General discussion
In this thesis on frailty in older adults, we describe several studies, which we have performed to gain more insight into risk factors for frailty and frailty outcomes. In particular, we studied the role of educational level (Chapter 2) and psychosocial resources (Chapters 3 and 4). Furthermore, we present studies on the accuracy of instruments to identify frailty in primary care (Chapter 5), and on the self-perceived care needs of frail older adults in primary care (Chapter 7). In addition, we present a study on the effectiveness of the Geriatric Care Model, a comprehensive care program based on the Chronic Care Model, for frail older adults in primary care (Chapters 6 and 8). To perform these studies, we used different types of datasets from various settings and countries (type: cross-sectional, longitudinal and randomised trial data; settings: population based, primary care and hospital; countries: the Netherlands and Australia). In this chapter, we give an overview of the main findings from Chapters 2 to 8, and we discuss our findings in the context current scientific literature. Next, we will discuss some conceptual and methodological issues. Finally, we will provide implications for clinical practice and directions for future research.

MAIN FINDINGS

Risk factors: educational level

It is well established that frailty affects some groups in the older population more than others. An important risk factor for frailty is educational level [1]. In Chapter 2, using data from the Longitudinal Aging Study Amsterdam (LASA), we examined the longitudinal association between educational level and frailty in older adults, and we investigated to what extent this association was explained by material, biomedical, behavioural, social and mental factors. We found that older adults (aged 65 and over) with a low educational level were more often frail compared to those with a high educational level, and that these differences remained during 13 years of follow-up. We confirmed findings from previous cross-sectional studies on the association between educational level and frailty [2, 3]. However, we also added to previous studies by investigating the educational gradient in frailty over an extended period of time. We showed that the overall frailty prevalence increased over time, but that the rate of increase did not vary across educational levels. In addition
to examining the longitudinal association between educational level and frailty, we also attempted to explain this association. By using a broad range of (time-varying) explanatory factors we were able to explain 76% of the longitudinal association between educational level and frailty. Our results showed that all factors, except social factors, contributed to the explanation. Individual factors that contributed most to the explanation were income, self-efficacy, cognitive functioning, obesity and chronic diseases. These results show that a multidimensional approach is needed for developing interventions aimed at reducing differences in frailty between groups with different educational levels.

As far as we know this was the first study focused on explanations for differences in frailty prevalence among groups with different educational levels. Therefore it is not possible to directly compare our results with other studies. Recently, a study was published on explanations for frailty worsening in 11 European countries [4]. This study found that lifestyle, health and social participation partly explained the association between educational level and frailty worsening. The explanatory power of the included factors was much lower than in our study, because in full model analyses only 5% to 31% (depending on the country) of the effect of educational level on frailty worsening was explained. Furthermore, this study [4] only included data over a period of 2 years, did not include biomarkers and detailed psychosocial factors, and was not based on time-varying explanatory factors.

**Risk factors: psychosocial resources**

So far, little is known about factors that may prevent or delay adverse outcomes in frail older adults. In **Chapters 3 and 4**, we focused on an important group of factors that may modify the pathways from frailty to adverse outcomes: the psychosocial resources of an individual. In **Chapter 3**, we investigated whether psychosocial resources modify the effects of frailty on functional decline and mortality. For that purpose, we used data of older adults aged 58 and above from LASA over a period of three years. Psychosocial resources in this study included sense of mastery, self-efficacy, instrumental support and emotional support. The results of this study showed that frail older adults had increased odds of both functional decline and mortality over a 3-year period. Higher levels of mastery and self-efficacy were associated with decreased odds of functional decline, but not mortality. However, we did not find evidence for the modifying role of psychosocial resources on frailty outcomes, because there were no statistical significant interaction effects between psychosocial resources and frailty on functional decline and mortality. In **Chapter 4**, we performed a similar study in a sample of hospital patients in sub-acute care. We investigated the association between psychosocial resources and frailty, and to what extent psychosocial factors modify the association between frailty and adverse outcomes. The adverse outcomes in this study
were 12-month mortality, long length of hospital stay, 1-month emergency rehospitalisation and discharge to a higher level of care. Data were used from patients aged 70 and over admitted to a Geriatric Evaluation and Management Unit (GEMU) in Australia. Psychosocial factors included wellbeing, sense of mastery, social activities, neighbourhood satisfaction, social relationships, anxiety and depression. Our results indicated that frail older adults in the hospital had elevated risks of all adverse outcomes compared to non-frail frail older adults. We found that poor wellbeing, anxiety, depression and low sense of mastery were associated with frailty, and that psychosocial resources impact the association between frailty and adverse outcomes. We found an interaction effect between frailty and sense of mastery for all adverse outcomes. In addition, interaction effects between frailty and respectively anxiety, wellbeing, social activities and neighbourhood satisfaction were observed for one or more of the adverse outcomes.

