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Chapter 1 is the general introduction to this thesis and describes proactive integrated care for older people in general practice. Integrated care was introduced in 2007 by the National Programme of Elderly Care (NPEC) and in 2008 by the Dutch College of General Practitioners (DCGP), as a response to poorly coordinated care for older people with complex problems in general practice.

Most older people have multiple functional, somatic, mental and social problems which often interact - these are generally covered by the umbrella term complex problems. Older people with complex problems might benefit from proactive integrated care. However, before general practitioners (GPs) can provide integrated care to older people, they need to properly identify older people with complex problems. In the work presented in this thesis, we tested the feasibility of five methods to identify this group of older people in general practice. These measures included a profile of laboratory measurements, the Fried frailty phenotype criteria, the clinical intuition of the GP, the ISCOPE screening questionnaire, and muscle strength measured as handgrip and quadriceps strength. These five measures were selected because: 1) laboratory measurements are regularly used by GPs to monitor older persons, 2) Fried’s frailty phenotype is an internationally recognized and validated measure, 3) most healthcare providers have a clear intuition about the vulnerability of older people, 4) the ISCOPE screening questionnaire is developed based on the definition of complex problems of the DCGP, and 5) hand grip and quadriceps strength are often used as a measure for sarcopenia (degenerative loss of skeletal muscle often associated with poor health outcomes) Therefore, all these measures might be effective in the aim to identify complex problems in general practice.

Primary care for older people with complex problems is sometimes sub-optimal because multiple (medical) specialists and (informal) caregivers are involved, and disease-specific guidelines do not always apply to older people with complex problems. To optimally address these complex problems it is suggested that GPs, medical specialists and (informal) caregivers should collaborate – this is known as integrated care. However, to our knowledge, when the research described in this thesis was started, no programs were available for integrated primary care. Therefore, we selected a method that is commonly used by elderly care -, and rehabilitation physicians in the Netherlands and implemented this method in primary care. Specifically, to support this integrated approach, the GP/physician (who has overall responsibility) in close collaboration with other healthcare workers (e.g. physiotherapist, psychologist, etc.) formulates a care plan which combines problems on all major health domains (i.e. functional, somatic, mental and social). This care plan was used in a pragmatic randomized controlled trial as an integrated care intervention to test the hypothesis that older people with complex problems might benefit from integrated care.
In Chapter 2 the dynamic nature of disability in the oldest old was studied. For this purpose, we used data from the Leiden 85-plus Study, a population-based study of 85-year-old individuals living in Leiden, the Netherlands. In this group, during the five-year follow-up, we examined transitions between disability states. A multi-state model was used to assess the risks of transitions between no disability, disability in instrumental activities of daily living (IADL disability), disability in basic activities of daily living (BADL disability), and death. At baseline, a large percentage of the population had IADL disability only, or IADL and BADL disability combined. During follow-up, an even larger percentage of the group made one or more transitions. Most of these transitions were directed to deterioration in disability, or death. We found that males had a lower risk of deterioration compared to females. The presence of depressive symptoms, chronic disease and cognitive impairment carried the highest risk of deterioration into disability. Based on these findings, we concluded that disability remains a dynamic process in the oldest old, with some older people experiencing a more rapid decline than others. These results are important, because the oldest old are the fastest growing segment of the general population. Therefore, these results might be used to develop preventive strategies directed towards disability. More studies are needed to further develop and implement these new strategies.

