General introduction
CHAPTER 1

THE CHALLENGE OF FRAILTY

Western societies are ageing, a trend that is expected to continue in the next decades [1]. Within these ageing societies, the care for the growing number of frail older adults (e.g., with multiple chronic conditions and/or functional disabilities) is a major challenge for healthcare systems [2-4]. The Netherlands is one of the countries facing this challenge. In order to be able to respond to the care needs of the rising number of older people, and especially frail older people, the Dutch Ministry of Health, Welfare and Sport initiated the National Care for the Elderly Program. This program started in 2008 and funded several research and implementation projects aimed at developing a more proactive and integrated health care system for older adults [5]. The ultimate goal of the program is to improve the quality of life and other outcomes in, especially frail, older people and to give older people more control over their care process. The program promoted research in frail older populations across different health-care settings, carried out by research groups of all eight university medical centers in the Netherlands, and included both cohort studies and randomised trials. This thesis is written as part of a research project within the framework of the National Care for the Elderly Program [6]. In this General introduction we provide background information on the scope of this thesis, followed by the research objectives and a thesis outline.

FRAILTY

Frailty is considered a relevant concept for both public health and clinical practice [7-11], which is used across different healthcare settings such as primary care and hospitals [12, 13]. In the past decades, various attempts have been made to define frailty [14-21]. Frailty is considered to be distinct from, but at the same time overlapping with, both comorbidity and functional disability [22]. Although there is still no generally accepted definition, there are three elements that all frailty definitions have in common:

1) Frailty is a geriatric syndrome associated with an increased risk of adverse health outcomes, such as functional decline, hospitalisation 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.
The loss of reserve capacity may be only physical or in multiple domains (physical, psychological, social) [4, 15, 23]. The choice of a single or a multi-dimensional approach depends on the purpose of an intervention in health care settings or the scope of a study. The physical definition is most widely used, and includes components such as loss of weight and muscle strength, exhaustion, reduced gait speed and reduced physical activity [16]. There is more or less international consensus on which components should be part of the physical frailty definition [15]. The multi-dimensional definition also includes psychological and social components, such as mood, personality characteristics, social support and social isolation [23-25]. However, there is still a debate on which components should be involved in the broader definition of frailty. One of the points of discussion is whether cognition should be included [26-28]. In the studies reported in this thesis, we use both the physical and the multi-dimensional definition of frailty, depending on the purpose of the particular study.

RESEARCH ON FRAILTY

The research field on frailty in older adults has rapidly increased in recent years. Figure 1 shows the number of published articles mentioned in PubMed, with “frailty” in the abstract. In 2004, 128 articles were published on this topic, which increased to more than 800 in 2014. This increase may even be sharper than the figure shows, because 10 years ago there was not a clear distinction between the concept of frailty and other concepts in geriatrics.

Figure 1. Number of articles published on frailty in the past 10 years (based on PubMed)
such as disability. The research on frailty can be divided in three main categories: studies
on the epidemiology of frailty, studies on instruments to measure frailty and studies on
interventions for frail older adults. In this thesis we contribute to each of these categories.

EPIDEMIOLOGY

In a recent systematic review it was estimated that between 4% and 59% of the population
aged 65 and over is considered to be frail [29]. The large variation in this estimation is the re-
sult of the different frailty definitions and the sampling procedures of the included studies.
Nevertheless, this would mean that in the Netherlands between 0.1 and 1.3 million older
adults are frail [30]. Various demographic and health-related factors are associated with
physical frailty, such as educational level, sex, social support, wellbeing, disability, chronic
diseases, biomarkers (e.g., inflammatory markers) and lifestyle [8, 31-41]. Many of the studies
on frailty determinants were cross-sectional, therefore it is difficult to draw conclusions on
the direction of associations between frailty and health-related factors. However, it is well
established that frailty (both the physical and the multi-dimensional definition) predicts
adverse health outcomes, such as functional decline, incident depression, falls, mortality,
and increased healthcare use such as hospitalisations and admission to nursing homes [16,
42-48]. This has been shown in many different settings and countries [13, 49-52].

Despite the large number of frailty studies, there is still a lot unknown about the epide-
miology of frailty. There are not many longitudinal studies on frailty with more than two
time points. Therefore, there is not much information available on changes over time in
frailty. In addition, risk factors for frailty, such as demographic and health-related factors
[24], have not been investigated extensively. Also, research on factors that may prevent or
delay adverse outcomes in frail older adults is lacking.

