HEALTHY AGEING IN EUROPE

Variation and **promotion** among older persons

Carmen B. Franse

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Chapter 1

General introduction

1.1 Background

Population ageing in Europe

Europe has the highest proportion of persons over 65 years compared with any other continent[1]. In 2015, Europeans over 65 years accounted for 19% of the population and by 2040 this will be 27% [2]. This demographic change is the result of people increasingly living longer and having less children compared with the post-war generation whose children are now ageing. At age 65, women in the European Union have an average life expectancy of 21.1 years and for men this is 17.7 years[3]. However, both men and women of 65 years live an average of only 8.5 years free from disability. Multimorbidity, which is the co-occurrence of two or more diseases, increases with age and has become a large problem in Europe[4 5]. In addition to physical health problems, older persons may also have relatively more social and mental health problems, which can be associated with higher disability and mortality[6-8].

Frailty

While some persons remain relatively healthy with aging, others become vulnerable to stressors. Frailty was introduced to capture this variability in the 'speed of aging'[9]. It has been described as a state of increased vulnerability to external stressors[10 11]. The concept of frailty offers a more holistic viewpoint of the patient and directs attention away from organ-specific diagnoses[10]. Frailty is an important risk factor for adverse outcomes such as hospital admission and mortality and a better predictor of adverse outcomes than age alone[9 12-14]. Frail older persons are two to four times as likely to develop or worsen disabilities in self-care tasks and household management tasks compared with non-frail older persons[15]. Furthermore, mortality is much higher among persons with chronic diseases who are also frail, compared with persons with chronic diseases who are not frail[16 17]. Frailty is manageable and early intervention slows functional decline and reduces hospital admissions and mortality[11 18 19]. One of the recommendations from an international consensus meeting consisting of experts in frailty and geriatrics from 6 major international, European, and US societies was to assess frailty in all persons of 70 years and older[11]. Further research is needed to identify which populations are frail or at a higher risk of developing frailty in order to target prevention strategies.

There has been a lot of discussion on the appropriate definition and way of measuring frailty. The two most popular models of frailty are the frailty phenotype; also known as physical frailty, developed by Fried et al., and Rockwood's accumulation-of-deficits model. In Fried's definition a person is frail if he/she presents with three or more of the following five symptoms: weight loss, exhaustion, low activity, slowness and weakness[20]. The Rockwood's deficits model consists of adding together an individual's number of impairments and conditions to create a Frailty Index[21 22]. While the original Frailty index focused on physical, psychological and cognitive impairments, there has been recent interest in using blood

biomarkers related to ageing[23]. Other recent models view frailty as a multidimensional concept which includes psychosocial vulnerability as well as physical vulnerability[24]. Examples of such multidimensional frailty tools are the Tilburg Frailty Index and Groningen Frailty Index[25 26]. These instruments include items related to loneliness, social isolation, sadness and nervousness in addition to items assessing physical health and cognition[25 26].

Falling

Falling is an adverse outcome of frailty[27]. Furthermore, falling and frailty have both been classified as geriatric syndromes; they are highly prevalent, have multiple causes, and are associated with poor outcomes[28 29]. Every year around 30% of community-dwelling older citizens over age 65 fall [30-32]. Around 5 to 10% of all falls result in serious injury such as a head injury or fracture [33 34]. Around 90% of fractures of the hip, one of the most debilitating injuries among older people, are the result of a fall. In 2000, the combined costs in Europe for hip fractures were estimated at €24.4 billion[35], these costs are expected to double in 2050 due to the ageing population. Falling can also have negative psychosocial effects such as fear of falling, activity avoidance and social isolation [36 37]. Due to the burden caused by falling and positive results from fall prevention interventions, prevention of falling is a priority of European health policy [32 38-40].

Variation in health

The health of older persons varies considerably between European countries. With 13.8 years, women in Sweden have the highest number of years without disability at age 65 and with 3.7 years, women in Slovakia the lowest (figure 1)[3]. In general, persons in Scandinavian (Denmark, Finland, Norway, Sweden), and Anglo-Saxon (Ireland, United Kingdom) regimes report better health in comparison with Bismarckian (Austria, Belgium, France, Germany, Luxembourg, Netherlands, Switzerland), East European (Croatia, Czech Republic, Hungary, Poland, Slovenia), and Southern (Greece, Italy, Portugal, Spain) countries[41-45]. Between-country differences in health and life expectancy have been linked to socioeconomic, political and cultural factors[45-48]. Persons living in richer countries on average live longer than persons living in poorer countries. A well-known illustration of this, is the association between the national income of a country and life expectancy at birth[46]. Improved population health has also been consistently linked to advanced levels of democracy and egalitarian political traditions[45 47]. Between-country differences have often been studied for certain outcomes such as mortality, healthy life years and disability. However, between-country differences in other outcomes such as falling have not been studied. Literature has focused on geographical differences in limb fractures and has found that hip fracture rates are highest in Scandinavian countries compared with other countries in Europe [49-51]. Insight into regional differences of falls and fall risk factors can help (inter)national policy makers to prioritise the right fall prevention strategies or continue successful efforts.

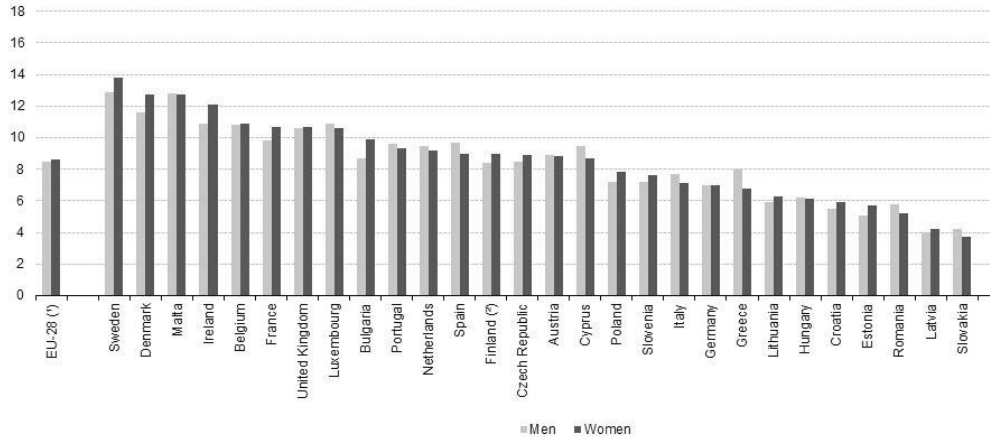

Figure 1: Healthy life years at age 65, by sex and European country in 2013. Source: Eurostat, 2015.

Inequalities in health are also present within populations of all European countries and pose a major challenge to public health. Persons with a lower education level, a lower occupational class or a lower income die at a younger age and have a higher prevalence of most health problems[52]. Inequalities in mortality have also increased in many countries in the past decades[52]. Studies among older persons have found that persons with a low socioeconomic status are frailer and become frailer over time compared with persons with a high socioeconomic status[53-55]. Older persons from ethnic minority groups have also found to be in poorer health compared with persons from native populations[56-60]. In Western Europe, large ethnic minority groups consist of immigrants settled during the decades after the Second World War. These immigrants are ageing. However, relatively little research is done on unravelling socioeconomic and ethnic differences in frailty. This increases the urgency to study the frailty level of these groups and associated factors, and to develop strategies to prevent frailty and adverse outcomes.

Primary care systems in Europe

As the number of older persons is increasing, there will be relatively fewer beds available in inpatient care facilities, such as hospitals, nursing homes or care homes. In addition, most older persons prefer to live independently as much as is possible, receive care at home and die at home[61 62]. Because of this, it is important to have a well-functioning primary care system that supports older persons in living independently for as long as possible. In many European countries, general practitioners provide day-to-day primary care for their communities and act as gatekeepers to specialised care. However, the importance and accessibility of general practitioners in community care differs by country. The Netherlands has a relatively high number of general practitioners, with over 15 per 10 000 inhabitants. Croatia, Spain and

the UK are in the middle with around 8 general practitioners per 10 000 inhabitants. Greece has one of the lowest numbers with 4 per 10 000 inhabitants[63]. The Primary Health Care Activity Monitor for Europe (PHAMEU) study has developed the following quality indicators for primary care: accessibility, availability of prevention and treatment services, continuity of care and coordination of care[64 65]. They found that population health is better in countries with relatively stronger primary care compared with countries with relatively weaker primary care[64].

The care system is currently often characterised by a monodisciplinary approach focussed on one disease or condition[64 66 67]. However, as described earlier, older persons may have multiple physical- and psychosocial health problems[6-8]. This could place a burden on health- and social care services. Because of this, the demand for cost-effective models of integrated and coordinated provision of different health and social care services has grown[64 68]. Multidisciplinary collaboration which is patient-centred instead of disease-centred and coordinated from primary care could provide a solution[64]. In addition, because of the pressure on the health care system due to population ageing, the interest in preventive interventions that increase healthy life years among older Europeans has increased[40 69].

Coordinated preventive care

Several models of coordinated preventive care approach for older persons have been proposed[70-74]. Common elements that these care models have is a single entry point for older persons and assessment of frailty and other geriatric syndromes. The gold standard for identifying frailty and geriatric syndromes among older persons is a comprehensive geriatric assessment; a multidimensional and multidisciplinary assessment of an older persons' physical, mental and social health[75 76]. However, this is time consuming and is preferably performed by a geriatrician[77]. Brief multidimensional frailty tools have therefore been developed to identify frailty in primary care[72-74]. After this frailty assessment, if needed, further assessment is done with short validated tools for particular health risks such as falls, polypharmacy or vision problems and a multidimensional care plan is developed. In complex cases a multidisciplinary consultation could be organised by the general practitioner together with other health professionals such as a nurse, pharmacist and physiotherapist. A nurse could alleviate the workload for the general practitioner and act as care coordinator. He/she coordinates the assessments and follow-up care services in consultation with the general practitioner. The health of the older person is monitored and the care plan is adjusted if needed. With the aim of improving interdisciplinary communication, an electronic patient system could be used through which health professionals from different disciplines communicate[71]. Table 1 provides an overview of differences between a coordinated preventive care approach and 'traditional' care for older persons.

Coordinated preventive interventions that integrate multiple disciplines often aim to reduce functional decline, nursing home admissions and mortality, and increase quality of life among older persons [78-80]. A smaller number of studies have focussed on reducing mental health problems or promoting social functioning among older persons[80-82]. Evidence for the effect of coordinated preventive interventions regarding these outcomes is mixed and more research is needed [78-82]. Most studies have been conducted in Northwest European or American settings, studies in Southern and Eastern European settings are lacking[19 78-80]. More insight is needed into what specific outcomes can be achieved with coordinated preventive care for older persons in diverse European settings. It is therefore important to evaluate the effectiveness of such care approaches in various European settings. A large meta-analysis of complex care interventions for older persons showed no evidence for any specific type or intensity of intervention and the authors suggest that tailoring of interventions to the context and client needs is key[19]. This suggests that care coordination and integration between disciplines could be organised in many ways depending on the availability and organizational structures in the local context.