In Chapter 3 we tested whether a combination of seven laboratory measurements has a better predictive accuracy in predicting mortality than gait speed and disability in IADL, which are other known predictors of mortality. This study was also embedded in the Leiden 85-plus Study. The seven laboratory measurements that were combined in a laboratory profile and were measured at baseline (age 85 years) were: high-density lipid cholesterol (HDL-C), albumin, alanine transaminase, hemoglobin, creatinine clearance homocysteine and C-reactive protein (CRP). These seven laboratory abnormalities were included as markers of different physiological systems; general health status (CRP), cardiovascular status (homocysteine), hematological status (hemoglobin), fatty acid metabolism (HDL-C), liver function (alanine transaminase), nutritional status (albumin), and renal function (creatinine clearance). It was found that 74% of our study population had one or more laboratory abnormalities at baseline and that an increasing number of abnormalities was associated with an increased mortality risk. Compared to low gait speed and disability in IADL, the predictive accuracy of the laboratory profile was similar. Therefore, the laboratory profile may be useful for clinicians as it provides information beyond age and sex. Moreover the laboratory profile is easily available, as most older people are regularly monitored by laboratory measurements. However, studies are needed to confirm these results in additional cohorts before implementation in clinical practice is possible. In addition, our study provides no etiological insight into the combinations of laboratory measurements; this is another topic for future studies.
In Chapter 2 it was found that functional, somatic and mental problems contribute to deterioration in disability. Most older people have problems not only on one domain, but on multiple domains. Therefore, in Chapter 4 we explored whether combinations of health problems interact and whether this interaction is associated with indicators of poor health, i.e. disability, poor cognitive function, depressive symptoms, loneliness, health-related quality of life, and GP contact time. This study was embedded in the Integrated Care for Older People (ISCOPE) study (Chapter 8). All participants (aged 75 years and over) of the ISCOPE study filled out the ISCOPE screening questionnaire; this consists of 21 questions on four domains (functional, somatic, mental and social). During home visits, the participants were interviewed to obtain data on health indicators at baseline and again 12 months later. GP contact time was extracted via the electronic medical records of the participant’s GPs. At baseline, over 80% of the participants had problems on more than one health domain. The number of health domains with problems was associated with poor health indicators, and problems on all four domains had an additional negative effect on these health indicators. At follow-up, an increased number of domains with problems was associated with an increased decline in health indicators, and the presence of problems on all four domains was associated with an additional negative effect on GP contact time. This implies that combinations of functional, somatic, mental and social problems interact, which may reflect the complexity of older individuals with problems on these domains. Future research should examine interventions for older people with problems on all four domains.

In chapter 4 it was shown that the ISCOPE screening questionnaire can be used to identify older people with complex problems. Chapter 5 investigates whether the ISCOPE screening questionnaire is also a valid and feasible questionnaire to identify complex problems in older people in primary care. It was found that the feasibility of the questionnaire could indeed be improved, as the response rate was not satisfactory (63%). Moreover, several studies have reported that non-responders tend to have more problems than responders. This was also the case in our study, i.e. older people who did not respond were appraised as being ‘vulnerable’ by their GP more often and more often received home visits. Of the responders, 99% filled out the entire questionnaire, which resulted in a minimal number of missing values. To determine the internal consistency, Cronbach’s alphas were calculated. These ranged from reasonable for the somatic (0.52) and mental domain (0.63) to good for the functional and social domain (0.81 and 0.70, respectively). Construct validity was evaluated by defining and testing 10 hypotheses about the associations of the four domains and the ISCOPE questionnaire, with adverse health indicators. All 10 hypotheses were confirmed, implying that the ISCOPE screening questionnaire has a good construct validity. To investigate the test-retest reliability, participants of five participating GPs were invited to fill out the questionnaire twice, within
two weeks. The test-retest reliability was highest for the functional domain (and the individual items within this domain) whereas the somatic domain had the lowest test-retest reliability. To determine the content validity, 16 geriatric experts agreed with the 21 original items of the ISCOPE screening questionnaire and suggested to add 11 items. These results imply that the ISCOPE screening questionnaire had a reasonable content validity. We conclude that the ISCOPE screening questionnaire is a short and reasonably feasible instrument, with satisfying clinimetric properties to identify complex problems in older people in primary care. Future research should investigate its responsiveness, generalizability and predictive validity. Moreover, the questionnaire needs to be further improved based on suggestions from the experts.

Apart from the ISCOPE screening questionnaire, other measures are available to identify complex problems. Chapter 6 describes a study which compares the ISCOPE screening questionnaire with two of these measures, i.e. the Fried frailty phenotype criteria and the GP’s clinical intuition regarding a patient’s vulnerability. Frailty is a biologic syndrome of decreased reserves and resistance to stressors. According to the Fried frailty phenotype criteria, frailty arises when $\geq 3$ of the following criteria are met: 1) unintentional weight loss, 2) self-reported exhaustion, 3) slow gait speed, 4) weak grip strength and 5) low level of physical activity. These latter criteria are often used in research but seldom in general practice, and never to identify older persons with complex problems. The GP and the older patient often have a long-term doctor-patient relationship and GPs often rely on a ‘gut feeling’ in their diagnostic process. However, although the clinical intuition of GPs has not yet been used as a measure for complex problems, GPs are known to take multiple domains into account, it is feasible that their intuition can be used as a measure to identify older persons with complex problems.

