlations [38]. In chapter 7, we reported that the interventions did not have a statistically significant result on adverse (health) outcomes. However, one must be cautious to make an inference about this result at the group level for the individual level. It is reasonable to think that for a certain group of participants, the interventions did work, while for others it did not. Therefore, a more in-depth analysis is necessary. In chapter 7, some extra subgroup analyses were performed for duration of intervention, a multi- versus unidimensional approach to frailty, average age, and recruitment method of the participants.

A trend showed that the results were better when the average age of the participants was 80 years or younger, although the results were not significant. In chapters 5 and 6, the analysis was done for men and women separately since the labor trajectories of men and women are very different throughout life [18]. In chapter 5, this yielded very different results for men and women.

Methodological considerations

In this section, several methodological considerations are discussed regarding the operationalization of frailty instruments, statistical errors, the limitations of a cross-sectional study design, and the sample size of the studies we performed.

Operationalization of frailty

The Fried Phenotype includes 5 criteria: weight loss, exhaustion, low physical activity, gait speed, and handgrip strength [25]. Therefore, low physical activity is operationalized using a short version of the Minnesota Leisure Time Activity questionnaire [25]. This criterion is often modified. Op het Veld et al. used an adjusted version of the Short Questionnaire to Assess Health-enhancing physical activity (SQUASH) [4]. In the present dissertation (chapter 2 and chapter 3), the criterion low physical activity was not operationalized in exactly the way it was initially proposed in the Fried Phenotype. In this dissertation, low physical activity was operationalized by asking the participant: 'Do you do sports activities (e.g., walking, swimming, or cycling)?' This difference in operationalization might have affected the results: the observed agreement of the three frailty stages between FRIED-P and FRIED-Q and the Cohen's kappa value, respectively [34].

Statistical errors: Specification error

In regression analysis, the aim of the statistical model is to be a best linear unbiased estimator (BLUE) [39]. Therefore, several assumptions must be tested (see the Gauss-Markov theorem) [40]. Unmet assumptions may be an indication of a biased estimator. One of these assumptions is related to building the statistical model or model specification. The specification of a model consists of selecting an appropriate functional form and the inclusion of variables. Consequently, a specification error can occur in different modes if 1) relevant variables are not included in the regression model, 2) irrelevant variables are included in the

regression model, and 3) a regression model with an incorrect functional form is used. Therefore, in chapters 5 and 6, the regression models were based on evidence found in the literature. To avoid misspecification by including irrelevant variables, a backward iteration was performed in chapter 5, and we used the same model in chapter 6. Misspecification because of missing relevant variables may be a problem in both chapters 5 and 6. Palmer et al. have shown that persons experiencing difficulties coping with the physical and mental demands of work are more (pre-)frail [41]. Lu et al. reported the importance of labor trajectories for frailty in later life (e.g., women who had a short break for family care and then did part-time work until they were 59 years old had a lower score on the Frailty Index after the age of 60 than those who undertook full-time work until they were 59 years old. Women who were largely family carers or non-employed throughout adulthood had higher levels of frailty at the age of 60 but experienced a slower decline with age.) [18]. These variables were not included in the statistical model of chapters 5 and 6; therefore, a specification error might have occurred.

Limitations of a cross-sectional study design

Some empirical studies of the present dissertation have a cross-sectional design. This mode of design enables us to find an association between variables; for instance, the relationship between frailty measurement outcomes (chapter 2). However, a cross-sectional design also has limitations; for instance, based on cross-sectional data, one cannot test for causality. The cross-sectional design in chapters 2 and 3 is not problematic since the direction of the relationship in these studies is not important. In chapter 6, this could be a problem; the aim was to assess the relationship between age of retirement and frailty in later life. However, it is initially reasonable to assume that some older adults were frail at a young age, thus affecting the age of retirement [42]. In the literature, this phenomenon is called reverse causality [42]. Reverse causality could lead to an endogeneity problem and may bias the results [43]. To address the issue of reverse causality between retirement for health-related reasons and the relation of retirement and frailty, we addressed the subpopulation that explicitly declined health issues (Likert score = 1) as a determining factor for retirement, a strategy also applied by Dave et al. [44]. Therefore, also in chapter 5, one must be cautious to interpret the results. In chapter 5, an association is found between frailty and retirement because of health-related reasons. However, it is reasonable to think that adults retiring were already (pre-)frail at the time of retirement [41]. Based on the results in chapter 5, one can state the existence of a

relationship between frailty in later life and retiring because of health-related reasons; however, one cannot make any statements on how the frailty trajectory evolved between the time of retirement and the time of the survey. Therefore, one needs longitudinal studies.

Sample size of studies

In chapter 2, the aim was to compare the characteristics of the frail sample according to the CFAI and the Fried Phenotype (FP) since the prevalence of frailty is rather unpredictable depending on the used frailty measurement and the setting (ranging 4% to 59.1%) [45, 46]. It was not possible to determine the number of participants needed exactly. The frail sample according to both frailty measurements was approximately 20%. In total, 23 participants (11.92%) were frail according to both the FP and the CFAI, 15 participants (7.77%) were solely frail according to FP, and 12 participants (6.21%) were solely high frail according to the CFAI. Because of the small sample size, many of the outcomes were not significant. However, some notable trends were present. Also, in chapter 7, in which the aim was to examine the effect of interventions in frail community-dwelling older adults, only a small sample of studies was included. For instance, for most interventions, it was not possible to perform a meta-analysis. This was mainly because frailty was operationalized in only a small number of studies.

Implications for future research

Towards a flexible use of frailty measurements

From the present dissertation, we learned that the choice of a frailty operationalization can have a large impact on both the estimates of frailty prevalence and the characteristics of the selected sample (chapter 2). We do not assume that one approach is better than the other. According to Rockwood, it is likely that some definitions of frailty will be more successful than others over time [47]. However, we disagree with this argument. We think it is incorrect to assume that one approach is better than the other. The choice of a specific conceptualization of frailty should depend on the context. Each researcher/clinician should ask some questions in advance: What is the setting of the study? What is the aim of the measurement, and who will administer the instrument? How much time is available? Who will be the participants? Based on these questions, a choice can be made for a particular instrument.