The studies performed in Chapters 3 and 4 are, as far as we know, the first studies focused on the modifying role of psychosocial resources on frailty outcomes. Previous research indicated that psychosocial resources may play a modifying role in the disablement process [5], but no study has examined this in relation to frailty in older adults. Our studies showed that psychosocial resources modify the effects of frailty on adverse outcomes in a hospital population, but not in a general older population. The findings of our two studies seem contradictory. However, sometimes mechanisms may not work for a whole group, but only for specific subgroups [6]. Our results suggest that although in a population based sample psychosocial resources do not seem to buffer against adverse health outcomes in frail older adults, they may still be effective in buffering against adverse outcomes in frail older adults in specific care settings.

**Assessment instruments**

In Chapter 5, we tested the accuracy of five simple instruments to identify frail older adults in primary care. Data were used from the Identification of Frail Elderly Study (IKO), a cross-sectional pilot study among 102 patients aged 65 and over from a primary care practice in the Netherlands. Five simple instruments (clinical judgement of the GP, polypharmacy (i.e., 5 or more medications), the Groningen Frailty Indicator, the PRISMA-7 questionnaire and self-rated health) were compared with two reference standards: frailty according to Fried’s frailty criteria and on the basis of clinical judgement by a multidisciplinary expert panel. From the five simple instruments compared in this study, the PRISMA-7 questionnaire had the best accuracy. This study is one of the first to compare several instruments to identify frailty in primary care. There is increasing attention for frailty identification in primary care [7], but most studies are focused on the validation of one instrument instead of comparing...
several instruments [8]. For example, a recently published study was focused on validating a frailty indicator extracted from electronic medical records, which is another simple method to identify frail older adults [9].

Comprehensive community care

The Frail older Adults: Care in Transition study (ACT) is a 24-month stepped wedge randomised controlled trial, in which we implemented a comprehensive care program, the Geriatric Care Model, for frail older adults aged 65 and over in 35 primary care practices in the Netherlands. The Geriatric Care Model is based on the Chronic Care Model [10], and aims to optimise quality and efficiency of care for frail older adults, and subsequently improve patient outcomes. The Geriatric Care Model is designed to target health risks at a timely stage, to stimulate active involvement of patients in the care process, and to improve the coordination between healthcare professionals, to optimise task division between professionals. It combines person centered care based on geriatric assessments with management by geriatric expert teams.

In Chapter 6, we described the design of the ACT study. It should be noted that in this thesis only the effectiveness of the Geriatric Care Model is reported. The economic and process evaluations are reported in the PhD projects of Karen van Leeuwen (economic evaluation) and Maaike Muntinga (process evaluation). The results of these evaluations will also become available in 2015.

The assessment of self-perceived care needs can provide additional insight into the care needs of frail older adults in primary care. In Chapter 7, we used baseline data of the ACT study to describe met and unmet care needs as perceived by frail older adults in primary care, and to explore the associations of care needs with socio-demographic and health-related characteristics. We assessed self-perceived care needs with the Camberwell Assessment of Need for the Elderly (CANE), a multi-dimensional needs assessment. The results showed that frail older adults report high number of needs in the environmental and physical domain, such as needs with regard to food preparation, running the household, treatment for physical illnesses, and mobility restrictions. However, most frail older adults reported to receive sufficient help for these needs. The highest proportion of unmet needs was found in the psychosocial domain, such as needs regarding loneliness, social isolation, appropriate day activities and receiving information on diseases, medication or treatment. ADL limitations and degree of frailty were the most important determinants of care needs, because frail older adults with more ADL limitations and a higher frailty score were more likely to report both met and unmet care needs across all domains. Previous studies showed similar results with regard to the domains of unmet needs. In primary care and in mental
health settings, the highest proportion of unmet care needs was also found in the psychosocial domain [11-14]. It seems that in medical settings, psychosocial needs require more attention, especially because older adults consider them as very important [15].