In a random sample of 823 participants aged $\geq 75$ years (taken from all participants of the ISCOPE study) we compared the yield on health indicators (including disability, multimorbidity, depressive symptoms, quality of life, use of GP care) of these three measures (i.e. the ISCOPE questionnaire, the Fried frailty criteria, and GP’s clinical intuition). Of the participants, over one third did not have complex problems according to the three measures. The remaining participants had complex problems, according to one, two or three of the measures. Irrespective of the measure, complex problems were associated with poor health indicators. When participants had complex problems according to two or three of the measures, the scores on these health indicators were even poorer. Of the three measures, the Fried frailty phenotype was most strongly associated with disability, whereas the ISCOPE screening questionnaire was most strongly associated with loneliness. However, from this study no clear conclusions can be drawn about the best instrument to use to identify complex problems in general practice. Therefore, the measure
of choice should perhaps depend on the intended intervention, as well as the workload and costs involved with each measure. In this study, the GP’s clinical intuition was associated with poor health indicators and is, therefore, suitable to identify older people with complex problems; however, when GPs are interested in disability or loneliness, then they should combine this intuition measure with the Fried frailty phenotype or the ISCOPE questionnaire, respectively. Further studies are needed to establish whether the combination of multiple measures improves the identification of complex problems in general practice.

In Chapter 7 we compared measurements of hand grip strength and quadriceps muscle strength (both as a measure for sarcopenia) for their association with poor health indicators. Because sarcopenia is thought to play a major role in functional impairment, measures to identify sarcopenia could identify older people at risk for functional decline. These analyses were performed in a subpopulation of the ISCOPE study of 823 older participants (aged ≥ 75 years) of whom 764 had valid hand grip and quadriceps strength measurements. These participants were visited at baseline to measure hand grip and quadriceps strength. Data on poor health indicators were obtained at baseline and again 12 months later. It was found that, although the association between hand grip and quadriceps strength was weak, both measurements were independently associated with poor health indicators at baseline. Participants with both weak hand grip and weak quadriceps strength were identified as having the poorest scores on health indicators at baseline, compared to participants with normal hand grip and quadriceps strength and to participants who had only weak hand grip strength or weak quadriceps strength. At follow-up, weak hand grip strength was associated with quality of life and disability in basic activities of daily living. Quadriceps weakness did not contribute to the prediction of poor health indicators at 12 months follow-up. The conclusion drawn from this study is that the combination of handgrip strength and quadriceps strength may help to identify older people with complex problems in primary care.

The aim of Chapter 8 was to investigate the introduction of an integrated care plan for older people (aged ≥75 years) with complex problems (identified with a postal questionnaire) in general practice. This was investigated within ISCOPE, which is a cluster randomized trial with 59 participating general practices (30 intervention practices, 29 control practices). Older people aged ≥75 years were screened with the ISCOPE screening questionnaire. Complex problems were defined as problems on ≥ 3 domains; 25% of the participants had complex problems. GPs from the intervention practices received training in making a care plan, and each GP made an integrated care plan for a random selection of 10 older persons with complex problems in his/her practice (resulting in a total number of 225 care plans). At 12 months follow-up there were no differences
in competence in the activities of daily living, quality of life and cost-effectiveness between the intervention and control group. Still, older patients with complex problems in the intervention group were slightly more satisfied with their GP. Moreover, GPs in the intervention group experienced better organization and more stability in the care for individual patients with complex problems. Therefore, the main conclusion drawn from this ISCOPE study is that GPs and older people with complex problems prefer a proactive integrated approach to geriatric care in general practice, but that this approach has no direct effect on functioning and quality of life of older people with complex problems, or on healthcare costs. There are several possible reasons for this lack of effect: 1) since the early 1990s, many changes have taken place in the care for older people in primary care. The present study started in a climate of growing interest in preventive and proactive care for older people, which ensured enthusiasm among the participating GPs - and government and healthcare professionals were already moving in this direction. GPs (also those in the control group) may have had increased awareness of the need to work proactively for their older patients, which might have caused dilution of the effect in the intervention group. 2) unsolicited care programs (or other devices) might not work because those who expect benefit from the offered service (or device) have already obtained it. 3) the intervention may have been too broad to cause an effect. 4) the intervention may not have been sufficiently intense to cause an effect. 5) a change in organization and/or delivery of care does not necessarily lead to an effect on the level of functioning and/or quality of life of the individual patient. 6) a randomized trial design may not be appropriate for this type of intervention, as it generally kind of as they consist of a complex mix of uncontrollable variables. Future research on integrated care interventions should take these points into consideration when setting up studies and planning integrated interventions. However, at the moment, there is no hard evidence for the effectiveness of integrated care for older people with complex problems in general practice.