In a clinical setting (e.g., hospital), a performance-based test might be easily applicable because most of the required tools (e.g., hydraulic dynamometer) are available in the setting.

However, in the case where one visits older people at home, this becomes more complicated since the researcher/clinician must bring all the equipment. Also, the aim of the measurement is important. Previous studies have shown that frail older adults are at a higher risk of experiencing complications after surgery [48, 49]. In the case where the aim of the frailty measurement is to know whether the patient is fit enough to undergo surgery or not, a frailty measurement focusing on physical frailty may be recommendable. Multidimensional frailty measurements, including domains such as social factors or environmental factors, can only bias the image of the patient's physical functioning/reserves. Lin et al. even suggested the possibility that different frailty tools may be best suited for different acuity and types of surgical patients [49]. However, after surgery, when determining the best place for the patient's recovery, a multidimensional approach can be more insightful since the social network or the home the patient is living in can make it feasible to recover at home or not. Also, if the aim is to facilitate aging well in place, a multidimensional approach can be more insightful instead of focusing solely on physical frailty. A systematic review showed limited evidence for the effectiveness of integrated care in frail older people. As a possible explanation for the limited effectiveness of integrated care, it was stated that older adults are still considered as a single group and that integrated care may be more beneficial for certain subpopulations of frail older people [50]. In conclusion, more research is needed to show which frailty operationalization is preferred for which aim and setting. Therefore, more comparative studies are needed to assess the impact of frailty measurements on sample and study/intervention outcomes. Based on the results of the present dissertation, one must ask whether it is possible to make a conceptual definition of frailty that takes the aim and setting (context) into account and that facilitates the use of tailored frailty operationalizations.

Life course approach

An aspect that should be added to the definition of frailty is the importance of the life course approach. In chapter 5, the results showed that the transition into retirement is related to frailty in later life. Consequently, one can conclude that frailty is an evolving process that starts at a younger age. Adding the aspect of the life course in the frailty definition could emphasize the importance of doing frailty research in older adults at a younger phase in life [51]. Studies have shown that the group of older adults is very heterogeneous [52]; some older adults age much faster in comparison with others. Therefore, one can assume that some aspects in life

can be a trigger for aging rapidly. According to Kuh, the origins of the components of frailty are already present in early life (prenatal, prepuberal) [51]. In the literature, frailty is seen as a state of vulnerability, whereby older adults experience a loss in resources or reserve capacity [53]. Because of this cumulative decline, minor stressor events can trigger disproportionate changes in health status [54]. However, it is still unclear what triggers these (biological) processes and the decline of these physiological systems. Wang et al. reported a decline in six physiological systems (biological processes) related to frailty: brain changes, endocrine dysregulation, enhanced inflammation, immune dysfunction, metabolic imbalance, and oxidative stress [55]. The results of the present dissertation suggest that the transition into retirement may be a trigger for frailty in later life, more specifically in case it is a push factor into retirement. Previous studies have shown that oxidative stress is caused by an unhealthy lifestyle characterized by a lack of exercise and by unhealthy food habits [56]. Perhaps the relationship between push factors to retirement and being frailer is associated with an unhealthy lifestyle in later life, increasing the level of oxidative stress. Conversely, the relationship between pull factors and being less frail may be associated with a healthy lifestyle, decreasing the level of oxidative stress. However, no current evidence exists to support this hypothesis; therefore, more research is needed. In addition, studies have also shown that life events affect psychological frailty in later life, and involuntary retirement is related to a lower well-being [57, 58]. Therefore, more focus on a life-course approach may be helpful in acquiring a better understanding of the development of frailty and might give insights into strategies to prevent (multidimensional) frailty proactively [51].

Frailty is dynamic

In chapter 7 (meta-analysis), we examined the effect of interventions on adverse outcomes. Since frailty is associated with adverse outcomes, an improvement in adverse outcomes could be an indication of an improved frailty level. However, the results of the meta-analysis for the interventions case management and information provision (chapter 7) did not indicate any improvements in the adverse outcomes. On the contrary, an increase in hospitalization was found in the intervention group. In the literature, mixed results are found with regard to the effect of interventions on (pre-)frailty and its adverse outcomes. Some reviews, especially with regard to physical activities, do find a positive effect [59-62]. However, interventions such as

group meetings and home visits were not found to be effective [63]. De Moraes et al. found no statistically significant effect of nutritional supplementation or nutritional education [64]. In some studies, the results suggest that the intervention was only beneficial for certain subgroups. Previously, it has been suggested that the reversibility of frailty at a later stage is rather limited and that frailty at a certain state becomes a point of no return. This raises the question of whether frailty is really dynamic, a recurring aspect in several frailty definitions [20]. We have to acknowledge that most of the frailty perspectives emerge from a negative and stereotypical view of aging, focusing on deficits and adverse (health) outcomes related to frailty. Several studies showed that older adults can still have a satisfying life or experience a good quality of life despite being frail or the deficits they experience [65, 66]. De Donder et al. argue that these positive outcomes are overlooked. Instead of explaining why frail older people report lower levels of well-being, one should rather identify factors that contribute to well-being despite being frail [67].

Complex interventions in frail older adults

To prevent or delay frailty and its adverse (health) outcomes, many intervention studies have been done. Until now, the results of these interventions are often disappointing [63, 64, 68]. During the course of the dissertation, some methodological issues raised questions regarding these intervention studies. First, many studies indicated to do an intervention study in frail older adults; however, one rarely motivated why the sample was frail or not frail [62, 68, 69]. Many studies did not operationalize the concept of frailty; consequently, we do not know whether the sample was frail or not. Future research should operationalize and describe the used frailty approach. This makes it more feasible to compare (intervention) studies and to do meta-analyses. Second, studies that did operationalize frailty did not motivate why a particular frailty operationalization was used. As reported above, the aim of the research may be relevant in the choice of the preferred frailty operationalization. In chapter 2, we found evidence that a chosen frailty operationalization can have an impact on the eligible sample and its characteristics. Based on these results, one can assume that the outcomes can be affected by the used frailty operationalization. To achieve a maximum effect of an intervention, we assume that the ability to recruit the targeted sample is essential, although more research is needed to find evidence that both approaches of frailty can be useful for