Table 1: Differences between coordinated preventive care and 'traditional' care for older persons (adapted from Looman et al. [82])

	Coordinated preventive care	'Traditional' care
Role general practitioner	Single entry point, coordinator of care supported by a nurse	Gatekeeper
Pro-activeness versus reactiveness	Preventive multidimensional assessment of frailty and other health risks	Care on own initiative and for specific health problems
Care plan	Multidisciplinary care plan	No or monodisciplinary care plan
Care coordination and monitoring	Case management monitoring, contact person professionals, evaluates care plan	No case management
Communication	Multidisciplinary meetings, support by electronic patient system	Bilateral communication by phone calls and letters

Promotion of healthy ageing

Rowe & Kayn argued that researchers have neglected the heterogeneity in the non-frail or 'normal' group of older persons[83]. They introduced a concept of successful ageing to describe older persons who have no or little loss of functioning and emphasised the importance of modifiable factors such as exercise, social support and diet for successful ageing. This called for a shift from management of chronic and age-related conditions towards prevention of health problems and promotion of healthy ageing. The World Health Organization focuses on promotion of healthy and active ageing, which is reflected in their definition of healthy and active ageing: "the process of optimising opportunities for health, participation, and security in order to enhance quality of life as people age"[84]. The promotion of healthy ageing is currently a priority of European policy[40 69]. A key initiative is the European Innovation Partnership on Active and Healthy Ageing[40]. They have funded actions that improve healthy

ageing and identified priority areas for healthy ageing, which are: appropriate medication prescription and adherence, falls prevention and management of frailty.

1.2 This thesis

Research questions

In order to identify target groups for intervention strategies aimed at healthy ageing it is important to study which populations are at a higher risk of poor health outcomes. In addition, the effectiveness and feasibility of coordinated preventive care interventions that promote healthy ageing should be evaluated in diverse European settings. Therefore, the aim of this thesis is twofold. Firstly, this thesis aims to study the variation in indicators of healthy ageing among populations in Europe. More specifically, variation in frailty according to socioeconomic status and ethnic background and between-country variation in falling and fall risk are studied. The second aim is to evaluate the effects and process components of a coordinated preventive care approach aimed at promoting healthy ageing among older persons in Europe. The following research questions will be answered:

- What is the association of socioeconomic status and ethnic background with frailty among older persons in the Netherlands?
- What is the rate of falling and intrinsic fall risk among older persons in Europe and can between-country variation in falling be explained by intrinsic fall risk?
- What are the effects of a coordinated preventive care approach on the lifestyle, health and quality of life among older persons in Europe and how does this approach perform in terms of process components?

Outline of this thesis

In this thesis six studies are presented. Table 2 provides an overview of the studies presented in this thesis. The research focus of these studies can be divided into two overarching topics, presented in two parts in this thesis. ***Part I*** of this thesis consists of studies on the variation in healthy ageing among community-dwelling older persons in Europe. In **chapter 2**, the associations of socioeconomic status with frailty and frailty components among community-dwelling older persons in the Netherlands are studied. In addition, the extent to which morbidities mediate the association of socioeconomic status with frailty components is studied. In **chapter 3**, the association of ethnic background with frailty and frailty components among community-dwelling older persons in the Netherlands is studied. In **chapter 4**, the rate of falling and intrinsic fall risk among community-dwelling older persons in twelve European countries is studied and whether between-country variation in falling can be explained by intrinsic fall risk among the populations of the countries. ***Part II*** of this thesis consists of studies on the design and evaluation of a coordinated preventive care

approach which integrated social and health care services and aimed to promote healthy ageing among older persons. This approach was implemented in five diverse European settings (Greater Manchester, United Kingdom; Pallini, Greece; Rijeka, Croatia; Rotterdam, the Netherlands; and Valencia, Spain). This study; Urban Health Centres Europe (UHCE), is described in more detail in the next paragraph. In **chapter 5**, the design of the UHCE study is described. In **chapter 6**, the effects of the UHCE approach are evaluated on the lifestyle, health and quality of life of community-dwelling older persons in five European cities. In **chapter 7,** specific process components of the UHCE approach are studied to evaluate how the approach is implemented, which persons are reached and what their experience is with the approach. Finally, in **chapter 8**, the results of the studies are summarised and interpreted alongside the literature. Strengths and limitations of these studies are discussed as well as recommendations for future research and implications for policy and practice.

Table 2: Overview of the studies presented in this thesis

Chapter	Study design	Study/data	Sample	N	Research focus
Part I - Variation in healthy ageing among older persons in Europe					
2	Cross-sectional	TOPICS-MDS	Community-dwellers aged ≥55 years in the Netherlands	26 014	The association of education level and neighbourhood socioeconomic status with frailty and frailty components
3	Cross-sectional	TOPICS-MDS	Ethnically diverse community-dwellers aged ≥55 years in the Netherlands	23 371	The association of ethnic background with frailty and frailty components
4	Longitudinal	SHARE	Community-dwellers aged ≥65 years in 12 European countries	18 596	The variation in falling across twelve European countries and extent to which this is explained by intrinsic fall risk factors
Part II – Promotion of healthy ageing among older persons in Europe					
5	Design paper	UHCE	NA	NA	Design of the UHCE study
6	Pre-post controlled trial	UHCE	Community-dwellers aged ≥70 years in 5 European cities	1836	Evaluation of effect of the UHCE approach on lifestyle, fall risk, appropriate medication use, loneliness, frailty, level of independence, health-related quality of life and care use
7	Mixed-methods study	UHCE	Community-dwellers aged ≥70 years and professionals participating in UHCE approach in 5 European cities	986 & 23	Evaluation of UHCE approach regarding process components: context, reach, dose delivered and received, satisfaction and experience.

1.3 Studies and data used

The UHCE project

The Urban Health Centres Europe (UHCE) project was set up to promote the lifestyle, health and quality of life of older European citizens by developing, implementing and evaluating a coordinated preventive health and social care approach (The UHCE approach) in primary care settings in Greater Manchester, United Kingdom; Pallini, Greece; Rijeka, Croatia; Rotterdam, the Netherlands; and Valencia, Spain (figure 2). The UHCE approach included an assessment of health risks and, if indicated, follow-up care in which different health and social care disciplines work together coordinated from a single point of care. The UHCE approach was specifically targeted at prevention of falling, management of polypharmacy, loneliness and frailty. In each city, 250 participants aged 75 years and older were recruited to receive the UHCE approach and compared with 250 participants who received 'care as usual'. By means of a baseline and 12-month follow up assessment, the effects of the UHCE approach on lifestyle, fall risk, appropriate medication use, loneliness, frailty, level of independence, quality of life and care use were assessed. In addition, process components were evaluated alongside the effects of the UHCE approach.

Figure 2: The five cities of the UHCE project

SHARE study

The Survey of Health, Ageing and Retirement in Europe (SHARE) is a multidisciplinary and cross-national panel database of micro data on health, socioeconomic status and social and family networks[85]. Persons are interviewed using standardised Computer Assisted Personal Interviews. Since its start in 2004, more than 120,000 individuals aged 50 or older have been interviewed in 27 European countries and Israel. Data are collected roughly every two years, and to date, data of six waves had been collected. The data are available to the research community free of charge and more than 6000 researchers from all over the world are registered as SHARE users. For this thesis, data from wave 4 (2010/2011) and wave 5 (2013) were used, collected in 12 European countries (Sweden, Denmark, Austria, Germany, the Netherlands, Belgium, Switzerland, France, Italy, Spain, Czech Republic and Estonia).

TOPICS-MDS

The Older Persons and Informal Caregivers Survey Minimum DataSet (TOPICS-MDS) is a public access data repository designed to capture essential information on the physical and mental well-being of older persons and informal caregivers in the Netherlands[86]. TOPICS-MDS was developed to collect uniform information from all studies funded under the program *Dutch National Care for the Elderly*[87]. Included survey items were based on the recommendations of an expert panel who identified the key outcomes in older persons' health relevant in a range of settings[86]. Data were collected between 2010 and 2013 in 50 different studies in the Netherlands. TOPICS-MDS consists of the pooled data of these studies. For this thesis, we used data from community-dwelling older persons collected in 2010.

REFERENCES

1. United Nations Department of Economic and Social affairs. World Population Prospects: United Nations; 2017 [Available from: https://esa.un.org/unpd/wpp/dataquery/.
2. Eurostat. Population structure and ageing: European Union, 1995-2013; 2014 [Available from: http://ec.europa.eu/eurostat/statistics-explained/index.php/Population_structure_and_ageing accessed 05/01/2017.
3. Eurostat. People in the EU – statistics on an ageing society: European Commission; 2015 [30/11/2017]. Available from: http://ec.europa.eu/eurostat/statistics-explained/index.php/People_in_the_EU_%E2%80%93_statistics_on_an_ageing_society.
4. Onder G, Liperoti R, Soldato M, et al. Case management and risk of nursing home admission for older adults in home care: results of the AgeD in HOme Care Study. *J Am Geriatr Soc* 2007;55(3):439-44. doi: JGS1079 [pii]10.1111/j.1532-5415.2007.01079.x [published Online First: 2007/03/08]
5. Navickas R, Petric VK, Feigl AB, et al. Multimorbidity: What do we know? What should we do? *J Comorb* 2016;6(1):4-11. doi: 10.15256/joc.2016.6.72
6. Andrew MK, Mitnitski A, Kirkland SA, et al. The impact of social vulnerability on the survival of the fittest older adults. *Age Ageing* 2012;41(2):161-65.
7. Fratiglioni L, Wang HX, Ericsson K, et al. Influence of social network on occurrence of dementia: a community-based longitudinal study. *Lancet* 2000;355(9212):1315-9. doi: 10.1016/S0140-6736(00)02113-9
8. Mendes de Leon CF, Glass TA, Berkman LF. Social engagement and disability in a community population of older adults: the New Haven EPESE. *Am J Epidemiol* 2003;157(7):633-42.
9. Theou O, Brothers TD, Mitnitski A, et al. Operationalization of frailty using eight commonly used scales and comparison of their ability to predict all-cause mortality. *J Am Geriatr Soc* 2013;61(9):1537-51. doi: 10.1111/jgs.12420 [published Online First: 2013/09/14]
10. Clegg A, Young J, Iliffe S, et al. Frailty in elderly people. *Lancet* 2013;381(9868):752-62. doi: S0140-6736(12)62167-9 [pii]10.1016/S0140-6736(12)62167-9 [published Online First: 2013/02/12]
11. Morley JE, Vellas B, van Kan GA, et al. Frailty consensus: a call to action. *J Am Med Dir Assoc* 2013;14(6):392-7. doi: S1525-8610(13)00182-5 [pii]10.1016/j.jamda.2013.03.022 [published Online First: 2013/06/15]
12. Romero-Ortuno R, Kenny RA. The frailty index in Europeans: association with age and mortality. *Age Ageing* 2012;41(5):684-9. doi: 10.1093/ageing/afs051
13. Song X, Mitnitski A, Rockwood K. Prevalence and 10-year outcomes of frailty in older adults in relation to deficit accumulation. *J Am Geriatr Soc* 2010;58(4):681-7. doi: 10.1111/j.1532-5415.2010.02764.x
14. Kojima G, Iliffe S, Walters K. Frailty index as a predictor of mortality: a systematic review and meta-analysis. *Age Ageing* 2017:1-8. doi: 10.1093/ageing/afx162
15. Kojima G. Frailty as a predictor of disabilities among community-dwelling older people: a systematic review and meta-analysis. *Disabil Rehabil* 2017;39(19):1897-908. doi: 10.1080/09638288.2016.1212282