In Chapter 8, we studied the effects of the Geriatric Care Model on quality of life of frail older adults in primary care. This was studied in a 24-month stepped wedge cluster randomised controlled trial. Primary care practices were randomised to one four allocation groups, which started the intervention at six month intervals (0, 6, 12 or 18 months after baseline). Until the start of the intervention the practices provided usual care. In the intervention group, every six months patients received a geriatric in-home assessment by a practice nurse, followed by a tailored care plan. Practice nurses worked together with GPs, and were supervised and trained by geriatric expert teams. If necessary, these geriatric expert teams organized multidisciplinary consultations for patients with complex care needs. We did not find any effect of the Geriatric Care Model on the primary outcome, i.e. quality of life measured by SF-12. In addition, no intervention effects were found for most secondary outcomes: health-related quality of life, ADL limitations, psychological wellbeing, self-rated health, social functioning and hospital admissions. However, we found a significant, but small effect on IADL limitations at 18 months after the start of the intervention. IADL limitations increased over time, but this increase was slower in the intervention group compared to the control group. These effects were stronger in three subgroups, where intervention effects were already present at 12 months after the start of the intervention: patients already receiving homecare at baseline, patients without partner and patients 80 years and over. The intervention effects on IADL, particularly in the subgroups, seem to be robust and potentially clinical relevant. There are two possible explanations of why we only found an effect on IADL and not on other outcomes: helping people with living independently is a core task of the usual work of practice nurses, and there is substantial attention in the Geriatric Care Model for increasing or maintaining independence of frail older adults. However, we do not exactly know why the effects of the intervention on IADL were stronger in the three subgroups.

Our findings are not surprising in the context of current research. Two recent studies on the effectiveness of comprehensive care programs in primary care in the Netherlands showed quite similar results. One study on the effectiveness of a 24-month comprehensive care program to reduce disability and functional decline did not find any difference between the intervention group and the usual care group on all the outcome measures [16]. Another study over a period of 12 months did only find a small effect of comprehensive community care on a combined ADL/IADL measure [17].
CONCEPTUAL AND METHODOLOGICAL CONSIDERATIONS

**Strengths**

This thesis contains several studies on frailty in older adults. A major strength is that our studies are relevant for both public health and clinical practice, and cover three important domains in frailty research: risk factors, assessment instruments and comprehensive community care. To be able to answer our research questions, we chose the best available datasets and research methods. We used different study designs, a broad range of quantitative analysis methods and data from various settings, including a large population-based sample. We believe that this approach gives a better picture of the impact of frailty in society, than just studying it in one specific setting or one research cohort.

**Generalisability**

The sampling procedures of the different study populations used in this thesis and drop-out in longitudinal studies should be considered when interpreting the results, because there may be limitations with regard to the generalisability of the findings of our studies. LASA is based on a randomly selected population-based sample in the Netherlands. However, as with all longitudinal studies, there is loss to follow-up. The attrition of respondents over time in longitudinal studies may lead to a relatively healthy sample. Therefore, the prevalence of frailty as presented in *Chapters 2 and 3* may have been underestimated. In *Chapter 4* we used GEMU data, which is a sample of older hospital patients. There is potential sampling bias, because patients from only one sub-acute care hospital setting in Australia were used. This may have led to under- or overestimation of the frailty prevalence in this study. Unfortunately, we were not able to compare the characteristics of study participants with the characteristics of excluded patients. The IKO study (*Chapter 5*) was designed to compare different frailty instruments. From one primary care practice in the Netherlands, a specific selection of study participants was made, based on age, sex and frailty score. This was done on purpose to obtain an optimal distribution of levels of frailty and thereby allow the diagnostic evaluation of frailty instruments. Although we weighted the results back to the composition of the population from which the selection was made, the sample might not be representative of all older adults in this primary care practice and the total population of Dutch older adults in primary care. The ACT study (*Chapters 6, 7 and 8*) consisted of frail older adults from 35 primary care practices in two regions in the northwest of the Netherlands. The question is whether the included patients are representative of the total population of frail older adults in these practices. Selection bias might have occurred in both the pre-selection of patients by the GP and when patients were approached for inclu-
sion. All included patients met the inclusion criteria, but it is possible we missed some frail older patients in the participating primary care practices. In addition, it is also possible that selective drop-out (of the most frail patients) during follow-up has influenced the external validity of the findings of our study. Efforts were made to reach as many people as possible, and to keep patients as long as possible in the study. The drop-out rate in the ACT study was comparable to other studies [16].