distinct purposes or contexts. Third, interventions are often done in different contexts. In the literature, the concept of 'context' refers to the spatial and institutional locations of social situations with the inherent norms, values, and interrelationships and describes those features of the conditions in which programs are introduced. For instance, Van Leeuwen did a study in two regions, West Friesland and Amsterdam [70]. Though both regions are close to each other, large differences exist in the population density and cultural background. Also, within the D-SCOPE project, the intervention study took place in three regions: Ghent, Knokke-Heist, and Thienen. These regions differ a lot in population density, income, cultural background, etc. Therefore, it is very reasonable that an intervention can be effective in a specific context while not in another setting. Current research often lacks a good description of the context [24]. The present dissertation presents a 5-step approach to get a better understanding of the context. This understanding can help with the clarification of the results; why was an intervention effective or not? Context is more than having data with regard to the availability of care or sociodemographic and socioeconomics data; it also involves the norms, values, and culture of an area. Although it is unreasonable to describe the context perfectly, more attention should at least be given to it. This can be done by using quantitative data but also by using qualitative data or mixed data. Fourth, interventions can generate more effects than solely those aimed in the study as outcome [71]. One must consider the extra awareness of services or (physical) problems that older adults gain through an intervention (e.g., home visits, case management). This may explain why in chapter 7, the number of hospitalizations in the intervention group was higher than in the control group. The extra awareness gained through the intervention should be taken into account during the preparation of the study protocol. Otherwise, a systematic bias will occur. This can be done by 1) collecting extra information, e.g., in the case of the variable hospitalization (chapter 7), information with regard to the reasoning for hospitalization and whether this was influenced by the intervention could give more insights into the effect of the intervention, and 2) having longer follow ups, which could give more insights into the patterns of hospitalization, need of care, and mortality [72]. Fifth, one must also be aware of the possibility of ecological fallacies meaning, making an inference about an individual based on aggregate data [38]. In chapter 7, we reported that the interventions did not have a statistically significant result on adverse (health) outcomes. However, one must be cautious to make an inference about this result at a group level for the individual level. Therefore, extra statistical analyses, such as sub-group

analysis or the minimal important change, could give extra insights into the real effect [73]. The minimal important change is a statistical approach in which patients are categorized as persons with an important improvement, an important deterioration, or without an important change [73].

Future research should not focus on the effect of an intervention solely but also address the questions why interventions were effective or not, for whom they were effective, and what contextual factors triggered the mechanisms required to make them work. This is described by Pawson and Tilley in 'realistic evaluation' (1997). They suggest that a realistic evaluation approach might provide a better understanding of the effect of an intervention. This approach is a theory-driven method that not only addresses the outcome of an intervention but also why interventions worked, when they worked, or for whom did they work [23].

Implications for policy

Various frailty measurements exist, each with their own specificities. In the present dissertation, the aim was not to prove the superiority of one frailty approach over another. We assume that both unidimensional and multidimensional approaches of frailty can be useful for distinct purposes. In chapter 2, the data suggested that the choice of a specific frailty measurement has an impact on the selected sample and the characteristics of the sample. Many initiatives/interventions exist at the local and national level to prevent frailty or fall incidences or to facilitate aging well in place. However, their effectiveness as such may depend on the extent to which one succeeds to reach the target group. Therefore, prior to the start of an initiative/intervention, policy makers must clearly define the aim/outcome of the initiative and the targeted population and how they aim to reach the targeted population.

The present dissertation shows that a case-finding strategy (chapter 4) based on risk factors could be helpful in detecting frail older people. Furthermore, the results in chapter 5 suggest that a transition from working life into retirement can influence the development of frailty in later life. Therefore, policies aiming to prevent or improve the frailty status should not start when an older adult is already frail or prefrail. Especially, older adults retiring because of health-related problems or dissatisfaction with the job content or working conditions have a higher risk of becoming frail. Hence, instead of screening the total population, a more targeted screening (case finding) based on risk profiles could be helpful and more efficient for

professionals in the community to detect/screen frail older people with an evidence-based strategy. Since early detection is important for the dynamic state of frailty, this might also imply that the efforts made by the professionals (i.e., extra care and support) could be more effective. Based on chapter 5, we learned about the possible added value of a life course approach. Life experiences early in life are related to the frailty score later in life. This might imply that it could be beneficial to start interventions to prevent or delay frailty or to promote aging well in place around the retirement phase, while frailty still may be reversible. Governmental policies should focus more on guiding older adults to the labor market in case the older adults were obliged to retire or already unemployed for some time.

Based on chapters 5 and 6, we concluded that why someone retires is more important for frailty in later life than when a person retires. The government must be aware that approximately 28.5% of the BAS participants indicated that health was an important motivation to retire. Therefore, a linear increase in the statutory retirement age will probably not be feasible for everyone. Therefore, a more tailored approach at the individual level is needed.

In the present dissertation, extra attention is given to the context of an intervention; therefore, a five-step approach is developed (chapter 8). The five-step approach can give an overview of the characteristics and care supply of these regions. Consequently, this approach can also be useful for governmental policies. In Flanders, the government created primary care regions (‘eerstelijnszones’). One of the main tasks of these primary care regions is to organize the coordination between care providers and stimulate interdisciplinary collaboration. Based on this five-step approach, each primary care region can get an overview of the specificities of their region. National data or data of other regions can be used as a benchmark to identify the strengths, weakness, opportunities, and threats (SWOT) of their region.

Implications for clinical practice

In the present dissertation, we discussed the flexible use of the frailty approach. The general practitioner is pre-eminently the person that should/could use this flexible approach in practice. The general practitioner is the expert in context. He/she often knows the patient for many years, is aware of the living conditions of the patient, the social network, the physical and mental state of the person, and of all services and facilities of the municipality. Therefore, the general practitioner is, for instance, the person who is able to give advice whether a person is physically fit enough to undergo surgery and to indicate whether a person could rehabilitate better at home or in an institution. This could be beneficial for the health and recovery of the patient. Based on the evidence of the present dissertation, the general practitioner must be empowered to take this role as advisor for the specialist in the hospital and the patient.