16. Cacciatore F, Testa G, Galizia G, et al. Clinical frailty and long-term mortality in elderly subjects with diabetes. *Acta Diabetol* 2013;50(2):251-60. doi: 10.1007/s00592-012-0413-2
17. Galizia G, Cacciatore F, Testa G, et al. Role of clinical frailty on long-term mortality of elderly subjects with and without chronic obstructive pulmonary disease. *Aging Clin Exp Res* 2011;23(2):118-25.
18. Theou O, Stathokostas L, Roland KP, et al. The effectiveness of exercise interventions for the management of frailty: a systematic review. *J Aging Res* 2011;2011:569194. doi: 10.4061/2011/569194 [published Online First: 2011/05/18]
19. Beswick AD, Rees K, Dieppe P, et al. Complex interventions to improve physical function and maintain independent living in elderly people: a systematic review and meta-analysis. *Lancet* 2008;371(9614):725-35. doi: S0140-6736(08)60342-6 [pii]10.1016/S0140-6736(08)60342-6 [published Online First: 2008/03/04]
20. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001;56(3):M146-56. [published Online First: 2001/03/17]
21. Rockwood K, Mitnitski A. Frailty in relation to the accumulation of deficits. *J Gerontol A Biol Sci Med Sci* 2007;62(7):722-7.
22. Mitnitski AB, Mogilner AJ, Rockwood K. Accumulation of deficits as a proxy measure of aging. *ScientificWorldJournal* 2001;1:323-36. doi: 10.1100/tsw.2001.58
23. Mitnitski A, Collerton J, Martin-Ruiz C, et al. Age-related frailty and its association with biological markers of ageing. *BMC Med* 2015;13:161. doi: 10.1186/s12916-015-0400-x
24. Gobbens RJ, Luijkx KG, Wijnen-Sponselee MT, et al. Towards an integral conceptual model of frailty. *J Nutr Health Aging* 2010;14(3):175-81.
25. Peters LL, Boter H, Buskens E, et al. Measurement properties of the Groningen Frailty Indicator in home-dwelling and institutionalized elderly people. *J Am Med Dir Assoc* 2012;13(6):546-51. doi: 10.1016/j.jamda.2012.04.007
26. Gobbens RJ, van Assen MA, Luijkx KG, et al. The Tilburg Frailty Indicator: psychometric properties. *J Am Med Dir Assoc* 2010;11(5):344-55. doi: 10.1016/j.jamda.2009.11.003
27. Kojima G. Frailty as a Predictor of Future Falls Among Community-Dwelling Older People: A Systematic Review and Meta-Analysis. *J Am Med Dir Assoc* 2015;16(12):1027-33. doi: 10.1016/j.jamda.2015.06.018
28. Isaacs B. Ageing and the doctor. In: Hobman D, ed. The Impact of Ageing. . London: Croom Helm 1981.
29. Inouye SK, Studenski S, Tinetti ME, et al. Geriatric syndromes: clinical, research, and policy implications of a core geriatric concept. *J Am Geriatr Soc* 2007;55(5):780-91. doi: 10.1111/j.1532-5415.2007.01156.x
30. Deandrea S, Lucenteforte E, Bravi F, et al. Risk factors for falls in community-dwelling older people: a systematic review and meta-analysis. *Epidemiology* 2010;21(5):658-68. doi: 10.1097/EDE.0b013e3181e89905 [published Online First: 2010/06/30]
31. Morrison A, Fan T, Sen SS, et al. Epidemiology of falls and osteoporotic fractures: a systematic review. *Clinicoecon Outcomes Res* 2013;5:9-18. doi: 10.2147/CEOR.S38721ceor-5-009 [pii] [published Online First: 2013/01/10]

32. Gillespie LD, Robertson MC, Gillespie WJ, et al. Interventions for preventing falls in older people living in the community. *Cochrane Database Syst Rev* 2012;9:CD007146. doi: 10.1002/14651858.CD007146.pub3
33. Tinetti ME, Williams CS. The effect of falls and fall injuries on functioning in community-dwelling older persons. *J Gerontol A Biol Sci Med Sci* 1998;53(2):M112-9. [published Online First: 1998/04/01]
34. Peeters G, van Schoor NM, Lips P. Fall risk: the clinical relevance of falls and how to integrate fall risk with fracture risk. *Best Practice & Research in Clinical Rheumatology* 2009;23(6):797-804. doi: DOI 10.1016/j.berh.2009.09.004
35. De Laet CE, van Hout BA, Burger H, et al. Incremental cost of medical care after hip fracture and first vertebral fracture: the Rotterdam study. *Osteoporos Int* 1999;10(1):66-72. doi: 90100066.198 [pii]10.1007/s001980050196 [published Online First: 1999/09/29]
36. Tinetti ME, Mendes de Leon CF, Doucette JT, et al. Fear of falling and fall-related efficacy in relationship to functioning among community-living elders. *J Gerontol* 1994;49(3):M140-7. [published Online First: 1994/05/01]
37. Jorstad EC, Hauer K, Becker C, et al. Measuring the psychological outcomes of falling: a systematic review. *J Am Geriatr Soc* 2005;53(3):501-10.
38. Tinetti ME, Kumar C. The patient who falls: "It's always a trade-off". *JAMA* 2010;303(3):258-66. doi: 303/3/258 [pii]10.1001/jama.2009.2024 [published Online First: 2010/01/21]
39. Gillespie LD, Robertson MC, Gillespie WJ, et al. Interventions for preventing falls in older people living in the community. *Cochrane Database Syst Rev* 2009(2):CD007146. doi: 10.1002/14651858.CD007146.pub2 [published Online First: 2009/04/17]
40. European Innovation Partnership on Active and Healthy Ageing. Specific Action on innovation in support of 'Personalized health management, starting with a Falls Prevention Initiative' Brussels: European Commision; 2013 [Available from: https://ec.europa.eu/eip/ageing/sites/eipaha/files/library/51a44f911f647_a2_action_plan.pdf.
41. Castro-Costa E, Dewey M, Stewart R, et al. Ascertaining late-life depressive symptoms in Europe: an evaluation of the survey version of the EURO-D scale in 10 nations. The SHARE project. *Int J Methods Psychiatr Res* 2008;17(1):12-29. doi: 10.1002/mpr.236
42. Santos-Eggimann B, Cuenoud P, Spagnoli J, et al. Prevalence of frailty in middle-aged and older community-dwelling Europeans living in 10 countries. *J Gerontol A Biol Sci Med Sci* 2009;64(6):675-81. doi: glp012 [pii]10.1093/gerona/glp012 [published Online First: 2009/03/12]
43. Etman A, Burdorf A, Van der Cammen TJ, et al. Socio-demographic determinants of worsening in frailty among community-dwelling older people in 11 European countries. *J Epidemiol Community Health* 2012;66(12):1116-21. doi: jech-2011-200027 [pii]10.1136/jech-2011-200027 [published Online First: 2012/05/01]
44. Jagger C, Gillies C, Moscone F, et al. Inequalities in healthy life years in the 25 countries of the European Union in 2005: a cross-national meta-regression analysis. *Lancet* 2008;372(9656):2124-31. doi: 10.1016/S0140-6736(08)61594-9

45. Muntaner C, Borrell C, Ng E, et al. Politics, welfare regimes, and population health: controversies and evidence. *Sociol Health Illn* 2011;33(6):946-64. doi: 10.1111/j.1467-9566.2011.01339.x
46. Mackenbach JP, Looman CW. Life expectancy and national income in Europe, 1900-2008: an update of Preston's analysis. *Int J Epidemiol* 2013;42(4):1100-10. doi: 10.1093/ije/dyt122
47. Mackenbach JP. Political conditions and life expectancy in Europe, 1900-2008. *Soc Sci Med* 2013;82:134-46. doi: 10.1016/j.socscimed.2012.12.022
48. Mackenbach JP. Cultural values and population health: a quantitative analysis of variations in cultural values, health behaviours and health outcomes among 42 European countries. *Health Place* 2014;28:116-32. doi: 10.1016/j.healthplace.2014.04.004
49. Dhanwal DK, Cooper C, Dennison EM. Geographic variation in osteoporotic hip fracture incidence: the growing importance of asian influences in coming decades. *J Osteoporos* 2010;2010:757102. doi: 10.4061/2010/757102
50. Dhanwal DK, Dennison EM, Harvey NC, et al. Epidemiology of hip fracture: Worldwide geographic variation. *Indian J Orthop* 2011;45(1):15-22. doi: 10.4103/0019-5413.73656
51. Litwic A, Edwards M, Cooper C, et al. Geographic differences in fractures among women. *Womens Health (Lond)* 2012;8(6):673-84. doi: 10.2217/whe.12.54
52. Mackenbach JP, Union UKPotE, Erasmus Universiteit R, et al. Health inequalities : Europe in profile. [London]: Produced by COI for the Dept. of Health 2006.
53. Stolz E, Mayerl H, Waxenegger A, et al. Impact of socioeconomic position on frailty trajectories in 10 European countries: evidence from the Survey of Health, Ageing and Retirement in Europe (2004-2013). *J Epidemiol Community Health* 2016 doi: 10.1136/jech-2016-207712
54. Chamberlain AM, St Sauver JL, Jacobson DJ, et al. Social and behavioural factors associated with frailty trajectories in a population-based cohort of older adults. *BMJ Open* 2016;6(5):e011410. doi: 10.1136/bmjopen-2016-011410
55. Hajizadeh M, Mitnitski A, Rockwood K. Socioeconomic gradient in health in Canada: Is the gap widening or narrowing? *Health Policy* 2016;120(9):1040-50. doi: 10.1016/j.healthpol.2016.07.019
56. Brothers TD, Theou O, Rockwood K. Frailty and migration in middle-aged and older Europeans. *Arch Gerontol Geriatr* 2014;58(1):63-8. doi: 10.1016/j.archger.2013.07.008
57. Hirsch C, Anderson ML, Newman A, et al. The association of race with frailty: the cardiovascular health study. *Ann Epidemiol* 2006;16(7):545-53. doi: 10.1016/j.annepidem.2005.10.003
58. Bandeen-Roche K, Seplaki CL, Huang J, et al. Frailty in Older Adults: A Nationally Representative Profile in the United States. *J Gerontol A Biol Sci Med Sci* 2015;70(11):1427-34. doi: 10.1093/gerona/glv133
59. Naharci MI, Engstrom G, Tappen R, et al. Frailty in Four Ethnic Groups in South Florida. *J Am Geriatr Soc* 2016;64(3):656-7. doi: 10.1111/jgs.14008
60. Pudaric S, Sundquist J, Johansson SE. Country of birth, instrumental activities of daily living, self-rated health and mortality: a Swedish population-based survey of people aged 55-74. *Soc Sci Med* 2003;56(12):2493-503.
61. Gomes B, Calanzani N, Gysels M, et al. Heterogeneity and changes in preferences for dying at home: a systematic review. *BMC Palliat Care* 2013;12:7. doi: 10.1186/1472-684X-12-7