**Study designs**

**Cross-sectional designs**

In order to test the accuracy of simple frailty instruments, a cross-sectional study was performed (*Chapter 5*). The IKO study was specifically designed for the purpose of our study. In another study, which described the self-perceived care needs of frail older adults in primary care we also used a cross-sectional design (*Chapter 7*). For this study we were able to use the baseline data of the ACT study, because these were collected before any intervention started. The cross-sectional designs are suitable to answer our research questions. However, cross-sectional designs make it difficult to say something about the directions of the associations that were found.

**Longitudinal designs**

In *Chapters 2, 3, and 4*, we used longitudinal study designs. In our study on explanations for educational differences in frailty we used multiple data measurements over a period of 13 years. We performed mediation models to examine which factors explain the association between educational level and frailty. A mediator is a variable in the causal pathway between an independent and dependent variable [18]. We performed the analyses using multilevel modelling, taking into account the dependency of repeated measures within individuals and missing values, which reduces the selection bias due to attrition. We believe that our analyses have provided insight into causal pathways linking educational level to frailty. A major strength of our study was the use of time-varying explanatory factors, which can make a greater contribution in explaining socio-economic differences in health outcomes [19]. However, we have not studied possible interrelations between explanatory factors. For example, income may affect lifestyles, and lifestyles may be related to the presence of chronic diseases. Our results showed that these interrelations exist, because there was an overlap of 31% between different factors explaining the association between educational level and frailty.
In the two studies on the role psychosocial factors as risk factors for frailty outcomes, we examined effect-modification, by testing interaction effects between frailty and psychosocial factors on adverse outcomes. These analyses are an innovative way to look at the impact of risk factors on frailty outcomes. Since we used longitudinal designs with measurements at two time points, we could use logistic regression and Cox regression techniques to analyse the data. The results in Chapters 3 and 4 show that some interaction effects have large confidence intervals, which is probably due to small numbers in subgroups. However, we believe that the initial samples were large enough to study effect-modification.

**Stepped wedge cluster randomised trial design**

To study the effects of the Geriatric Care Model, we chose to carry out a stepped wedge cluster randomised trial. Randomised controlled trials may provide the most reliable evidence for effects of an intervention. In this specific case, the stepped wedge cluster design was chosen for several logistic, ethical and analytical reasons. The sequential roll-out of the intervention makes a randomised trial with a large sample better manageable, and in the end, all frail patients who might benefit from the intervention will start with the intervention. This played an important role in motivating GPs to participate in our study. In addition, the design makes it possible to study the effects of the duration of the intervention on outcome measures. At the same time, this is a novel design. When planning the ACT study, the advantages and disadvantages of the stepped wedge design were not completely clear. Currently, there is still discussion among experts about when to use the stepped wedge design for clinical trials [20-26]. Looking back at the implementation of the ACT study and the performance of the effect evaluation, we believe that a classical cluster randomised trial may be a better choice of design for trials focused on care programs. When using a stepped wedge design, statistical analyses are complex, and the design may not be suitable for interventions showing a delayed effect. The stepped wedge design makes it possible to study the effects of the duration of the intervention, but if the effect appears in the last measurement period, there may not be enough statistical power to show this effect [27]. More research is needed into the use and analysis methods of stepped wedge designs.

The methods used in this thesis were quantitative in nature. Sometimes a mix of different methods, both qualitative and quantitative, can be helpful in understanding the subjects or processes being studied. A mixed method approach may especially be helpful for interpreting the effects of a care intervention [28]. Additional qualitative data would perhaps have made the interpretation of the effects of the Geriatric Care Model on certain outcomes as presented in Chapter 8 more easy.
Measurements

In all studies in this thesis (except the ACT study) frailty was measured using Fried’s frailty criteria [29]. This is a widely used and well-validated frailty measure, based on clinical tests and questionnaires [30]. In the ACT study we identified frailty based on the PRISMA-7 questionnaire, which showed good agreement with Fried’s frailty criteria [31]. A limitation of the ACT study is that frailty was not measured during follow-up. Therefore, we do not know if the degree of frailty of participants changed during the study period.