Also, the risk factors for frailty (chapters 4 and 5) can be useful for the general practitioner. The knowledge of these risk factors enables the general practitioner to screen and act proactively for older adults meeting the criteria. This could facilitate healthy aging and aging (well) in place. To screen his/her patients, the general practitioner can make use of the Fried Phenotype criteria with replacement questions (chapter 3). This measurement is short and feasible to apply, which makes it possible to assess the patient's physical frailty level more often and in a larger population. Since the performance-based tests have been replaced, the general practitioner can also assess the patient's physical frailty level during home visits.

Overall conclusion

Overall, this dissertation provides evidence that: (1) different frailty approaches measure only partly the same 'frailty construct'. Therefore, it has become clear that the difference in approach has a major impact on the composition of 'the frail sample' and its characteristics; (2) risk factors/profiles can have an added value in the detection of frail older adults and the importance of previous life events for the development of frailty in later life; (3) interventions might not be protective against the included adverse outcomes of frailty and show the importance of context in studies. Based on the evidence of the present dissertation, researchers should be more aware of the shortcomings in the present research, especially in researching complex interventions. Important questions such as why (or more importantly, why not) did the intervention work, in which context or subgroup did the intervention work, etc., could give important insights into the mechanisms of a complex intervention.

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Summary

In the European Union (EU-28), at the beginning of the year 2018, the percentage of people being 65 years and older was 19.7%. Demographic studies indicate that this number will increase to approximately 30% in the year 2060. Consequently, the number of frail older adults with high needs of care and support is expected to increase.

Frailty is an emerging concept, and no agreement exists about its definition. In general, two approaches of the frailty concept are described. The first, a unidimensional approach often designated as physical frailty, emphasizes frailty as a biological/medical concept, defined as: "A medical syndrome with multiple causes and contributors that is characterized by diminished strength, endurance, and reduced physiologic function that increases an individual's vulnerability for developing increased dependency and/or death". The second approach focuses on frailty from a multidimensional perspective. In addition to physical features, this perspective emphasizes cognitive, social, and psychological factors as well. Consequently, many instruments for identifying frail older adults have been developed. Studies show that the different methods to conceptualize and operationalize frailty result in widely differing prevalence figures of frailty. According to a systematic review, the prevalence of frailty in older adults ranges from 4.0% to 59.1%. Ntanasi et al. (2020) compared five frailty scales whereby the prevalence ranged from 4.1% up to 30.2%, but less than 1% was frail according to all scales. Depending on the used frailty scale the characteristics of the 'frail sample' showed important differences. For instance, 50% of the 'frail sample' according to the 'Fried Phenotype' was 80 years and over, while this was only 20.1% of the frail older persons as assessed according to the 'Groningen Frailty Indicator' (GFI). Therefore, one can assume that the choice for a particular frailty measurement in a study, could also have a strong impact on its outcomes. Research shows that frailty is associated with adverse outcomes such as mortality, institutionalization, and hospitalization. Some authors assume that early detection and intervention are important to prevent or delay frailty, improve quality of life, and reduce costs of care. Nevertheless, it is unclear if interventions in frail community-dwelling older adults can be protective against adverse frailty outcomes. There is evidence that frailty in an early state may be reversible. However, the evidence for reversibility of frailty in a later stage

is rather limited. Critics argue the methodological approaches to assess the effect of interventions, which fail to address the interaction of intervention components with each other and with the local context.

Therefore, the objectives of this dissertation are threefold: (1) to study how unidimensional and multidimensional frailty assessments are related with each other; (2) to study strategies which enable early detection and a proactive approach of frailty in older persons; and (3) to expand our knowledge with regard to the aspects that should be taken into account when doing a complex intervention study.

Chapter 1 provides information about the epidemiological situation and expectations regarding frailty in the future. We discuss also the main topics of the present dissertation: the concept of frailty and its many operationalizations, the importance of early detection and a proactive approach of frailty, and complex interventions. The chapter ends with the main objectives and the outline of this dissertation.

During the past decades, many frailty scales have been developed, although it is unknown how these frailty scales are related to each other. Therefore, in **chapter 2** a cross-sectional study was conducted among 196 community-dwelling older adults (≥60 years). Unidimensional frailty was operationalized according to the Fried Phenotype and multidimensional frailty was measured with the Comprehensive Frailty Assessment Instrument (CFAI). The results of the study showed that the Fried Phenotype Criteria and the CFAI measure partly the same 'frailty concept'. The moderate association between both measurements was attributed to by the physical domain of the CFAI, and (to a lesser extent) by the psychological domain. The social domain and environmental domains of the CFAI were not related with the Fried Phenotype. Differences were found in the prevalence of frailty, the composition of the 'frail participants' and their characteristics. Participants who were solely frail according to the CFAI had a lower level of life satisfaction and net income, but were physically more active. Since 'being frail' is an inclusion criterion in many studies, researchers must be aware that the choice of a frailty measurement has an impact on both the estimates of frailty prevalence and the characteristics of the selected sample.

To screen large populations on frailty, a short and feasible measurement is needed. Therefore, performance-based tests are often replaced by self-report questions. In **chapter 3** the

psychometric properties of a set of questions replacing the performance-based measures slowness and weakness as part of the Fried Phenotype were tested in community-dwelling older adults (N = 196). We observed that the concordance between the Fried Phenotype including the 6 replacement questions and the Fried Phenotype including the 2 performance-based measures is substantial. The replacement questions have the ability to correctly identify those without physical frailty, whereas their ability to correctly identify those with physical frailty seems to be less adequate. The concordance between the Fried Phenotype performance-based measures (slowness and weakness) and the set of replacement questions at item level was fair. Therefore, one might consider the scale with the replacement questions as a step in a sequential process to detect frailty in large populations.

In **chapter 4** we validated a set of risk factors of frailty. The results indicated an increase in the percentage of older adults who were mildly and highly frail from a physical, psychological, social, and environmental perspective. Therewith, the odds of identifying people who were mildly or highly frail were higher if one screens people who met at least three risk factors. According to the results in chapter 4, selecting older people based on these risk factors is an effective strategy of identifying frail older people.