62. Gomes B, Higginson IJ, Calanzani N, et al. Preferences for place of death if faced with advanced cancer: a population survey in England, Flanders, Germany, Italy, the Netherlands, Portugal and Spain. *Ann Oncol* 2012;23(8):2006-15. doi: 10.1093/annonc/mdr602
63. Eurostat. Healthcare personnel statistics - physicians: European Commission; 2017 [Available from: http://ec.europa.eu/eurostat/statistics-explained/index.php/Healthcare_personnel_statistics_-_physicians#Further_Eurostat_information accessed 17/11/2017 2017.
64. Kringos DS, Boerma WGW, Hutchinson A, et al. Building primary care in a changing Europe2015.
65. World Health Organization. Primary health care : now more than ever2008.
66. Hunt L. Test and learn: Working towards integrated services. *Nurs Older People* 2014;26(7):16-20. doi: 10.7748/nop.26.7.16.e624
67. Glasby J. The holy grail of health and social care integration. *BMJ* 2017;356:j801. doi: 10.1136/bmj.j801
68. Nolte E, Knai C, McKee M, et al. Managing chronic conditions : experience in eight countries. Copenhagen: World Health Organization on behalf of the European Observatory on Health Systems and Policies 2009.
69. World Health Organization Europe. Strategy and action plan for healthy ageing in Europe, 2012-2020. 2012
70. Veras RP, Caldas CP, Motta LB, et al. Integration and continuity of Care in health care network models for frail older adults. *Rev Saude Publica* 2014;48(2):357-65.
71. Waterson P, Eason K, Tutt D, et al. Using HIT to deliver integrated care for the frail elderly in the UK: current barriers and future challenges. *Work* 2012;41 Suppl 1:4490-3. doi: 10.3233/WOR-2012-0750-4490
72. Metzelthin SF, van Rossum E, de Witte LP, et al. The reduction of disability in community-dwelling frail older people: design of a two-arm cluster randomized controlled trial. *BMC Public Health* 2010;10:511. doi: 1471-2458-10-511 [pii]10.1186/1471-2458-10-511 [published Online First: 2010/08/25]
73. Fabbricotti IN, Janse B, Looman WM, et al. Integrated care for frail elderly compared to usual care: a study protocol of a quasi-experiment on the effects on the frail elderly, their caregivers, health professionals and health care costs. *BMC Geriatr* 2013;13:31. doi: 1471-2318-13-31 [pii]10.1186/1471-2318-13-31 [published Online First: 2013/04/17]
74. Ruikes FG, Meys AR, van de Wetering G, et al. The CareWell-primary care program: design of a cluster controlled trial and process evaluation of a complex intervention targeting community-dwelling frail elderly. *BMC Fam Pract* 2012;13:115. doi: 1471-2296-13-115 [pii]10.1186/1471-2296-13-115 [published Online First: 2012/12/12]
75. Ellis G, Whitehead MA, Robinson D, et al. Comprehensive geriatric assessment for older adults admitted to hospital: meta-analysis of randomised controlled trials. *BMJ* 2011;343:d6553. doi: 10.1136/bmj.d6553
76. Rubenstein LZ, Josephson KR, Wieland GD, et al. Effectiveness of a Geriatric Evaluation Unit. *New England Journal of Medicine* 1984;311(26):1664-70. doi: 10.1056/nejm198412273112604

77. Morley JE, Arai H, Cao L, et al. Integrated Care: Enhancing the Role of the Primary Health Care Professional in Preventing Functional Decline: A Systematic Review. *J Am Med Dir Assoc* 2017;18(6):489-94. doi: 10.1016/j.jamda.2017.03.015
78. Stuck AE, Egger M, Hammer A, et al. Home visits to prevent nursing home admission and functional decline in elderly people: systematic review and meta-regression analysis. *JAMA* 2002;287(8):1022-8. doi: jma10044 [pii] [published Online First: 2002/02/28]
79. Huss A, Stuck AE, Rubenstein LZ, et al. Multidimensional preventive home visit programs for community-dwelling older adults: a systematic review and meta-analysis of randomized controlled trials. *J Gerontol A Biol Sci Med Sci* 2008;63(3):298-307. doi: 63/3/298 [pii] [published Online First: 2008/04/01]
80. Mayo-Wilson E, Grant S, Burton J, et al. Preventive home visits for mortality, morbidity, and institutionalization in older adults: a systematic review and meta-analysis. *PLoS One* 2014;9(3):e89257. doi: 10.1371/journal.pone.0089257PONE-D-13-47215 [pii] [published Online First: 2014/03/14]
81. Bouman A, van Rossum E, Nelemans P, et al. Effects of intensive home visiting programs for older people with poor health status: a systematic review. *BMC Health Serv Res* 2008;8:74. doi: 1472-6963-8-74 [pii]10.1186/1472-6963-8-74 [published Online First: 2008/04/05]
82. Looman WM, Fabbricotti IN, de Kuyper R, et al. The effects of a pro-active integrated care intervention for frail community-dwelling older people: a quasi-experimental study with the GP-practice as single entry point. *BMC Geriatr* 2016;16:43. doi: 10.1186/s12877-016-0214-5
83. Rowe JW, Kahn RL. Human aging: usual and successful. *Science* 1987;237(4811):143-9.
84. World Health Organization. Active ageing : a policy framework. Geneva, Switzerland: World Health Organization 2002.
85. Börsch-Supan A, Alcser KH, Mannheim Research Institute for the Economics of A. The survey of health, aging [ageing], and retirement in Europe methodology ; [SHARE, survey of health, ageing and retirement in Europe]. Mannheim: MEA 2005.
86. Lutomski JE, Baars MA, Schalk BW, et al. The development of the Older Persons and Informal Caregivers Survey Minimum DataSet (TOPICS-MDS): a large-scale data sharing initiative. *PLoS One* 2013;8(12):e81673. doi: 10.1371/journal.pone.0081673
87. BeterOud. Nationaal Programma Ouderenzorg 2017 [Available from: http://www.beteroud.nl/ouderen/nationaal-programma-ouderenzorg-npo.html.

Part 1

Variation in healthy ageing among older persons in Europe

Chapter 2

Socioeconomic inequalities in frailty and frailty components among community-dwelling older citizens

Carmen B. Franse, Amy van Grieken, Li Qin, René J. F. Melis, Judith A. C. Rietjens, Hein Raat

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ABSTRACT

Background

So far, it has not yet been studied whether socioeconomic status is associated with distinct frailty components and for which frailty component this association is the strongest. We aimed to examine the association between socioeconomic status and frailty and frailty components. In addition we assessed the mediating effect of the number of morbidities on the association between socioeconomic status and other frailty components.

Methods

This is a cross-sectional study of pooled data of The Older Persons and Informal Caregivers Survey Minimum DataSet in the Netherlands among community-dwelling persons aged 55 years and older (n=26,014). Frailty was measured with a validated Frailty Index that consisted of 45 items. The Frailty Index contained six components: morbidities, limitations in activities of daily living (ADL), limitations in instrumental ADL (IADL), health-related quality of life, psychosocial health and self-rated health. Socioeconomic indicators used were education level and neighbourhood socioeconomic status.

Results

Persons with primary or secondary education had higher overall frailty and frailty component scores compared to persons with tertiary education (P<.001). Lower education levels were most consistently associated with higher overall frailty, more morbidities and worse self-rated health (P<.05 in all age groups). The strongest association was found between primary education and low psychosocial health for persons aged 55-69 years and more IADL limitations for persons aged 80+ years. Associations between neighborhood socioeconomic status and frailty (components) also showed inequalities, although less strong. The number of morbidities moderately to strongly mediated the association between socioeconomic indicators and other frailty components.

Conclusion

There are socioeconomic inequalities in frailty and frailty components. Inequalities in frailty, number of morbidities and self-rated health are most consistent across age groups. The number of morbidities a person has play an important role in explaining socioeconomic inequalities in frailty and should be taken into account in the management of frailty.

INTRODUCTION

Frailty can be defined as a state of increased vulnerability to external stressors and adverse outcomes such as death and hospitalization[1 2]. Frailty is a better predictor of adverse outcomes than age[3]. Hence, it is important to identify persons or groups at risk of developing frailty in order to target prevention strategies. Older persons with a low socioeconomic status (SES) are more frail and become more frail over time compared to persons with a high SES[4-6]. Many indicators of SES such as education level, occupation, income and wealth have been linked to frailty[4 7-9].

A widely used approach to measure frailty is the accumulation-of-deficits approach that results in a Frailty Index (FI)[10 11]. The FI is calculated by adding up the number of health deficits a person has, divided by the total of possible health deficits included in the index. Theou et al. found that of eight commonly use frailty scales, the FI most accurately predicted mortality[12]. A standard procedure to construct a FI was developed by Searle et al., who recommended to include the following components in the index: morbidities, disability in Activities of Daily Living (ADL) and Instrumental ADL (IADL), restricted activity, impairments in general cognition and physical performance, psychological health and self-rated health (SRH)[13]. In addition to the study of 'overall' frailty, the assessment of frailty components could uncover important information about the specific domain in which a person is frail. Recently, Yang et al. have studied the associations of frailty components with mortality and found that IADL and ADL limitations played a greater role in mortality compared to other components[14].

It is not yet studied which frailty component contributes most strongly to socioeconomic inequalities in frailty. By uncovering this, interventions could be directed towards narrowing the gap in frailty between persons with a higher versus a lower SES. In the FI approach and other frailty measures such as the FRAIL scale, morbidities are considered as part of frailty[2 12]. Theoretically morbidities precede the other frailty components of the FI, as proposed in different health models[15 16]. Having certain morbidities at a younger age, such as depression or cardiovascular disease, could lead to an increase in ADL and/or IADL limitations at older age[17]. Studies using Fried's frailty phenotype have showed that both number and specific morbidities such as obesity partly explained why persons with a lower SES were more frail compared to persons with a higher SES[9 18]. Therefore we hypothesize that the presence of morbidities could mediate the association between SES and other components of the FI.

The aim of this study was, 1) to assess the association between SES indicators and a) 'overall' frailty and b) the distinct frailty components (morbidities, ADL, IADL, health-related quality of life (HRQoL), psychosocial health and SRH), and 2) to assess whether and to what extent the number of morbidities mediates the association between SES and the other frailty components (ADL, IADL, HRQoL, psychosocial health and SRH).

METHODS

Study design and population

We applied a cross-sectional study design using data from The Older Persons and Informal Caregivers Survey Minimum DataSet (TOPICS-MDS)[19]. TOPICS-MDS is a data-base designed to capture information on the well-being of older persons in the Netherlands. TOPICS-MDS was developed to collect uniform information from studies funded under the National Care for older citizens Programme[20]. Included survey items were based on the recommendations of experts who identified key outcomes in older persons' health[19]. Data were collected between 2010 and 2013 in 50 studies in the Netherlands. TOPICS-MDS consists of pooled data of these studies which differ across study design, sampling framework, and inclusion criteria. TOPICS-MDS is a fully anonymized data set, and therefore this analysis was exempt from ethical review (Radboud University Medical Centre Ethical Committee review reference number: CMO: 2012/120).

Our analysis was restricted to data from independently living Dutch persons aged 55 years and older. We further excluded persons with more than 15 missing items for the FI (n=3658), missing education level (n=221) or country of birth (n=1569). The final sample comprised of data from 30 studies of 26,014 persons (see figure 1).

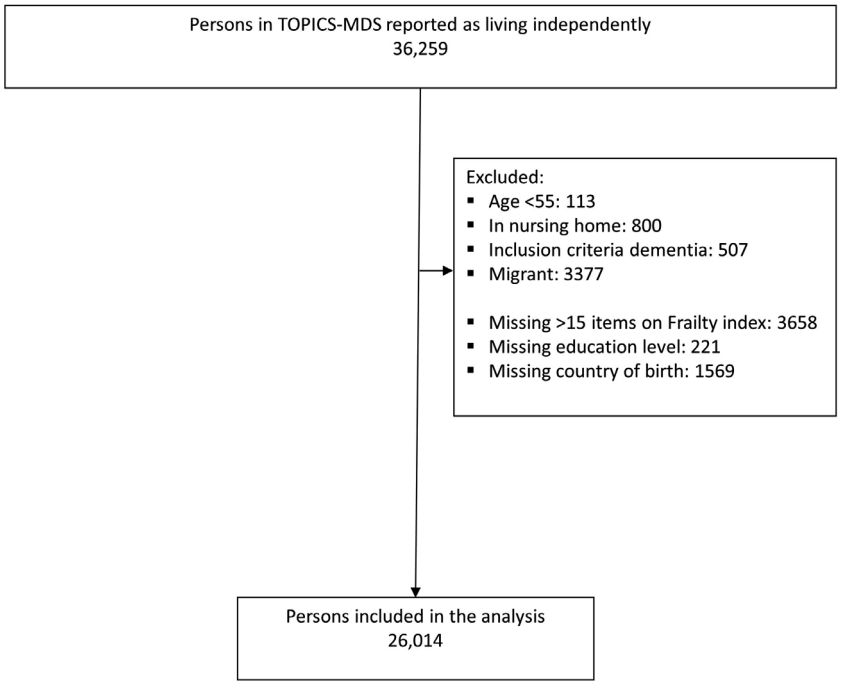

Figure 1: Population of analysis.