The outcome measures of the ACT study are all validated and widely used. However, a limitation is that the responsiveness (i.e., the ability of measures to detect clinically important changes over time [32]) of most of the outcome measures is unknown. Responsive measures are very important in longitudinal intervention studies to be able to show effects of an intervention.

In the studies in this thesis, various explanatory factors, covariates and outcome measures were based on self-report. The use of self-reported data is a potential source of bias, and could lead to an under- or overestimation of the contribution of predictors or changes in outcomes. For example, chronic diseases are in most of our studies based on self-reported data.

Deviations from protocol

Performing the ACT study, a 24-month stepped wedge randomised trial with 1147 participants, was a logistic challenge, but with strong logistic and intervention teams we were able to organise the intervention and the data collection within a short time period. Between May 2010 and March 2013, the intervention was enrolled in 35 primary care practices (finally, one practice did not start with the intervention due to practical circumstances) and more than 4500 interviews were completed. The large number of included patients enabled us to do subgroup analyses. However, not everything was performed as described in our design paper (Chapter 6). One major deviation from the protocol occurred in the part of the study focused on primary caregivers. The inclusion of primary caregivers was difficult, mainly because primary caregivers did not have time to participate in our study or older adults did not want to bother their primary caregiver, often a family member, with questionnaires. We did not reach the numbers needed to be able to study the effects of the Geriatric Care Model on outcomes in primary caregivers, and the number of participating caregivers was not equally spread over the four allocation groups. Therefore we did not perform effectiveness analyses with data of the primary caregivers who were included (N = 118).
Effectiveness of the intervention in the ACT study

As described under 'Main findings' we did not find any effect of the Geriatric Care Model on the primary outcome and on most secondary outcomes in frail older adults. We found a small beneficial effect on IADL functioning. The most likely explanation for our findings is that the Geriatric Care Model has no added value to usual care. In the Netherlands, primary care has a strong position in the healthcare system and plays an important role in the organisation of community care for older adults. Primary care is easily accessible, and the quality is considered to be good [16]. The development of the Geriatric Care Model was based on the assumption that finding a solution for three major barriers to optimal care for frail older adults in primary care (i.e. health risks are not timely identified, the lack of autonomy of older adults in their own care process, and the lack of coordination between health care professionals) would result in better patient outcomes. However, before developing the Geriatric Care Model there was limited evidence from studies in primary care supporting this assumption. Moreover, our study on self-perceived care needs in Chapter 7 showed that frail older adults report high numbers of physical and environmental needs, but that most of them already receive sufficient help for these needs. This may also indicate that primary care for frail older adults in the Netherlands is already at a relatively high level. However, there may be several other explanations for our findings:

1) Shortcomings of the performed intervention

The limited effects of the Geriatric Care Model may be the result of shortcomings of the intervention as implemented. It could be that the intensity of the intervention was too low to have influence on patient outcomes. Nurses visited the patients every six months. For frail older adults, this period may be too long. Another possibility is that the intervention was not implemented as intended. However, the first results of the process evaluation indicate that adherence to the Geriatric Care Model was high for most of the elements of the intervention (geriatric assessments, tailored care plan, care team meetings, multidisciplinary consultations and local networks of care organisations). The PhD project of Maaike Muntinga will provide more insight into the level of implementation of the intervention in the ACT study.

2) Not the right target group

There was much heterogeneity in the characteristics of the included patients. Some people had several chronic conditions and disabilities, others had no care needs at all. Therefore, the question arises if we included the right target population. Perhaps, the Geriatric Care Model has more beneficial effects in specific high risk groups, such as older adults with high risk of functional decline or hospital admissions [33]. In our subgroup analyses we already identified three subgroups that benefitted more from the intervention with regard to IADL
functioning: patients already receiving homecare at baseline, patients without partner and patients 80 years and over. However, more research is needed to find out which older adults would benefit most from the Geriatric Care Model.