In chapter 5 and chapter 6 we focused on the transition into retirement. Retirement can be accompanied by opportunities (e.g., extra leisure, healthier lifestyle) as well as by adverse events (e.g., loss of income, loss of social support). A better understanding whether this transition into retirement is related with frailty in later life and in which specific circumstances, can be insightful to develop a proactive approach against frailty; since the transition into retirement occurs in an earlier phase in life, in which most people are not (yet) frail. So far, only a few studies focused on retirement and its relation with frailty. Therefore, a cross-sectional study was performed. Based on chapter 5 and 6, one can conclude that *when* a person retires is not important, but *why* someone retires is important for frailty in later life.

Previous studies have shown that frailty is associated with adverse (health) outcomes. Since frailty is seen as dynamic, many interventions are done to prevent or delay frailty. Nevertheless, it is still largely unclear if interventions in frail community-dwelling older adults can be protective against adverse frailty outcomes. In **chapter 7,** we present the results of a systematic review and meta-analysis in which we assessed the effect of interventions in frail community-dwelling older adults in terms of mortality, hospitalization, formal health costs,

accidental falls, and institutionalization. In total, 16 studies were included. Two included studies described a significant effect. In a study of Hall et al. (1992), the intervention of case management resulted in a lower institutionalization rate. Perttila et al. (2016) performed a study with a physical intervention, which resulted in a lower number of accidental falls. However, based on the results of the meta-analysis no significant results were found for the observed adverse outcomes. A sub-analysis for some variables yielded no significant effects as well. In the present study no evidence was found that interventions might be protective against the included adverse outcomes of frailty.

Based on the interpretation of this literature review we recognized the need of more emphasis on the context and setting in which an intervention is implemented. Therefore, the aim of **chapter 8** was to assess whether it is feasible to make an in-depth study of the local context and how this should be done. This resulted in a 5-step approach, which we applied on the three municipalities (Ghent, Knokke-Heist and Thienen) participating in the D-SCOPE trial. Based on the explorative case study one can conclude: 1) a large amount of standardized data (contextual factors) is accessible on public web-based datasets; 2) it is very feasible to get an in-depth analysis of a local setting in order to get a better understanding of the effect of an intervention and the mechanisms related to the intervention.

Chapter 9 summarizes and discusses the main findings. In addition, implications for clinical practice and future research are given.

Overall this dissertation provides evidence that (1) different frailty approaches measure only partly the same 'frailty concept'. Thereby it has become clear that the difference in approach has a major impact on the composition of 'the frail sample' and its characteristics. (2) Risk factors/profiles can have an added value in the detection of frail older adults and the importance of previous life events for the development of frailty in later life. (3) Interventions might not be protective against the included adverse outcomes of frailty and show the importance of context in studies. Based on the evidence of the present dissertation, researchers should be more aware of the shortcomings in present research, especially in researching complex interventions. Important questions such as why (or more important why not) did the intervention work and in which context or subgroup did the intervention work, could give important insights in the mechanisms of a complex intervention.

Samenvatting

In de Europese Unie (EU-28) bedroeg het percentage mensen van 65 jaar en ouder in het jaar 2018 19.7%. Demografische studies wijzen uit dat dit aantal zal stijgen tot ongeveer 30% in 2060. Bijgevolg wordt verwacht dat het aantal kwetsbare ouderen met behoefte aan zorg en ondersteuning de komende jaren zal toenemen.

In de wetenschappelijke literatuur bestaat er geen consensus over het concept 'frailty' (kwetsbaarheid). Er zijn in feite twee benaderingen van het begrip 'frailty'. De eerste is de unidimensionale, ook aangeduid als fysieke frailty. Deze benadert frailty als een biologisch/medisch concept, gedefinieerd als: "Een medisch syndroom met meerdere oorzaken dat wordt gekenmerkt door verminderde kracht, gedaald uithoudingsvermogen en een afname van het fysiologisch functioneren welke tot gevolg kan hebben dat een individu afhankelijk wordt en/of komt te overlijden". De tweede benadering bekijkt frailty vanuit een multidimensionaal perspectief. Naast fysieke kenmerken, voegt deze benadering ook cognitieve, sociale en psychologische factoren toe. In de afgelopen decennia zijn derhalve tal van frailty-meetschalen ontwikkeld om kwetsbare ouderen te identificeren. Studies tonen aan dat de verschillende methoden om frailty te conceptualiseren en te operationaliseren, resulteren in sterk uiteenlopende prevalentiecijfers. Volgens een literatuurstudie varieert de prevalentie van frailty bij ouderen van 4.0% tot 59.1%. Ntanasi et al. (2020) vergeleken vijf frailty-meetschalen waarbij de prevalentie varieerde van 4.1% tot 30.2%, daarbij was minder dan 1% van de ouderen fragiel volgens alle meetschalen. Een diepgaandere analyse wees uit dat 50% van de ouderen die fragiel waren volgens de 'Fried Criteria', 80 jaar en ouder waren, terwijl dit slechts 20.1% was volgens de 'Groningen Frailty Indicator' (GFI). Daarom kan men vermoeden dat de keuze voor een bepaalde frailty-meetschaal in een studie, een sterke invloed kan hebben op de resultaten.

Onderzoek toont aan dat frailty gekoppeld is aan sterfte, institutionalisering en ziekenhuisopname. Onderzoekers gaan ervan uit dat vroegtijdige detectie en interventie belangrijk zijn om frailty te voorkomen of te vertragen, de kwaliteit van leven te verbeteren en de kosten van de zorg te verminderen. Desondanks is het onduidelijk of interventies bij fragiele thuiswonende ouderen wel protectief zijn tegen deze ongunstige uitkomsten. Er zijn

aanwijzingen dat frailty in een vroeg stadium nog omkeerbaar kan zijn. Het bewijs voor omkeerbaarheid in een later stadium is echter vrij beperkt. De methodologische aanpak om het effect van deze interventies te beoordelen wordt door onderzoekers bekritiseerd. Zo wordt onder meer gesteld dat de huidige manier van effectonderzoek te weinig/geen rekening houdt met de (lokale) context van de interventie.

Daarom zijn de doelstellingen van dit proefschrift drieledig: (1) bestuderen hoe unidimensionale en multidimensionale frailty-meetschalen zich tot elkaar verhouden; (2) bestuderen van strategieën die vroegtijdige detectie en een pro-actieve benadering van frailty bij ouderen mogelijk maken; en (3) onze kennis met betrekking tot het evalueren van (complexe) interventies uitbreiden.