ASSESSMENT INSTRUMENTS

There are many instruments available to identify frail older adults. A lack of a universal
consensus on the definition of frailty, has resulted in the development of numerous instru-
ments. Examples are the FRAIL questionnaire, the Tilburg Frailty Indicator, the Groningen
Frailty Indicator, the Gerontopole Frailty Screening Tool, the PRISMA-7 questionnaire and
various instruments based on single markers such as gait speed [42, 53-58]. The instru-
ments differ by frailty definition (physical or multi-dimensional), purpose (frailty screening
or observation of changes in frailty), content (variable or fixed) and the target population (e.g., general population, primary care). Also, the sources of information may differ, such as clinical tests, questionnaires, data collected in routine care or observations by healthcare professionals [59-61]. Despite the large number of newly developed instruments, two well-validated instruments are most often used: Fried’s frailty phenotype and Rockwood’s Frailty Index (FI) [16, 22, 62, 63]. The frailty phenotype consists of five pre-defined criteria (weight loss, exhaustion, slowness, poor grip strength, and low physical activity), based on both clinical tests and questionnaires. The instrument distinguishes between three different states, based on the number of criteria present in a person: non-frail, pre-frail and frail [16]. The FI counts deficits in health, such as diseases, disabilities and symptoms. The FI is a continuous score ranging between 0 and 1, and indicates the proportion of deficits present [64]. The FI can be based on questionnaires, clinical tests, or can be generated from routine care data [65-67]. Figure 2 shows a classification system for frailty instruments based on frailty definition and content, and some examples of frailty instruments.

Most frailty instruments are validated in research cohorts. However, how these instruments should be used in clinical practice is not always clear. Many instruments are time-consuming or too difficult to apply in health-care settings. Although some studies were conducted on simple frailty instruments for clinical practice [55, 68, 69], there is still much unknown on which instruments are most suitable for the identification of frail older adults in health-care settings, such as primary care [70].

Figure 2. Classification of frailty instruments
INTERVENTIONS

Given the high number of frail older adults in the community and the severe consequences frailty may have, it is important to develop interventions. Frailty interventions may be focused on preventing frailty, on reducing the severity of frailty, or on preventing or delaying adverse outcomes in frail older adults. So far, there is not much evidence for the prevention of frailty. This is not surprising, because it requires insight into the pathophysiology of frailty, which is still largely unknown [3, 4]. There may be some effective interventions for reducing the severity of frailty, such as physical exercise, nutrient supplementation and reducing polypharmacy [71-75]. However, the majority of the interventions aim to prevent or delay adverse outcomes, such as disability [76].

Most interventions focused on frail older adults are provided in primary care settings, because in many countries general practitioners have a central position in the care for older adults [77]. This is also in line with the "ageing in place" principle, which is preferred by older people: independent living at home, as long as possible [78]. Interventions to improve community care for frail older adults are most of the time delivered in the form of comprehensive care programs. Comprehensive community care was often disease-oriented, but it is nowadays shifting to a more integrated approach [79]. Many variations of comprehensive care programs exist, but they usually include patient-centered care based on comprehensive geriatric assessments. Care needs of frail older adults are assessed, followed by tailor-made care and interventions, often described in a care plan. Care needs may be assessed by performing a comprehensive geriatric assessment by a healthcare professional (e.g., by a practice nurse) [80] or by assessing the self-perceived needs of frail older adults [81, 82]. Generally, comprehensive care programs cover a broad range of interventions for specific goals, such as preventing functional decline or malnutrition [83, 84].

In the past decades, much research has been conducted on the effectiveness of comprehensive care programs. These studies show mixed results, effects are often small, and the outcomes on which effects are found vary across studies [85]. There are still research gaps with regard to the effectiveness of comprehensive community care for frail older adults. First, it has been suggested that comprehensive care programs for frail older adults should be modelled after the Chronic Care Model (CCM) [86, 87]. Interventions following a CCM approach found beneficial effects on quality of care and patient outcomes in other settings, and in patients with specific chronic conditions [88-90]. Second, there is a lack of effectiveness studies combining different types of evaluations. Not only effect evaluations are important. Economic and process evaluations can provide additional insights, and may be linked to the results of the effect evaluation [91, 92].
THE CURRENT STUDY

This thesis on frailty in older adults contains studies on topics relevant for public health and clinical practice, covering three main research areas: risk factors, assessment instruments and comprehensive community care. We performed several studies to enhance our understanding of risk factors for frailty and frailty outcomes, to increase our insights into the accuracy of frailty assessment instruments, and to gain more insight into the care needs of frail older adults. In addition, we evaluated the effectiveness of the Geriatric Care Model, a comprehensive care program for frail older adults in primary care. Various datasets from different settings were used to perform these studies (Table 1), which are described below.

Table 1. Datasets used in this thesis

<table>
<thead>
<tr>
<th>Dataset</th>
<th>Setting</th>
<th>Country</th>
<th>Thesis part</th>
<th>Chapter</th>
</tr>
</thead>
<tbody>
<tr>
<td>LASA</td>
<td>Population based sample</td>
<td>The Netherlands</td>
<td>Risk factors</td>
<td>Chapters 2, 3</td>
</tr>
<tr>
<td>GEMU</td>
<td>Hospital (sub-acute care)</td>
<td>Australia</td>
<td>Risk factors</td>
<td>Chapter 4</td>
</tr>
<tr>
<td>IKO</td>
<td>Primary care</td>
<td>The Netherlands</td>
<td>Assessment instruments</td>
<td>Chapter 5</td>
</tr>
<tr>
<td>ACT</td>
<td>Primary care</td>
<td>The Netherlands</td>
<td>Comprehensive community care</td>
<td>Chapters 6, 7, 8</td>
</tr>
</tbody>
</table>