Frailty and components

Frailty was measured by the TOPICS-Frailty Index (TOPICS-FI), which was developed and validated using TOPICS-MDS data by Lutomski et al.[21]. In our study we included the 45 item TOPICS-FI, after exclusion of the item measuring prostatism. Searle et al. showed that a FI with 30–40 variables is accurate for predicting adverse outcomes[13 22]. The TOPICS-FI was calculated when at least 30 items were available. This was done by adding up the number of health deficits a person reported, divided by the total health deficits measured for this person, following Searle et al.[13]. This resulted in a score between 0-1, where higher scores represent higher frailty.

The TOPICS-FI as used in this study consists of 45 items that belong to six components, each measured by validated instruments; morbidities, ADL, IADL, HRQoL, psychosocial health and SRH[13]. The component 'Morbidities' was measured by 16 items regarding the self-reported presence (yes/no) of diabetes, stroke, heart failure, cancer, respiratory condition (asthma, chronic bronchitis, lung emphysema or Chronic obstructive pulmonary disease (COPD), incontinence, joint damage of hips or knees, osteoporosis, hip fracture, fractures other than hip, dizziness with falling, depression, anxiety/panic disorder, dementia, hearing problems, vision problems. The component 'ADL limitations' was measured by 6 items using a modified version of the Katz instrument[23 24]. Persons could indicate whether they needed help (yes/no) with the following activities: bathing, dressing, toileting, incontinence, sitting down, eating. The component 'IADL limitations' was measured by 9 items using a modified version of the Katz instrument[23 24]. Persons could indicate whether they needed help (yes/no) with the following activities: using the telephone, travelling, shopping, preparing a meal, cleaning, taking medications, handling finance, brushing hair and walking. The component 'HRQoL' was measured by 6 items of the EuroQol 5D+C[25]. Persons could indicate whether they had problems (no/some/extreme) with the following: mobility, self-care, usual activities, pain/discomfort, anxiety/depression and cognition. The component 'Psychosocial health' was measured with 5 items of the RAND-36 [26]. Persons could indicate how much of the time in the past month (none/a little/ some/a good bit/most/all) they had been the following: nervous, calm, downhearted, happy and down in the dumps, and how much time (none/a little/some/most/all) health problems had interfered with social activities. The component 'SRH' was measured with 2 items of the RAND-36[26], one regarding perceived current health status (poor/fair/good/very good/excellent) and one regarding perceived changes in health in the past year (much worse/slightly worse/about the same/a little better/much better). The score for each component of the TOPICS-FI were calculated analogous to the FI, by adding up the health deficits within the FI component that a person had, divided by the total of possible health deficits included in the component[13]. This resulted in a score between 0-1, where higher scores represent worse health. We accepted no missing variables for SRH and a maximum of 1 of 3 missing variables for other FI component scores.

Indicators of SES

In this study we applied two indicators of SES; education level and neighbourhood SES. TOPICS-MDS used the 1997 International Standard Classification of Education[27] to assess education level; participants were asked whether they had completed: fewer than 6 years of primary school; 6 years of primary school; further uncompleted education; vocational school; secondary professional education or university entrance level or tertiary education. We categorized the education level into "primary education or less", "secondary education" and "tertiary education or higher", based on the definition by Statistics Netherlands[28].

For the neighbourhood SES, the 2006 reference scores for area codes were used, as calculated by The Netherlands Institute for Social Research[29] based on the education level, income and labor market position of persons living in each area code. Scores were categorized into quartiles, quartile 1 is the least deprived quartile (high education, high income, high labor market position), while quartile 4 is the most deprived.

Potential confounders

Gender, age, living arrangement, marital status and level of urbanization were incorporated as potential confounders in this study based on literature and availability in TOPICS-MDS. Age was assessed by asking year of birth. Living arrangement was assessed by asking whether participants were living: independent alone, independent with others, care or nursing home. Only persons living independently were included and categorized into "not alone" and "alone". Marital status was assessed by asking whether participants were: married, divorced, widowed, unmarried, long term cohabitation unmarried. Answers were categorized into "married/cohabitant partners", "divorced", "widowed" and "single". Level of urbanization was based on the density of addresses in an area code and categorized as by Statistics Netherlands into "not urban", "little urban", "somewhat urban", "urban" and "very urban"[30].

Statistical analysis

The statistical significance of differences in socio-demographic characteristics, frailty and frailty components (morbidities, ADL limitations, IADL limitations, psychosocial health, HRQoL and SRH) among persons from different education levels was calculated using chi-squared tests for categorical variables and one-way ANOVA for continues variables.

To examine the association between SES, frailty and frailty components (model 1), we estimated multilevel random-intercept models because data were clustered in studies[31]. As such, dependency between the observations of participants of a study because of sampling design and/or inclusion criteria, was taken into account. Only potential confounders that led to a substantial change in effect estimates (i.e. ≥10% change) were included in models[32]. Subsequently, we examined the presence of mediation by the number of morbidities in

the association between SES and other frailty components, by following the causal step approach proposed by Baron and Kenny (figure 2)[33]. When SES indicators were significantly associated with the morbidities component and when the morbidities component was significantly associated with the other frailty components, the morbidities component was considered a 'true' mediator. Only then, the morbidities component was added to model 1 (model 2). To assess the mediating effect, the percentages of attenuation of effect estimates were calculated by comparing model 2 relative to model 1.

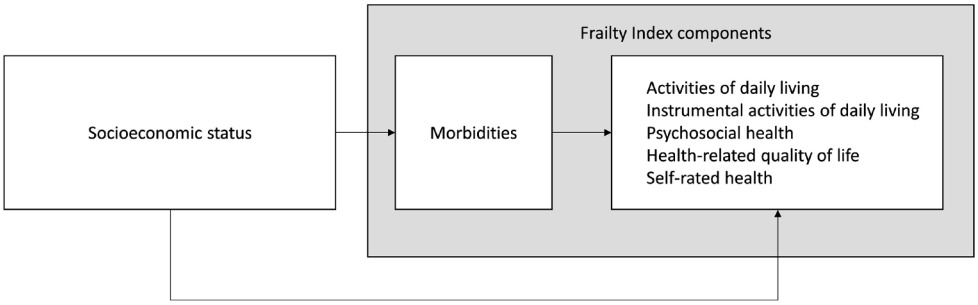

Figure 2: Conceptual framework for the association between socioeconomic status and Frailty Index components, where the morbidities component mediates the association between socioeconomic status and other Frailty Index components.

We explored the presence of interaction between the indicators of SES and sex, age and living arrangement in the association between SES and frailty and frailty components. We also explored interaction between the indicators of SES and morbidities (exposure-mediator interaction) in the association between SES and frailty and frailty components. After applying Bonferroni correction for multiple testing[34], we found significant interactions between SES and age on overall frailty and on all frailty components, and therefore stratified all analyses by age in three groups: 55-69 years, 70-79 years, and 80 years and older.

Percentages of missing values in the potential confounders were 2% or less (table 1). Missing data on potential confounders were imputed using multiple imputation. We computed five imputation datasets using a fully conditional specified model[35]. Pooled estimates from these datasets were used to report regression coefficients and 95% confidence intervals (CIs). We considered a p-value of .05 or lower to be statistically significant for main analyses and used Bonferroni correction for testing interactions[34]. Descriptive analyses were performed using SPSS version 23.0 (IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp). Multilevel linear regression analysis were performed using R-3.3.2.

Non-response analysis

A comparison of persons included in the study (N=26,014) with persons not included due to missing values for education level, FI and/or country of birth (N=5448) did not indicate significant differences in terms of sex (p=.882) and living arrangement (p=.113). However, excluded persons were older (p<.001), more often single (p<.05), more often living in rural areas and in deprived neighbourhoods (p<.001) than persons included in the study.

RESULTS

Table 1 shows the characteristics of the study population. Of all persons, 10.5% of the persons had tertiary education, and 32.8% had primary education or less. Compared with persons who received tertiary education, persons who received primary education or less were older, more often female, more often living alone, more often widowed and less often married, single or divorced and more often living in deprived neighbourhoods (P<.001). Frailty was highest in persons who received primary education or less (mean=0.23; SD=0.13), followed by persons who received secondary education (mean=0.20; SD=0.12) and persons who received tertiary education (mean=0.16; SD=0.11).

Education level was significantly associated with frailty; frailty was higher in persons of all age groups with secondary and primary or less education as compared to persons with tertiary education (p<.05; table 2-model 1). This was also found for the frailty components morbidities and SRH. Persons with lower education levels generally had higher scores (i.e. worse health) for IADL limitations, psychosocial health and HRQoL, although not significant in all age groups for secondary education. ADL limitations were only worse in persons aged 70-79 years with primary education or less compared to persons with tertiary education (p<.05). Among all frailty components, the association between education level and psychosocial health was strongest in persons aged 55-69 years, while for persons aged 80+ years this was IADL limitations. For frailty and all frailty components except IADL limitations, stronger associations were observed in persons aged 55-69 compared to older age groups. The number of morbidities mediated the association between education level and other frailty components, attenuations ranged between 19% and 80% (table 2-model 2).

Neighbourhood SES was significantly associated with frailty, morbidities, IADL limitations, psychosocial health, HRQoL and SRH (p<.05; table 3-model 1). Persons living in more deprived neighbourhoods (third or fourth quartile) had higher scores compared to those living in the least deprived neighbourhoods (first quartile). The number of morbidities mediated the association between neighbourhood SES and other frailty components, attenuations ranged between 20% and 90% (table 3-model 2).

Table 1: Socio-demographic characteristics and frailty outcomes by education level of 26,014 persons of The Older Persons and Informal Caregivers Survey Minimum DataSet (TOPICS-MDS).

		Education level			
	Total N=26,014	**Tertiary N=2723**	**Secondary N=14,762**	**Primary or less N=8529**	***P*-value***
Age in years (mean, SD)	78.0 (6.8)	76.1 (7.1)	77.7 (6.7)	79.3 (6.7)	<0.001
Sex, N (%)					<0.001
Male	10,825 (41.6)	1800 (66.1)	6394 (43.3)	2631 (30.8)	
Female	15,189 (58.4)	923 (33.9)	8268(56.7)	5898 (69.2)	
Living arrangement, N (%)					<0.001
Alone	11,689 (44.9)	860 (31.6)	6377 (43.2)	4452 (52.2)	
With others	14,325 (55.1)	1863 (68.4)	8385 (56.8)	4077 (47.8)	
Marital status, N (%)					<0.001
Married/Cohabitant partners	13,954 (53.6)	1836 (67.4)	8261 (56.0)	3857 (45.2)	
Divorced	1562 (6.0)	189 (7.0)	878 (5.9)	494 (5.8)	
Widowed	9288 (35.7)	491 (18.0)	4940 (33.5)	3857 (45.2)	
Single	1211 (4.7)	206 (7.6)	684 (4.6)	321 (3.8)	
Neighbourhood SES, N (%)					<0.001
First quartile	7277 (28.5)	1298 (48.2)	4369 (30.1)	1610 (19.4)	
Second quartile	6988 (27.4)	649 (24.1)	4012 (27.7)	2327 (28.0)	
Third quartile	5259 (20.6)	427 (15.9)	2958 (20.4)	1874 (22.6)	
Fourth quartile	5970 (23.4)	320 (11.9)	3165 (21.8)	2485 (30.0)	
Level of urbanization, N (%)					<0.001
Not urban	5802 (22.3)	592 (21.7)	3232 (21.9)	1978 (23.2)	
Little urban	7031 (27.0)	578 (21.2)	4177 (28.3)	2277 (26.7)	
Somewhat urban	4114 (15.8)	637 (23.4)	2410 (16.3)	1067 (12.5)	
Urban	6313 (24.3)	704 (25.9)	3497 (23.7)	2112 (24.8)	
Very urban	2754 (10.6)	213 (7.8)	1445 (9.8)	1096 (12.8)	
Overall Frailty mean FI (SD)†	0.20 (0.12)	0.16 (0.11)	0.20 (0.12)	0.23 (0.13)	<0.001
Morbidities, mean FI (SD)†	0.17 (0.12)	0.14 (0.11)	0.16 (0.12)	0.18 (0.13)	<0.001
Number morbidities, mean (SD)	2.61 (1.90)	2.16 (1.69)	2.55 (1.87)	2.88 (1.98)	<0.001
ADL limitations, mean FI (SD)†	0.11 (0.19)	0.08 (0.17)	0.11 (0.19)	0.13 (0.20)	<0.001
Number ADL limitations, mean (SD)	0.65 (1.10)	0.47 (0.97)	0.62 (1.08)	0.78 (1.16)	<0.001
IADL limitations, mean FI (SD)†	0.21 (0.24)	0.14 (0.21)	0.20 (0.23)	0.26 (0.25)	<0.001
Number IADL limitations, mean (SD)	1.48 (1.67)	0.96 (1.47)	1.39 (1.62)	1.81 (1.74)	<0.001
Psychosocial health, mean FI (SD)†	0.26 (0.18)	0.22 (0.16)	0.25 (0.17)	0.28 (0.19)	<0.001
Health-related quality of life, mean FI (SD)†	0.22 (0.17)	0.18 (0.16)	0.21 (0.17)	0.25 (0.17)	<0.001
Self-rated Health, mean FI (SD)†	0.58 (0.17)	0.54 (0.17)	0.57 (0.17)	0.60 (0.17)	<0.001