Hoofdstuk 1 geeft informatie over de epidemiologie en de verwachtingen ten aanzien van frailty in de toekomst. Ook worden de belangrijkste concepten van het proefschrift besproken, met name: het concept frailty en de vele operationaliseringen ervan, het belang van vroegtijdige detectie en een pro-actieve benadering van frailty én ook de complexe interventies. Het hoofdstuk eindigt met de belangrijkste doelstellingen en een schets van dit proefschrift.

In de afgelopen decennia zijn tal van frailty-meetschalen ontwikkeld, maar het is onbekend hoe deze frailty-schalen zich tot elkaar verhouden. Daarom wordt in hoofdstuk 2 een cross-sectionele studie uitgevoerd bij 196 thuiswonende ouderen (≥60 jaar). De unidimensionale benadering werd geoperationaliseerd a.h.v het Fried fenotype en de multidimensionale benadering door middel van het Comprehensive Frailty Assessment Instrument (CFAI). De resultaten van de studie tonen aan dat het Fried fenotype en de CFAI gedeeltelijk hetzelfde ‘frailty concept’ meten. De associatie tussen beide metingen kan toegeschreven worden aan het fysieke domein van de CFAI en (in mindere mate) aan het psychologische domein. Het sociale domein en het omgevingsdomein van de CFAI waren niet gerelateerd aan het Fried fenotype. Er werden verschillen gevonden in de prevalentie van frailty, de samenstelling van de 'fragiele deelnemers' en hun karakteristieken. Deelnemers die uitsluitend volgens de CFAI 'fragiel' waren, hadden een lager niveau van levenstevredenheid en netto-inkomen, maar waren lichamelijk actiever. Aangezien ‘frailty’ in veel studies een inclusiecriterium is, moeten onderzoekers zich er dus bewust van zijn dat de methode om frailty te operationaliseren

impact heeft op zowel de prevalentie van frailty, de samenstelling van de fragiele groep alsook op de karakteristieken van de geselecteerde steekproef.

Om op grote schaal ouderen te kunnen screenen op frailty, is een kort en makkelijk frailty-instrument nodig. Daarom worden fysieke testen vaak vervangen door vragen. In hoofdstuk 3 wordt onderzocht hoe goed 6 vragen de 2 fysieke testen (polskracht en wandelsnelheid) van het Fried fenotype kunnen vervangen. Dit onderzoek werd uitgevoerd bij thuiswonende ouderen(N=196). We observeerden dat de overlap tussen de fysieke testen (itemniveau) en de vervangende vragen redelijk is. De overlap tussen het Fried fenotype met de 6 vervangende vragen en het Fried fenotype met de 2 fysieke testen was substantieel. De vervangende vragen hebben het vermogen om mensen die niet fysiek fragiel zijn, correct te identificeren, terwijl hun vermogen om mensen die wel fysieke fragiel zijn, minder goed lijkt te zijn. Het Fried Fenotype met vervangende vragen voor de fysieke testen zou gebruikt kunnen worden als een eerste evaluatie om frailty te screenen.

In hoofdstuk 4 hebben we een groep risicofactoren, ontwikkeld door Dury et al. (2017), voor frailty gevalideerd. De resultaten wezen op een toename van het aantal ouderen die respectievelijk licht en zeer fragiel waren. Deze toename werd gevonden op alle domeinen van de frailty-meetschaal (CFAI): fysiek, psychologisch, sociaal en omgeving. Volgens de resultaten in hoofdstuk 4 is het selecteren van ouderen op basis van deze risicofactoren een effectieve strategie om kwetsbare ouderen te identificeren.

In hoofdstuk 5 en hoofdstuk 6 wordt gefocust op de overgang van werken naar pensionering. Pensionering kan gepaard gaan met opportuniteiten (bv. extra vrije tijd, een gezondere levensstijl) maar kan ook nadelige gevolgen hebben (bv. verlies van inkomen, verlies van sociale steun). Een beter inzicht in de overgang van werken naar pensionering in relatie tot frailty op latere leeftijd, kan helpen bij het ontwikkelen van een proactieve aanpak van frailty. De overgang naar pensionering vindt namelijk veelal plaats op een moment waarop de meeste mensen (nog) niet fragiel zijn. Er werd een cross-sectionele studie uitgevoerd, op basis waarvan geconcludeerd kan worden dat, in het kader van frailty op latere leeftijd, het niet zozeer belangrijk is wanneer iemand met pensioen gaat, maar waarom iemand met pensioen gaat.

Eerdere studies hebben aangetoond dat frailty geassocieerd is met negatieve (gezondheids)uitkomsten. Omdat frailty in principe als dynamisch wordt beschouwd, worden interventies gedaan om frailty te voorkomen of het proces te vertragen. Desondanks is het nog grotendeels onduidelijk of interventies bij fragiele thuiswonende ouderen wel protectief werken tegen deze negatieve uitkomsten. In hoofdstuk 7 presenteren wij de resultaten van een literatuurstudie en meta-analyse waarin wij het effect van interventies bij kwetsbare, thuiswonende ouderen hebben onderzocht op het gebied van mortaliteit, ziekenhuisopname, gezondheidskosten, valincidenten, en institutionalisering. In totaal werden 16 studies geïncludeerd. Twee geïncludeerde studies beschreven een significant effect. Zo toonden Hall et al. (1992) aan dat casemanagement leidt tot een lagere institutionalisering; en Perttila et al. (2016) implementeerden een fysieke interventie, dit resulteerde in een lager aantal accidentele valincidenten. Op basis van de resultaten van de meta-analyse werden echter geen significante resultaten gevonden voor de geselecteerde uitkomstmaten. Een subanalyse voor sommige variabelen leverde ook geen significante effecten op. Kort samengevat: er werd geen bewijs gevonden dat interventies protectief zijn tegen de geselecteerde negatieve uitkomsten van frailty.