3) **Outcome measures: responsiveness and appropriateness**

Two issues with regard to the outcome measures may have resulted in the absence of relevant effects on most outcome measures. First, it is possible that we were not able to show more effects, because of the low responsiveness of our outcomes. As already mentioned in previous sections, there is limited evidence for the responsiveness of the outcome measures used in our study. Second, it possible we did not choose the appropriate outcome measure for this intervention. A broad range of actions were formulated in the tailored care plans for frail older adults. The question is whether a general quality of life questionnaire is able to capture the effects of such a broad intervention. Perhaps, for heterogeneous interventions with person centered care, we also need person centered outcomes, such as goal attainment measures [34].

4) **Follow-up was too short**

The follow-up period may have been too short to show significant effects of the Geriatric Care Model on the outcome measures. When implementing an intervention in routine care, it may take a while until the intervention is carried out as intended and starts to show effects. Our study had a follow-up period of 24 months, which may be too short to show long-term and durable effects. A stepped wedge design makes it even more difficult to show a long-term effect. It has been argued that stepped wedge designs are not suitable to show delayed intervention effects, because statistical power is generally higher for short-term effect estimates compared to long-term effects [27]. This happens because there are not enough participants who receive the intervention during the whole study period. In the ACT study, only one of four allocation groups received the intervention during 24 months. The other allocation groups received the intervention for 6, 12 and 18 months.

**IMPLICATIONS FOR PRACTICE**

**Attention for low educated older people**

Given the severe consequences frailty may have, it is important to pay attention to frail older adults in clinical practice [35]. However, there are specific groups that may require more attention. One of these is the group of lower educated older people. The results of Chapter 2 show that older adults with a low educational level were more often frail compared to higher educated people, and that these differences remained the same during
later life. First, it is important that health care professionals are aware of the association between educational level and frailty. Second, preventive strategies may be targeted at lower educated older people. In Chapter 2, we showed that a broad range of factors explained educational differences in frailty, such as material conditions, psychosocial factors, chronic diseases and lifestyle. Health care professionals may inform lower educated older adults proactively about the importance of healthy lifestyles, and may encourage them to visit their GP regularly to monitor their chronic conditions. However, our results also indicate that reducing frailty in lower educated older adults is not only a challenge for health care professionals in elderly care, but also for national policy makers. Material conditions explained a large part of the effect of educational level on frailty. To reduce the impact of material disadvantage on health, major revisions of the welfare state (e.g., social security, public housing) may be needed, which is very difficult to establish [36].

The importance of psychosocial factors

The results of two studies in this thesis (Chapters 4 and 7), show the importance of psychosocial resources for frail older adults. Healthcare professionals could pay more attention to the psychosocial resources of frail older adults who are transferred to a new location, especially from hospital to home. In Chapter 4, we showed that hospitalised older adults with poor psychosocial resources had a higher risk of adverse outcomes. Psychosocial resources could be assessed, and interventions to improve these resources may be offered, such as organising social support for older adults after hospitalisation [37].

In Chapter 7, we showed that frail older adults in primary care reported high numbers of physical and environmental needs, but that most needs were already met. This is positive news, because it may show that primary care for frail older adults in the Netherlands is of high quality. However, we also found that most unmet needs were found in the psychosocial domain. Loneliness, social isolation, appropriate day activities and the provision of information to patients are topics that require more attention of the GP. For example, GPs may refer patients with psychosocial needs to social services and may improve the information provision on medical conditions and treatment to frail older adults [38, 39].

Frailty identification in primary care

Based on the results presented in Chapter 5, the PRISMA-7 questionnaire seems an easy and accurate instrument to identify frail older adults in primary care. However, before the PRISMA-7 questionnaire can be broadly used in clinical practice, an extended validation of the instrument is needed, in particular on its ability to predict adverse health outcomes.
Future use of the Geriatric Care Model

The results of the stepped wedge randomised trial (Chapter 8) demonstrated that comprehensive community care, and in this particular study the Geriatric Care Model, had no effects on quality of life, ADL functioning, self-rated health, psychological wellbeing, social functioning and hospital admissions of frail older adults. However, we observed a small effect on IADL: patients in the intervention groups showed better maintenance of IADL functioning compared to usual care. These effects were stronger in three distinct subgroups.

At this moment, we do not know enough to explain our findings. First we need to know more about which elements of this comprehensive care program lead to the beneficial effects, and why this care program showed stronger effects on IADL functioning in some subgroups.

FUTURE RESEARCH

This thesis has contributed to three research areas in the field of frailty: risk factors, assessment instruments and comprehensive community care. However, more research in each of these areas is needed.