In Chapter 9, we summarize and reflect on the main results of this thesis. In addition, we discuss implications for general practice and make some recommendations for further research. The results of this thesis shed new light on two important issues for evidence-based general practice care for older people: 1) the feasibility (or not) of the (proactive) identification of older people with complex problems and 2) the effectiveness (or not) of proactive integrated care for older people with complex problems in general practice.

We investigated five measures for their feasibility to identify older people with complex problems in general practice, i.e. a profile of laboratory measurements, handgrip and quadriceps muscle strength, Fried’s frailty phenotype criteria, the clinical intuition of the GP, and the ISCOPE screening questionnaire. Each of these measures identified
different groups of older people with complex problems; moreover, the association between these five measures and health indicators also differed. Therefore, none of these measures can be specifically recommended as the gold standard. Even though all five measures identified a complex group of older people, based on the present results we cannot recommend one of the measures as being the most feasible for general practice. As a result, the measure of choice in general practice could depend on the intended intervention of the GP, the workload involved with each measure, and the intention of the GP for a systematic inventory of the older population. In the ISCOPE study, systematic screening for complex problems was used to identify complex problems. We checked this systematic screening against the 10 Wilson and Jungner criteria for screening for disease; this revealed that systematic screening for complex problems fulfils 3 of the 10 Wilson and Jungner criteria. Since systematic population screening for complex problems is not yet appropriate another method is needed to identify older people with complex problems in general practice. Case finding involves screening of a smaller group of people based on the presence of known risk factors. This might prove to be an appropriate method to identify older people with complex problems.

In the ISCOPE study, a proactive integrated care plan did not have a direct effect on functional decline or quality of life among older people with complex problems. However, this does not mean that integrated care is not a good way to deal with older people with complex problems as in fact, it has become a standard in some practices to the satisfaction of both GPs and their older patients. In addition to the reasons described in Chapter 8, the lack of effect of the ISCOPE study might also be attributed to the target group for integrated care. Older people with complex problems may have been too complex to show improvement in functioning. An intervention directed to older people at risk to become complex, might have had more a more obvious effect on these older people. Also, the sample size of the ISCOPE study may have been too small to demonstrate an effect. Therefore, an individual patient data meta-analysis of all studies in the context of the NPEC is recommended. The lack of effect of the ISCOPE study might also be due to the intervention, because unmet needs were not specifically considered in the integrated care plan. In addition, collaboration with elderly care physicians and GPs with expertise in geriatrics, might also improve integrated care in general practice. The above-mentioned items and recommendations could be used to design future studies and integrated care interventions for older people with complex problems in general practice.

In conclusion, the main findings emerging from this thesis are:

1. Older people with complex problems in general practice can be identified with relatively simple measures
2) No direct benefit from proactive integrated care for older people with complex problems can be demonstrated; this might be attributed to the study design used and/or to the intervention itself.

Based on the results of the work presented here, some recommendations can be made for a revision of the DCGP statement on the care for older people in general practice. Although we could not demonstrate a direct effect of integrated care for older people in general practice, this population warrants attention from GPs as they are at risk of adverse health outcomes. Future studies will reveal whether an intervention for older people at risk has some effect in the prevention of further deterioration. Our studies also provide evidence for the value of the clinical intuition of GPs regarding the ‘vulnerability’ of older people; this intuition can be used by GPs as a measure to identify older people with complex problems. Moreover, the four other measures that were investigated can also be used individually, or in combination, to identify these older people. Although we found no direct effect of integrated care on functional status or quality of life of these older people, in our opinion integrated care still remains the best type of care available for this specific group. We believe this is confirmed by the level of satisfaction of both older people and the GPs who were included in the intervention group of our ISCOPE study.