Op basis van de resultaten van deze meta-analyse concludeerden wij dat er meer aandacht gegeven moet worden aan de context en setting waarin een interventie wordt geïmplementeerd. Daarom was het doel van hoofdstuk 8 om na te gaan of het haalbaar is om een diepgaande studie te maken van de lokale context en hoe dit gedaan zou moeten worden. Dit resulteerde in een aanpak in 5 stappen. We pasten deze aanpak toe op de drie gemeenten die participeerden in de D-SCOPE-interventiestudie (Gent, Knokke-Heist en Tienen). Op basis van deze exploratieve casestudy konden we besluiten dat: 1) een grote hoeveelheid gestandaardiseerde gegevens (contextuele factoren) toegankelijk zijn voor het brede publiek; 2) het haalbaar is om een diepgaande analyse te maken van een lokale setting om tot een beter inzicht te komen van het effect van een interventie en de mechanismen die met de interventie samenhangen.

In hoofdstuk 9 worden de belangrijkste bevindingen van dit proefschrift samengevat en besproken. Daarnaast bespreken we ook de implicaties voor de klinische praktijk en toekomstig onderzoek. In het algemeen leren we van dit proefschrift dat verschillende frailty benaderingen slechts gedeeltelijk hetzelfde ‘frailty concept’ meten. Daarbij is duidelijk

geworden dat het verschil in benadering een grote impact kan hebben op het categoriseren van personen als fragiel of niet fragiel en de karakteristieken van deze groep. Ook leren we dat risicofactoren/-profielen een toegevoegde waarde kunnen hebben bij de opsporing van kwetsbare ouderen en t.a.v. het belang van belangrijke levensgebeurtenissen voor de ontwikkeling van frailty op latere leeftijd. Verder leren we dat interventies zeker niet altijd werken tegen de negatieve gezondheidsuitkomsten van frailty en dat derhalve met name de context in interventiestudies meer aandacht verdient. Bovendien is het best makkelijk om snel een diepgaande analyse te maken van de context.

Op basis van de resultaten uit dit proefschrift zouden onderzoekers zich meer bewust moeten zijn van de tekortkomingen in het huidige onderzoek, vooral bij onderzoek naar complexe interventies. Belangrijke vragen zoals waarom (of waarom niet) werkt een interventie en ook in welke context of groep werkt de interventie, worden zelden beantwoord, terwijl beantwoording ervan een beter inzicht zou kunnen geven in de werking van complexe interventies.

Impact

This dissertation describes studies that aimed: (1) to study how unidimensional and multidimensional frailty assessments are related to each other; (2) to study strategies that enable early detection and a proactive approach of frailty in older persons; and (3) to expand our knowledge with regard to aspects that should be taken into account when doing a complex intervention study in the frailty domain.

This chapter discusses (1) the scientific impact, new scientific views, new scientific approaches, and the dissemination of the study results; and (2) the societal impact for the public health sector and, in particular, for general practitioners and older people themselves.

Scientific impact

New scientific views

The worldwide aging of the population leads to increasing numbers of frail old people. In the past decades, frailty has therefore been of increasing interest to researchers and policy makers. Despite this attention, a clear conceptualization and definition of frailty is still lacking. From the present dissertation, we have learned that the choice of a frailty operationalization can have a large impact on both the estimates of frailty prevalence and the characteristics of the selected sample of older people (chapter 2). We argue that the choice for a specific conceptualization of frailty should depend on the aim and the context of the study. Therefore, we think that it is important and relevant to determine which frailty operationalization is recommendable for which aim and in which specific context. This flexible approach of frailty could be beneficial to optimize the effectiveness of interventions and might facilitate aging well in place.

In the field of frailty, the research mainly focuses on old people or even the oldest of the old. In chapter 5 of this thesis, the results show that the transition into retirement is related to frailty in later life. Consequently, one can conclude that frailty is an evolving process that starts in the younger years. Therefore, we plea to add the aspect of the life course in the frailty definition; this may trigger researchers to do research in adults at an earlier phase of life to prevent or delay frailty in later life.

New scientific approaches

In the literature, it is argued that some contexts are supportive for an intervention while others are not. Based on the results of the meta-analysis performed in chapter 7, we recognized the need for more emphasis on the context and setting in which an intervention is implemented. Current research often lacks a good description of the context. Therefore, we developed a 5-step approach (chapter 8) to get a better understanding of the context. This understanding can help future research with the clarification of the results.

During the course of the dissertation, methodological issues with regard to (complex) interventions were raised (chapter 7, the meta-analysis). Based on the evidence of the present dissertation, researchers should be more aware of the shortcomings in current research practice. Future research should not solely focus on the effect of an intervention but also address the questions: Why did interventions work or not work?; For whom did they work?; and What contextual factors triggered the mechanisms required to make them work? In the general discussion, we enlisted the aspects that future studies should take into consideration during the preparation of the study protocol: 1) operationalization of the required frailty approach, 2) motivation of why a particular frailty operationalization is used based on an aim and/or targeted population, 3) description of the context of a study, 4) awareness of unexpected effects an intervention can generate, and 5) awareness that results at the group-level cannot always be transferred towards the individual-level (ecological fallacies). By taking these aspects into account during the preparation of an intervention study, we will get a better understanding of the effect of interventions aiming to prevent or delay frailty.

Dissemination of study results

Findings of this dissertation have been disseminated in the past years in several ways. First, findings were presented during national and international conferences. They also have been disseminated among healthcare professionals who participated in the D-SCOPE project, for example, by organizing meetings and sending regular newsletters to healthcare professionals and participants in the project. Further information about the D-SCOPE project is available on the website (www.d-scope.be). In addition, most chapters have been published in scientific journals, of which most are freely available (open access).

Societal impact

Public sector

Many initiatives/interventions exist at local and national level to prevent frailty or to facilitate aging well in place. In chapter 2, the data showed that the choice of a specific frailty measurement has an impact on the selected sample and the characteristics of the sample. Therefore, the effectiveness of these initiatives as such may depend on the extent to which one succeeds in reaching the target group. To optimize the effect of these initiatives, prior to the start of an initiative/intervention, policy makers must clearly define the aim/outcome of the initiative and the targeted population and how they will reach the targeted population. Furthermore, the results in chapter 5 suggest that a transition from working life into retirement is associated with frailty in later life. This might imply that it could be beneficial to start interventions to prevent or delay frailty or to promote aging well in place already around the retirement phase. Policies aiming to prevent or improve frailty in old age should probably not start when an older adult is already frail or prefrail.