More studies are needed to understand the complex interrelations between frailty determinants, onset of frailty and adverse outcomes. First, more life course research is needed, because frailty in old age may originate from earlier stages in life. There is not much research done linking factors earlier in life (e.g., midlife) with frailty in older adults [40, 41]. Second, more research is needed on factors that may prevent or delay adverse outcomes in frail older adults. These studies should look at different risk factors at the same time, to observe which factors are the most important. A starting point may be the development of prediction models for frailty outcomes based on data with many different variables. Third, in future studies on risk factors for frailty and frailty outcomes attention should be paid to different populations and settings, because these risk factors may differ over populations and settings.

There is an ongoing discussion about instruments to identify frail older adults. The continuing development of new instruments is a serious problem for the field, because it hinders the comparison of different studies and makes it almost impossible for healthcare professionals to choose an instrument to use in practice. Current comparative research is only cross-sectional, or based on secondary analyses of cohort data [42-45]. These studies have limitations, because the data are collected for different purposes and are not based on older adults in healthcare settings. We need more research to determine which of the exist-
ing frailty instruments are best for each setting. More comparative studies on measurement properties such as content validity and predictive validity should be conducted in general older populations and in specific healthcare settings. In addition to these suggestions for future clinimetric studies, international associations in the field of geriatrics (e.g., EUGMS, IAGG) may attempt to find agreement among their members on the definition of frailty, and subsequently make evidence-based decisions about which instruments are preferred for different settings.

With regard to comprehensive community care for frail older adults, we have several recommendations for future research. **First**, in the ACT study, we do not exactly know why we only found effects of the Geriatric Care Model on IADL functioning, and why these effects were stronger among patients already receiving homecare at baseline, patients without partner and patients aged 80 years and over. Additional research is needed to understand these findings, such as qualitative interviews with participants and practice nurses, and in-depth investigation of the content of the personalised care plans. **Second**, there was much heterogeneity in the characteristics of patients included in the ACT study and in the performed interventions. It may be worth to apply future comprehensive care programs in populations with older adults at high risk of adverse health outcomes, such as hospitalisations [33]. This may be done by selecting older adults with specific risk profiles, and focus the interventions within the care program on delaying or preventing specific outcomes. **Third**, when implementing comprehensive care programs in routine practice, it may take a while before effects become visible. In the ACT study, only a small part of the participants received the interventions during 24 months. More studies are needed with a longer follow-up time, to determine to what extent long-term and durable effects of comprehensive care programs are present. **Finally**, other research designs may be needed to find out which elements of comprehensive care programs in primary care are most beneficial. In the National Care for the Elderly Program in the Netherlands, several randomised trials were performed to test the effectiveness of comprehensive community care for frail older adults [16, 17, 46]. However, it is difficult to compare the results of these trials, because of the differences in target population, selection procedure, intervention elements and outcome measures. In future research, a parallel cluster design should be used to compare several comprehensive care programs within one study. In such a design, a control group is compared with two or more intervention groups, which receive different interventions. In this way, one can directly compare the effectiveness of care programs with slightly different elements.

As already mentioned, the use of stepped wedge designs in clinical trials is recently debated [20-26]. At the moment, it is not completely clear when this design should be used, and how effectiveness of interventions should be evaluated when using this design.
More research should be conducted into the usefulness of the stepped wedge design, to make clear for what kind of interventions the stepped wedge design is recommended (e.g., stepped wedge designs may be more appropriate for implementation studies than effectiveness studies). In addition, to determine the best method to analyse intervention effects in stepped wedge trials, future research should focus on the various existing methods to analyse stepped wedge data.

**OVERALL CONCLUSION**

In this thesis, we contributed to current knowledge on risk factors for frailty and frailty outcomes, the use of simple frailty instruments in primary care, and care needs of frail older adults. We also gained insight into the effectiveness of a comprehensive care program for frail older adults in primary care. The intervention showed small effects on one of the secondary outcomes, and therefore confirms that it is difficult to improve outcomes of frail older adults by means of comprehensive community care. Much is still unknown about frailty and its determinants, and ways to provide optimal care to frail older adults across different healthcare settings. We conclude that the **challenge of frailty in older adults** is ongoing. It requires attention in clinical practice and in future research.
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