**Longitudinal Aging Study Amsterdam (LASA)**

LASA is a large population based cohort study on physical, emotional, cognitive, and social functioning of older adults in the Netherlands [93]. LASA is a nationally representative study, and started in 1992-93 with 3107 respondents aged 55 to 85 (birth years 1908-1937). Every 10 years, a new cohort was added to the study (e.g., 1002 persons were added in 2002-03 from the birth years 1938-1947). LASA is still ongoing, and has follow-up measurements every three to four years. The data collection of LASA covers various domains of functioning, and consists of questionnaires, clinical tests and blood samples.

**Geriatric Evaluation and Management Unit (GEMU)**

This is a prospective, observational study of patients aged 70 years and over recruited from a geriatric sub-acute care unit at The Queen Elizabeth Hospital in Adelaide, South Australia [13]. From 172 patients, data on various demographic and health-related characteristics were collected from October 2010 to December 2011. Outcomes, such as mortality were assessed at 6 and 12 months after the baseline measurement.
Identification of Frail Elderly study (IKO)
The IKO study is a cross-sectional pilot study on the identification of frail older adults in primary care [94], and consists of 102 patients from a primary care practice in Amsterdam, the Netherlands. The data were collected from October 2009 to December 2009, and contained demographic and health measures (including a comprehensive geriatric assessment), and the assessment of various frailty instruments.

Frail older Adults: Care in Transition study (ACT)
The ACT study [6] is a 24-month stepped wedge cluster randomised controlled trial designed to evaluate the Geriatric Care Model, a comprehensive care program for frail older adults in primary care. The study took place between May 2010 and March 2013. Participants (1147 frail older adults aged 65 and over) were recruited through 35 primary care practices in the northwest of the Netherlands, and were followed for 2 years. During that period the intervention started, and every six months follow-up measurements were collected. The study consists of five measurements: the baseline and 4 follow-up measurements at 6, 12, 18 and 24 months. The collected data include a broad range of measures, such as demographic characteristics, quality of life, health, disability, morbidity, care needs and use of health care services.

OBJECTIVES AND OUTLINE OF THIS THESIS

The objectives of this thesis are:

Risk factors
1. To investigate explanations for the association between educational level and frailty in older adults (Chapter 2)
2. To investigate the role of psychosocial resources as risk factors for adverse outcomes in frail older adults (Chapters 3 and 4)

Assessment instruments
3. To compare the accuracy of simple instruments to identify frail older adults in primary care (Chapter 5)

Comprehensive community care
4. To provide insight into the care needs of frail older adults in primary care (Chapter 7)
5. To evaluate the impact of the Geriatric Care Model on quality of life and other patient outcomes in frail older adults in primary care, by performing a stepped wedge cluster randomised controlled trial (Chapters 6 and 8)
In Chapter 2, we examine the longitudinal association between educational level and frailty in older adults over a period of 13 years, and we investigate the role of material, biomedical, behavioural, social and mental factors in explaining this association.

In Chapters 3 and 4 we focus on the role of psychosocial factors as risk factors for adverse outcomes in frail older adults. In Chapter 3, we investigate whether psychosocial resources modify the effects of frailty on functional decline and mortality, by using data over 3 years from a population based study. In Chapter 4, we examine the association between psychosocial factors and frailty in the hospital setting, and the extent to which psychosocial factors modify the associations between frailty and several adverse outcomes.

In Chapter 5, in a cross-sectional study we compare the accuracy of five simple instruments to identify frail older adults in primary care.

In Chapter 6, we describe the study design of the ACT study, which is a stepped wedge cluster randomised trial on the effectiveness of the Geriatric Care Model, a comprehensive care program for frail older adults in primary care.

In Chapter 7, we focus on the met and unmet care needs of frail older adults in primary care, and examine cross-sectional associations of care needs with socio-demographic and health-related characteristics.

In Chapter 8, we investigate the effects of the Geriatric Care Model on the quality of life and other outcomes of frail older adults in primary care, in a 24-month stepped wedge cluster randomised trial.

Finally, in Chapter 9 we provide a general discussion of this thesis: we summarise the main findings and reflect on these findings, discuss methodological limitations, and elaborate on the implications for clinical practice and future research.
REFERENCES

21. Gobbens RJJ, Luijckx KG, Wijnen-Sponselee MT, Schols JMGA. In search of an integral


41. Strandberg TE, Stenholm S, Strandberg AY, Salomaa VV, Pitkala KH, Tilvis RS. The 'obesity


61. de Vries NM, Staal JB, van Ravensberg CD, Hobbelen JSM, Olde Rikkert MGM, Nijhuis-van der Sanden MWG. Outcome instruments to


81. Peters LL, Boter H, Slaets JPJ, Buskens E. Development and measurement properties of