The present results show that a case-finding strategy based on risk factors could be additionally helpful in detecting frail older people. Hence, instead of screening the total population, a more targeted screening (case finding) based on risk profiles could be helpful for professionals in the community to detect/screen frail older people with an evidence-based strategy, which is more efficient. Since early detection is important with regard to the dynamic state of frailty, this might also imply that the efforts made by professionals (i.e., extra care and support) could be more effective.

In the present dissertation, extra attention is given to the context of an intervention, for which a five-step approach has been developed (chapter 8). The five-step approach can give an overview of the characteristics and care supply of these regions. Consequently, this approach can also be useful for governmental policies. In Flanders, for instance, the government created primary care regions (‘eerstelijnszones’). One of the main tasks of these primary care regions is to organize the coordination between care providers and stimulate interdisciplinary collaboration. Based on our five-step approach, each primary care region can get an overview of the specificities of their region. National data or data of other regions can be used as a

benchmark to identify the strengths, weaknesses, opportunities, and threats (SWOT) of their region.

This dissertation was part of the Detection, Support and Care for Older people: Prevention and Empowerment (D-SCOPE) project (www.d-scope.be), on behalf of which several activities were organized. The results from the D-SCOPE project were presented to healthcare professionals and policy makers in a large conference. Furthermore, reports and many scientific papers have been published.

General practitioners

In the present dissertation, we discussed the flexible use of the frailty approach. The general practitioner is pre-eminently the person that should/could use this flexible approach in practice. The general practitioner is the ultimate expert in context. He/she often knows the patient for many years and is aware of the living conditions of the patient, the social network, the physical and mental state of the person, but also of most supporting health and social services of the municipality. Therefore, the general practitioner is THE professional who is able to give advice on whether a person is physically frail or fit enough to undergo surgery and to indicate whether a person could rehabilitate at home or in an institution (context!). This might be beneficial for the health and recovery of the patient. Based on the evidence of the present dissertation, the general practitioner must be empowered to take this role.

Also, the risk factors for frailty (chapters 4, 5, and 6) can be useful for the general practitioner. The knowledge of these risk factors enables the general practitioner to screen and act proactively for older adults prone to these risk factors. This might also facilitate healthy aging and aging (well) in place. To screen his/her patients, the general practitioner can, for instance, use the Fried Phenotype criteria with replacement questions (chapter 3). This measurement is short and feasible to apply, which makes it possible to assess the patient's physical frailty level more often and in a larger population. Since the performance-based tests are replaced, the general practitioner can also assess the patient's physical frailty level during home visits.

Older adults

Finally, the main goal of the present dissertation is to contribute to an improved care for older adults by which a society can facilitate healthy aging and aging well in place. Based on the

present dissertation, we hope to reach this goal by providing a better understanding of how interventions work, for whom they work, and in which context they work.

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21 april 2015. Met een klein hartje stapte ik ’s ochtends in de auto op weg naar de eerste dag van mijn D-SCOPE avontuur. Aangekomen op het bureau dat ik de komende jaren zou gebruiken, werd ik overvallen door één gedachte: wat moet ik hier in godsnaam de hele dag doen? Ik ging onderzoek doen naar frailty, een concept dat ik helemaal niet kende als politicoloog en econoom. Met veel twijfel en onzekerheid zette ik de computer aan en begon ik te zoeken naar iets, zonder te weten naar wat. Laat staan dat ik een idee had van wat ik zou kunnen vinden! Hoe zou dit aflopen? Gelukkig zaten er twee leuke Nederlandse dames en een charismatische Nepalees aan hetzelfde bureau. Doch twijfel en onzekerheid waren troef de eerstkomende maanden. Maar geleidelijk aan begon zich een pad te ontwikkelen dat stap voor stap geleid heeft naar dit doctoraat. Een doctoraat dat niet tot stand was gekomen zonder de hulp van vele andere mensen:

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About the author

Michaël C.J. Van der Elst was born on May 6th, 1987 in Aalst (Oost-Vlaanderen, Flanders). In 2005 he completed secondary school at Sint-Aloysiuscollege in Ninove. He graduated as master in Political Sciences (2010) and master in economics (2013) at the University of Ghent (Flanders). In April 2015, he started working as a scientific researcher in the D-SCOPE project which aimed to enable community-dwelling (frail) older people to age in place with a good quality of life. In June 2019, he started his PhD trajectory at Maastricht University (department of Health Services Research) as external PhD student. Since July 2019, he is working at the university hospital of Leuven as scientific researcher in a HORIZON 2020 project called 'Palliative Sedation' (department Laboratory of Experimental Radiotherapy, KU Leuven). Alongside his work and PhD trajectory, he followed several statistical courses in preparation of a master in statistics.

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D-SCOPE

The present doctoral dissertation is written in the frame of the D-SCOPE project (Detection - Support, Care for Older People: Prevention and Empowerment). D-SCOPE is a four-year international research project, financed by the Flemish government agency for Innovation by Science and Technology [IWT-140027 Strategisch Basis Onderzoek (SBO)] (2015-2018). The D-SCOPE consortium is a multidisciplinary group composed of researchers from five universities/colleges: Maastricht University, Universiteit Antwerpen, Hogeschool Gent, KU Leuven and Vrije Universiteit Brussel. The focus of D-SCOPE has been the targeted detection of frail older adults in their local environment. The project contributes to the development of new methodologies for the prevention of frailty in older adults, so they can age in their own homes in good quality of life. The D-SCOPE project starts from a multidimensional perspective on frailty, including physical, cognitive, psychological, social and environmental frailty and focuses on positive outcomes like mastery, life satisfaction and meaning in life. In order to achieve this, the D-SCOPE project was divided in three research phases. In the first phase, risk profiles were determined through data from the Belgian Ageing Studies. In the second phase, balancing factors and life events were explored by means of 121 individual interviews with frail older people. The third and last phase consisted of a randomized controlled trial (RCT) in three municipalities (Ghent, Knokke-Heist and Thienen) among 869 older adults. The respondents in the experimental group received a home visit from a social worker of the municipality and were referred to tailored care and support when needed.