* P-values are based on Chi-squared test for categorical variables and one-way ANOVA for continues variables.
† Mean FI=mean number of health deficits reported/total health deficits measured in instrument; score between 0-1 where higher scores represent worse health. Missing N (%) for variables: Age=544 (2%); sex=8 (<1%); living arrangement=0 (0%); marital status=50 (<1%); Neighbourhood SES=520 (2%); Level of urbanization=199 (1%); morbidities=531 (2%); ADL=45 (<1%); IADL=124 (<1%); psychosocial health=281 (1%); Health-related quality of life=521 (2%); Self-rated health=100 (<1%). FI=frailty index; (I)ADL= (instrumental) activities of daily living; SES=socioeconomic status.

Table 2. Association of education level with overall frailty and with its six components (Model 1) and change in association of education level with the five other frailty components after adjustment for the morbidities component (Model 2); stratified by age group among 26,014 persons of The Older Persons and Informal Caregivers Survey Minimum DataSet (TOPICS-MDS).

	Overall Frailty	Morbidities	ADL limitations		IADL limitations		Psychosocial health		Health-related quality of life		Self-rated health	
	B (95% CI)	B (95% CI)	B (95% CI)	%†	B (95% CI)	%†	B (95% CI)	%†	B (95% CI)	%†	B (95% CI)	%†
Model 1												
Age 55-69 years												
Secondary education	0.016** (0.005-0.026)	0.019*** (0.008-0.030)	0.007 (-0.008-0.022)		0.005 (-0.013-0.023)		0.016 (-0.003-0.036)		0.020* (0.003-0.038)		0.028** (0.011-0.046)	
≤ Primary education	0.047*** (0.035-0.059)	0.052*** (0.039-0.064)	0.013 (-0.005-0.030)		0.034** (0.013-0.055)		0.074*** (0.051-0.096)		0.056*** (0.036-0.076)		0.064*** (0.044-0.085)	
Age 70-79 years												
Secondary education	0.007* (0.001-0.013)	0.008** (0.002-0.014)	-0.002 (-0.010-0.007)		0.011* (0.000-0.021)		0.006 (-0.003-0.015)		0.005 (-0.004-0.014)		0.016*** (0.007-0.025)	
≤ Primary education	0.027*** (0.021-0.033)	0.022*** (0.015-0.028)	0.010* (0.000-0.019)		0.039*** (0.028-0.051)		0.034*** (0.024-0.044)		0.029*** (0.019-0.038)		0.043*** (0.033-0.053)	
Age ≥ 80 years												
Secondary education	0.015*** (0.006-0.024)	0.012** (0.003-0.021)	0.001 (-0.014-0.016)		0.019* (0.001-0.036)		0.022*** (0.009-0.035)		0.018** (0.005-0.031)		0.014* (0.001-0.026)	
≤ Primary education	0.026*** (0.017-0.036)	0.019*** (0.009-0.028)	0.012 (-0.003-0.028)		0.044*** (0.026-0.063)		0.026*** (0.012-0.040)		0.033*** (0.019-0.046)		0.022*** (0.007-0.035)	
Model 2												
Age 55-69 years												
Secondary education	NA	NA	0.001 (-0.014-0.16)	NA	-0.003 (-0.021-0.014)	NA	0.003 (-0.015-0.022)	NA	0.009 (-0.007-0.025)	55%	0.017* (0.001-0.034)	39%
≤ Primary education	NA	NA	-0.003 (-0.021-0.014)	NA	0.014 (-0.007-0.034)	59%	0.040*** (0.019-0.062)	46%	0.026** (0.007-0.044)	54%	0.036*** (0.016-0.056)	44%
Age 70-79 years												
Secondary education	NA	NA	-0.005 (-0.014-0.004)	NA	0.006 (-0.004-0.016)	45%	0.002 (-0.007-0.011)	NA	0.001 (-0.007-0.008)	NA	0.013** (0.004-0.021)	19%
≤ Primary education	NA	NA	0.002 (-0.008-0.011)	80%	0.028*** (0.017-0.039)	28%	0.024*** (0.014-0.034)	29%	0.016*** (0.007-0.025)	45%	0.032*** (0.023-0.042)	26%

Table 2 continued

	Overall Frailty	Morbidities	ADL limitations		IADL limitations		Psychosocial health		Health-related quality of life		Self-rated health	
	B (95% CI)	B (95% CI)	B (95% CI)	%†	B (95% CI)	%†	B (95% CI)	%†	B (95% CI)	%†	B (95% CI)	%†
Age ≥ 80 years												
Secondary education	NA	NA	-0.005 (-0.020-0.010)	NA	0.011 (-0.006-0.028)	42%	0.016** (0.003-0.028)	27%	0.010 (-0.002-0.022)	44%	0.008 (-0.004-0.020)	43%
≤ Primary education	NA	NA	0.003 (-0.012-0.019)	NA	0.032*** (0.015-0.050)	27%	0.017** (0.003-0.030)	35%	0.021*** (0.008-0.033)	36%	0.013* (0.001-0.025)	41%

Values are derived from multilevel multivariable linear regression, tertiary education is the reference group. Model 1 is adjusted for confounders: age, sex, and living arrangement (alone/not alone). Model 2 is additionally adjusted for morbidities. * p<0.05; ** p<0.01; ** p<0.001. † % represents the % change in effect estimates relative to model 1 after adjustment for morbidities; this was calculated by: 100x $((B_{model1}-B_{model2})/B_{model1})$. B=effect estimate; CI=confidence interval; (I)ADL=(instrumental) activities of daily living.

Table 3. Association of neighbourhood socioeconomic status with overall frailty and with its six components (Model 1) and change in association of neighbourhood socioeconomic status with the five other frailty components after adjustment for the morbidities component (Model 2); stratified by age group among 25,494 persons of The Older Persons and Informal Caregivers Survey Minimum DataSet (TOPICS-MDS).

	Overall Frailty	Morbidities	ADL limitations		IADL limitations		Psychosocial health		Health-related quality of life		Self-rated health	
	B (95% CI)	B (95% CI)	B (95% CI)	%†	B (95% CI)	%†	B (95% CI)	%†	B (95% CI)	%†	B (95% CI)	%†
Model 1												
Age 55-69 years												
Second quartile	0.008 (-0.004-0.020)	0.006 (-0.007-0.018)	0.005 (-0.012-0.022)		-0.005 (-0.025-0.016)		0.020 (-0.002-0.042)		0.017 (-0.003-0.036)		0.021* (0.0011-0.041)	
Third quartile	0.012* (0.001-0.023)	0.013 (-0.001-0.025)	-0.004 (-0.021-0.012)		0.005 (-0.015-0.025)		0.023* (0.001-0.044)		0.028** (0.010-0.047)		0.021* (0.001-0.040)	
Fourth quartile	0.023*** (0.012-0.033)	0.025*** (0.014-0.036)	-0.002 (-0.017-0.013)		0.016 (-0.002-0.034)		0.043*** (0.024-0.063)		0.028** (0.011-0.045)		0.036*** (0.018-0.053)	
Age 70-79 years												
Second quartile	0.003 (-0.001-0.008)	0.007** (0.002-0.012)	-0.001 (-0.008-0.006)		0.000 (-0.009-0.009)		0.001 (-0.007-0.009)		0.006 (-0.001-0.013)		0.002 (-0.006-0.009)	
Third quartile	0.010*** (0.004-0.015)	0.012*** (0.006-0.018)	0.002 (-0.006-0.010)		0.007 (-0.003-0.017)		0.010* (0.001-0.018)		0.013** (0.005-0.022)		0.008 (-0.001-0.017)	
Fourth quartile	0.014*** (0.008-0.019)	0.015*** (0.009-0.021)	0.004 (-0.005-0.012)		0.010* (0.000-0.021)		0.016*** (0.007-0.025)		0.018*** (0.009-0.026)		0.025*** (0.016-0.033)	
Age ≥ 80 years												
Second quartile	0.005 (-0.001-0.011)	0.006 (-0.001-0.012)	0.002 (-0.008-0.013)		0.012 (-0.001-0.024)		-0.003 (-0.012-0.007)		0.010* (0.001-0.019)		-0.002 (-0.011-0.007)	
Third quartile	0.003 (-0.004-0.010)	0.008* (0.001-0.015)	-0.002 (-0.014-0.010)		0.002 (-0.012-0.015)		0.000 (-0.011-0.010)		0.003 (-0.007-0.013)		0.003 (-0.007-0.013)	
Fourth quartile	0.012*** (0.005-0.019)	0.008* (0.001-0.015)	0.004 (-0.008-0.016)		0.017* (0.003-0.030)		0.017** (0.006-0.027)		0.025*** (0.015-0.035)		0.010* (0.000-0.020)	

Table 3 continued

	Overall Frailty	Morbidities	ADL limitations		IADL limitations		Psychosocial health		Health-related quality of life		Self-rated health	
	B (95% CI)	B (95% CI)	B (95% CI)	%†	B (95% CI)	%†	B (95% CI)	%†	B (95% CI)	%†	B (95% CI)	%†
Model 2												
Age 55-69 years												
Second quartile	NA	NA	0.003 (-0.014-0.20)	NA	-0.007 (-0.027-0.013)	NA	0.015 (-0.006-0.036)	NA	0.014 (-0.005-0.032)	NA	0.019* (0.000-0.038)	NA
Third quartile	NA	NA	-0.007 (-0.023-0.009)	NA	0.001 (-0.019-0.020)	NA	0.015 (-0.005-0.035)	NA	0.023** (0.006-0.040)	NA	0.015 (-0.003-0.033)	NA
Fourth quartile	NA	NA	-0.009 (-0.024-0.006)	NA	0.005 (-0.013-0.022)	NA	0.027** (0.008-0.045)	37%	0.014 (-0.002-0.029)	50%	0.022** (0.005-0.039)	39%
Age 70-79 years												
Second quartile	NA	NA	-0.004 (-0.011-0.004)	NA	-0.004 (-0.013-0.004)	NA	-0.003 (-0.010-0.005)	NA	0.002 (-0.004-0.009)	NA	-0.002 (-0.010-0.005)	NA
Third quartile	NA	NA	-0.003 (-0.011-0.005)	NA	0.000 (-0.010-0.010)	NA	0.003 (-0.006-0.011)	70%	0.006 (-0.002-0.014)	54%	0.000 (-0.008-0.008)	NA
Fourth quartile	NA	NA	-0.003 (-0.011-0.006)	NA	0.001 (-0.008-0.011)	90%	0.008 (-0.001-0.016)	50%	0.008* (0.001-0.016)	56%	0.016*** (0.007-0.024)	36%
Age ≥ 80 years												
Second quartile	NA	NA	0.000 (-0.011-0.010)	NA	0.008 (-0.004-0.020)	NA	-0.006 (0.015-0.003)	NA	0.006 (-0.002-0.015)	NA	-0.005 (-0.014-0.003)	NA
Third quartile	NA	NA	-0.006 (-0.017-0.006)	NA	-0.004 (-0.017-0.010)	NA	-0.004 (-0.014-0.006)	NA	-0.001 (-0.010-0.008)	NA	-0.001 (-0.011-0.008)	NA
Fourth quartile	NA	NA	0.001 (-0.010-0.013)	NA	0.012 (-0.001-0.026)	29%	0.013** (0.003-0.023)	24%	0.020*** (0.011-0.030)	20%	0.007 (-0.003-0.016)	30%

Values are derived from multilevel multivariable linear regression, First Quartile is the reference group. Model 1 is adjusted for confounders: age, sex, and living arrangement (alone/not alone). Model 2 is additionally adjusted for morbidities.* p<0.05; ** p<0.01; ** p<0.001. † % represents the % change in effect estimates relative to model 1 after adjustment for morbidities; this was calculated by: 100x ((B_{model1}-B_{model2})/B_{model1}). B=effect estimate; CI=confidence interval; (I)ADL=(instrumental) activities of daily living.

DISCUSSION

This study showed that persons with the lowest SES, e.g. the lowest education level or living in the most deprived neighbourhoods, had the highest overall frailty and frailty component scores. The number of morbidities mediated the association between SES indicators and other frailty components.

In our study, education level was most consistently associated with overall frailty, morbidities and SRH. Former research found that lower educated persons are on average more frail compared to higher educated persons[5-8]. Education level has been associated with frailty components, such as ADL, IADL and SRH, although few studies compare multiple outcomes[36-38]. We found associations of neighborhood SES as indicator of individual SES with frailty and with frailty components, but these were generally less strong. Additionally, we examined the isolated effect of neighbourhood SES after adjustment for individual education level and found consistent associations for the most deprived neighbourhoods (S1 table). Few studies have investigated the association between neighbourhood SES and frailty[39]. The association between the SES indicators and ADL limitations was not consistent in our study, which might be due to a ceiling effect for the instrument used in a community-dwelling population[40].

We found the strongest association between education level and psychosocial health for persons aged 55-69 years and with IADL limitations for persons aged 80 years and over. Vaughan et al. found that persons who had no cardiovascular disease when aged between 65-80 years maintained good physical functioning over the age of 80 years[17]. As certain morbidities are more prevalent among persons with a lower SES, this could at a younger age result in worse psychosocial health or self-rated health, but may as one ages increasingly impact on functional health[17 41]. Socioeconomic inequalities in frailty and all frailty components except for IADL limitations, were larger among persons aged 55-69 years compared to older persons. This finding is often explained by a 'healthy survivor effect', where unhealthier persons with a low SES have died at a younger age and is found in cross-sectional research for various health outcomes[42-45]. However, longitudinal research has found confirming and contradicting results, depending on the indicator by which SES and health is measured[4 46]. Further research is needed to understand the mechanisms behind these findings.

The number of morbidities moderately to strongly mediated the association between SES indicators and other frailty components. Former research has found that both specific morbidities and number of morbidities mediate socioeconomic inequalities in frailty[9 18 47 48]. Hoogendijk et al. found that cognitive impairment, obesity, and number of chronic diseases had the largest contributions to socioeconomic inequalities in frailty[18], while Soler-Vila et

al. found largest contributions for obesity, depression and musculoskeletal disease[9]. These studies have looked at physical frailty as developed by Fried[49]. A study by Gobbens et al. that used a multidimensional concept of frailty found that multi-morbidity could explain income differences in psychological and physical frailty, but not social frailty[47]. More longitudinal research is needed on the role of specific morbidities and number of morbidities in explaining socioeconomic inequalities in frailty and frailty components. Furthermore, this means that frailty and morbidities more often coexist in persons with a low SES. It is important to manage the progression of morbidities in this group, as the presence of frailty in persons with chronic diseases such as diabetes and COPD has shown to strongly increase mortality[50 51].

The main strengths of this study are the size and diversity of the study population, this study included data from a large number of older persons from different regions in the Netherlands. Furthermore, we used validated instruments to measure frailty and frailty components. This study has some limitations. First, this study had a cross-sectional design, which limits conclusions regarding causality. Health could also impact a person's SES, which is defined as health selection, however the effect of health selection is small for education level[52]. Second, there was considerable variation between the 30 included projects regarding sampling frame, inclusion criteria, study design, sample size, and data collection method. We used meta-analyses techniques to correct for clustering between subjects in projects. However, we believe that these pooled data are likely to reflect reality better than data from a single project based on one nonrandom sample. Third, due to item non-response there were some missing data. To deal with this we used multiple imputation methods for potential confounders. A non-response analysis showed that there were some socio-demographic differences between persons who were excluded and who were included, although it is unclear how this could have affected the size of the effect. We additionally performed a series of sensitivity analyses restricted to persons who had a complete number of items for the FI and for each FI component, changes were marginal.

In conclusion, there are socioeconomic inequalities in frailty and frailty components. Inequalities in frailty, number of morbidities and SRH are most consistent across age groups. The number of morbidities a person has play a role in explaining socioeconomic inequalities in frailty and should be considered in the management of frailty.

REFERENCES

1. Clegg A, Young J, Iliffe S, et al. Frailty in elderly people. *Lancet* 2013;381(9868):752-62. doi: S0140-6736(12)62167-9 [pii]10.1016/S0140-6736(12)62167-9 [published Online First: 2013/02/12]
2. Morley JE, Vellas B, van Kan GA, et al. Frailty consensus: a call to action. *J Am Med Dir Assoc* 2013;14(6):392-7. doi: S1525-8610(13)00182-5 [pii]10.1016/j.jamda.2013.03.022 [published Online First: 2013/06/15]
3. Romero-Ortuno R, Kenny RA. The frailty index in Europeans: association with age and mortality. *Age Ageing* 2012;41(5):684-9. doi: 10.1093/ageing/afs051
4. Stolz E, Mayerl H, Waxenegger A, et al. Impact of socioeconomic position on frailty trajectories in 10 European countries: evidence from the Survey of Health, Ageing and Retirement in Europe (2004-2013). *J Epidemiol Community Health* 2016 doi: 10.1136/jech-2016-207712
5. Chamberlain AM, St Sauver JL, Jacobson DJ, et al. Social and behavioural factors associated with frailty trajectories in a population-based cohort of older adults. *BMJ Open* 2016;6(5):e011410. doi: 10.1136/bmjopen-2016-011410
6. Hajizadeh M, Mitnitski A, Rockwood K. Socioeconomic gradient in health in Canada: Is the gap widening or narrowing? *Health Policy* 2016;120(9):1040-50. doi: 10.1016/j.healthpol.2016.07.019
7. Harttgen K, Kowal P, Strulik H, et al. Patterns of frailty in older adults: comparing results from higher and lower income countries using the Survey of Health, Ageing and Retirement in Europe (SHARE) and the Study on Global AGEing and Adult Health (SAGE). *PLoS One* 2013;8(10):e75847. doi: 10.1371/journal.pone.0075847
8. Romero-Ortuno R. Frailty Index in Europeans: association with determinants of health. *Geriatr Gerontol Int* 2014;14(2):420-9. doi: 10.1111/ggi.12122
9. Soler-Vila H, Garcia-Esquinas E, Leon-Munoz LM, et al. Contribution of health behaviours and clinical factors to socioeconomic differences in frailty among older adults. *J Epidemiol Community Health* 2016;70(4):354-60. doi: 10.1136/jech-2015-206406
10. Mitnitski AB, Mogilner AJ, Rockwood K. Accumulation of deficits as a proxy measure of aging. *ScientificWorldJournal* 2001;1:323-36. doi: 10.1100/tsw.2001.58
11. Rockwood K, Mitnitski A. Frailty in relation to the accumulation of deficits. *J Gerontol A Biol Sci Med Sci* 2007;62(7):722-7.
12. Theou O, Brothers TD, Mitnitski A, et al. Operationalization of frailty using eight commonly used scales and comparison of their ability to predict all-cause mortality. *J Am Geriatr Soc* 2013;61(9):1537-51. doi: 10.1111/jgs.12420 [published Online First: 2013/09/14]
13. Searle SD, Mitnitski A, Gahbauer EA, et al. A standard procedure for creating a frailty index. *BMC Geriatr* 2008;8:24. doi: 1471-2318-8-24 [pii] 10.1186/1471-2318-8-24 [published Online First: 2008/10/02]
14. Yang F, Gu D. Predictability of frailty index and its components on mortality in older adults in China. *BMC Geriatr* 2016;16:145. doi: 10.1186/s12877-016-0317-z
15. World Health O. International classification of functioning, disability and health : ICF. Geneva: World Health Organization 2001.

16. Wilson IB, Cleary PD. Linking clinical variables with health-related quality of life. A conceptual model of patient outcomes. *JAMA* 1995;273(1):59-65.
17. Vaughan L, Leng X, La Monte MJ, et al. Functional Independence in Late-Life: Maintaining Physical Functioning in Older Adulthood Predicts Daily Life Function after Age 80. *J Gerontol A Biol Sci Med Sci* 2016;71 Suppl 1:S79-86. doi: 10.1093/gerona/glv061
18. Hoogendijk EO, van Hout HP, Heymans MW, et al. Explaining the association between educational level and frailty in older adults: results from a 13-year longitudinal study in the Netherlands. *Ann Epidemiol* 2014;24(7):538-44 e2. doi: 10.1016/j.annepidem.2014.05.002
19. Lutomski JE, Baars MA, Schalk BW, et al. The development of the Older Persons and Informal Caregivers Survey Minimum DataSet (TOPICS-MDS): a large-scale data sharing initiative. *PLoS One* 2013;8(12):e81673. doi: 10.1371/journal.pone.0081673
20. BeterOud. Nationaal Programma Ouderenzorg 2017 [Available from: http://www.beteroud.nl/ouderen/nationaal-programma-ouderenzorg-npo.html.
21. Lutomski JE, Baars MA, van Kempen JA, et al. Validation of a frailty index from the older persons and informal caregivers survey minimum data set. *J Am Geriatr Soc* 2013;61(9):1625-7. doi: 10.1111/jgs.12430
22. Mitnitski A, Song X, Skoog I, et al. Relative fitness and frailty of elderly men and women in developed countries and their relationship with mortality. *J Am Geriatr Soc* 2005;53(12):2184-9. doi: 10.1111/j.1532-5415.2005.00506.x
23. Katz S, Ford AB, Moskowitz RW, et al. Studies of Illness in the Aged. The Index of Adl: A Standardized Measure of Biological and Psychosocial Function. *JAMA* 1963;185:914-9.
24. Laan W, Zuithoff NP, Drubbel I, et al. Validity and reliability of the Katz-15 scale to measure unfavorable health outcomes in community-dwelling older people. *J Nutr Health Aging* 2014;18(9):848-54. doi: 10.1007/s12603-014-0479-3
25. Krabbe PF, Stouthard ME, Essink-Bot ML, et al. The effect of adding a cognitive dimension to the EuroQol multiattribute health-status classification system. *J Clin Epidemiol* 1999;52(4):293-301.
26. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;30(6):473-83.
27. Organisation for Economic Co-operation and Development. Classifying educational programmes: manual for ISCED-97 implementation in OECD countries. Paris: Organisation for Economic Co-operation and Development 1999.
28. Statistics Netherlands (CBS). Standaard Onderwijsindeling. Voorburg [etc.]: Centraal Bureau voor de Statistiek, 1999.
29. Knol F. Van hoog naar laag; van laag naar hoog : de sociaal-ruimtelijke ontwikkeling van wijken tussen 1971-1995. Den Haag: Sociaal en Cultureel Planbureau 1998.
30. Statistics Netherlands (CBS). Kerncijfers postcodegebieden (2008-2010). Den Haag/Heerlen, 2012.
31. Snijders TAB, Bosker RJ. Multilevel analysis : an introduction to basic and advanced multilevel modeling. Los Angeles: SAGE 2012.

32. Mickey RM, Greenland S. The impact of confounder selection criteria on effect estimation. *Am J Epidemiol* 1989;129(1):125-37.
33. Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *J Pers Soc Psychol* 1986;51(6):1173-82.
34. McDonald JH, University of D. Handbook of biological statistics. Baltimore, Maryland: Sparky House Publishing 2009.
35. Greenland S, Finkle WD. A critical look at methods for handling missing covariates in epidemiologic regression analyses. *Am J Epidemiol* 1995;142(12):1255-64.
36. Palacios-Cena D, Jimenez-Garcia R, Hernandez-Barrera V, et al. Has the prevalence of disability increased over the past decade (2000-2007) in elderly people? A Spanish population-based survey. *J Am Med Dir Assoc* 2012;13(2):136-42. doi: 10.1016/j.jamda.2010.05.007
37. Leopold L, Engelhardt H. Education and physical health trajectories in old age. Evidence from the Survey of Health, Ageing and Retirement in Europe (SHARE). *Int J Public Health* 2013;58(1):23-31. doi: 10.1007/s00038-012-0399-0
38. Tsai Y. Education and disability trends of older Americans, 2000-2014. *J Public Health (Oxf)* 2016 doi: 10.1093/pubmed/fdw082
39. Lang IA, Hubbard RE, Andrew MK, et al. Neighborhood deprivation, individual socioeconomic status, and frailty in older adults. *J Am Geriatr Soc* 2009;57(10):1776-80. doi: 10.1111/j.1532-5415.2009.02480.x
40. Lutomski JE, Krabbe PF, den Elzen WP, et al. Rasch analysis reveals comparative analyses of activities of daily living/instrumental activities of daily living summary scores from different residential settings is inappropriate. *J Clin Epidemiol* 2016;74:207-17. doi: 10.1016/j.jclinepi.2015.11.006
41. Edjolo A, Proust-Lima C, Delva F, et al. Natural History of Dependency in the Elderly: A 24-Year Population-Based Study Using a Longitudinal Item Response Theory Model. *Am J Epidemiol* 2016;183(4):277-85. doi: 10.1093/aje/kwv223
42. Huisman M, Kunst AE, Mackenbach JP. Socioeconomic inequalities in morbidity among the elderly; a European overview. *Soc Sci Med* 2003;57(5):861-73.
43. Enroth L, Raitanen J, Hervonen A, et al. Is socioeconomic status a predictor of mortality in nonagenarians? The vitality 90+ study. *Age Ageing* 2015;44(1):123-9. doi: 10.1093/ageing/afu092
44. Gobbens RJ, van Assen MA, Schalk MJ. The prediction of disability by self-reported physical frailty components of the Tilburg Frailty Indicator (TFI). *Arch Gerontol Geriatr* 2014 doi: S0167-4943(14)00101-0 [pii]10.1016/j.archger.2014.06.008 [published Online First: 2014/07/22]
45. Bell CL, Chen R, Masaki K, et al. Late-life factors associated with healthy aging in older men. *J Am Geriatr Soc* 2014;62(5):880-8. doi: 10.1111/jgs.12796
46. Benzeval M, Green MJ, Leyland AH. Do social inequalities in health widen or converge with age? Longitudinal evidence from three cohorts in the West of Scotland. *BMC Public Health* 2011;11:947. doi: 10.1186/1471-2458-11-947
47. Gobbens RJ, van Assen MA, Luijkx KG, et al. Determinants of frailty. *J Am Med Dir Assoc* 2010;11(5):356-64. doi: 10.1016/j.jamda.2009.11.008

48. Etman A, Kamphuis CB, van der Cammen TJ, et al. Do lifestyle, health and social participation mediate educational inequalities in frailty worsening? *Eur J Public Health* 2014 doi: cku093 [pii] 10.1093/eurpub/cku093 [published Online First: 2014/07/26]
49. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001;56(3):M146-56. [published Online First: 2001/03/17]
50. Cacciatore F, Testa G, Galizia G, et al. Clinical frailty and long-term mortality in elderly subjects with diabetes. *Acta Diabetol* 2013;50(2):251-60. doi: 10.1007/s00592-012-0413-2
51. Galizia G, Cacciatore F, Testa G, et al. Role of clinical frailty on long-term mortality of elderly subjects with and without chronic obstructive pulmonary disease. *Aging Clin Exp Res* 2011;23(2):118-25.
52. Kroger H, Pakpahan E, Hoffmann R. What causes health inequality? A systematic review on the relative importance of social causation and health selection. *Eur J Public Health* 2015;25(6):951-60. doi: 10.1093/eurpub/ckv111

SUPPLEMENTAL MATERIAL

Table S1. Association of neighbourhood socioeconomic status with frailty by age group and with frailty components by age group , corrected for individual education level, among 25,494 persons of The Older Persons and Informal Caregivers Survey Minimum DataSet (TOPICS-MDS).

	Frailty Index	Morbidities	ADL limitations	IADL limitations	Psychosocial health	Health-related quality of life	Self-rated health
	B (95% CI)	B (95% CI)	B (95% CI)	B (95% CI)	B (95% CI)	B (95% CI)	B (95% CI)
Age 55-69 years							
Second quartile	0.004 (-0.008-0.016)	0.001 (-0.012-0.014)	0.003 (-0.014-0.020)	-0.007 (-0.028-0.013)	0.014 (-0.008-0.036)	0.012 (-0.008-0.031)	0.016 (-0.004-0.036)
Third quartile	0.007 (-0.005-0.018)	0.007 (-0.005-0.019)	-0.006 (-0.023-0.010)	0.001 (-0.019-0.021)	0.014 (-0.007-0.035)	0.022* (0.003-0.040)	0.014 (-0.005-0.033)
Fourth quartile	0.014** (0.003-0.024)	0.015** (0.004-0.026)	-0.005 (-0.020-0.011)	0.009 (-0.009-0.028)	0.030** (0.010-0.050)	0.018* (0.000-0.035)	0.024** (0.006-0.041)
Age 70-79 years							
Second quartile	0.002 (-0.003-0.007)	0.005* (0.000-0.012)	-0.002 (-0.009-0.006)	-0.002 (-0.011-0.006)	-0.001 (-0.009-0.007)	0.004 (-0.003-0.012)	-0.001 (-0.009-0.007)
Third quartile	0.008** (0.002-0.013)	0.010*** (0.005-0.016)	0.001 (-0.007-0.009)	0.001 (-0.007-0.009)	0.007 (-0.002-0.016)	0.011** (0.003-0.019)	0.004 (-0.004-0.013)
Fourth quartile	0.011*** (0.005-0.016)	0.013*** (0.007-0.018)	0.002 (-0.006-0.011)	0.002 (-0.006-0.011)	0.012** (0.003-0.020)	0.014*** (0.006-0.023)	0.019*** (0.011-0.028)
Age ≥ 80 years							
Second quartile	0.002 (-0.004-0.009)	0.004 (-0.002-0.011)	0.000 (-0.011-0.011)	0.006 (-0.006-0.018)	-0.005 (-0.014-0.005)	0.007 (-0.003-0.016)	-0.004 (-0.013-0.005)
Third quartile	0.001 (-0.006-0.008)	0.007 (-0.001-0.014)	-0.004 (-0.016-0.008)	-0.003 (-0.017-0.011)	-0.002 (-0.012-0.009)	0.000 (-0.010-0.011)	0.001 (-0.009-0.011)
Fourth quartile	0.009* (0.002-0.016)	0.006 (-0.001-0.013)	0.002 (-0.010-0.014)	0.011 (-0.003-0.024)	0.014** (0.004-0.024)	0.021** (0.011-0.031)	0.007 (-0.003-0.017)

Values are derived from multilevel multivariable linear regression, First Quartile is the reference group. Model is adjusted for: age, sex, living arrangement (alone/not alone) and education level.
* p<0.05; ** p<0.01; ** p<0.001.
B=effect estimate; CI=confidence interval; (I)ADL=(instrumental) activities of daily living.

Chapter 3

Ethnic differences in frailty: a cross-sectional study of pooled data from community-dwelling older persons in The Netherlands

Carmen B. Franse, Amy van Grieken, Li Qin, René J.F. Melis, Judith A.C. Rietjens, Hein Raat

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ABSTRACT

Objective

Few European studies examined frailty among older persons from diverse ethnic backgrounds. We aimed to examine the association of ethnic background with frailty. In addition, we explored the association of ethnic background with distinct components that are considered to be relevant for frailty.

Design and setting

This was a cross-sectional study of pooled data of The Older Persons and Informal Caregivers Survey Minimum DataSet (TOPICS) in the Netherlands.

Participants

Community-dwelling persons aged 55 years and older with a Dutch, Indonesian, Surinamese, Moroccan or Turkish ethnic background were included (n=23,371).

Measurements

Frailty was assessed with the validated TOPICS-Frailty Index that consisted of 45 items. The TOPICS-Frailty Index contained six components: morbidities, limitations in activities of daily living (ADL), limitations in instrumental ADL, health-related quality of life, psychosocial health and self-rated health. To examine the associations of ethnic background with frailty and with distinct frailty components, we estimated multilevel random-intercept models adjusted for confounders.

Results

TOPICS-Frailty Index scores varied from 0.19 (SD=0.12) among persons with a Dutch background to 0.29 (SD=0.15) in persons with a Turkish background. After adjustment for age, sex, living arrangement and education level, persons with a Turkish, Moroccan or Surinamese background were frailer compared with persons with a Dutch background ($p<.001$). There were no significant differences in frailty between persons with an Indonesian compared with a Dutch background. The IADL component scores were higher among all groups with a non-Dutch background compared with persons with a Dutch background ($p<.05$ or lower for all groups).

Conclusions

Compared with older persons with a Dutch background, persons with a Surinamese, Moroccan or Turkish ethnic background were frailer. Targeted intervention strategies should be developed for the prevention and reduction of frailty among these older immigrants.

INTRODUCTION

The concept of frailty was introduced to capture the variability in the rate of ageing[1]. Frailty can be defined as a state of increased vulnerability to external stressors[2 3]. Frailty is an important risk factor for adverse outcomes such as institutionalisation and mortality[1 4]. Early intervention in frail older persons could improve functional health and reduce hospital admissions[5 6]. A widely used approach to measure frailty is the accumulation-of-deficits approach developed by Rockwood and Mitnitski that results in a Frailty Index [7 8]. Theou et al found that of eight commonly used approaches to measure frailty, frailty measured with a Frailty Index most accurately predicted mortality[1]. A standard procedure to construct a Frailty Index was developed by Searle et al., who recommended to include the following components in the index: morbidities, disability in activities of daily living (ADL) and instrumental ADL (IADL), restricted activity, impairments in general cognition and physical performance, psychological health and self-rated health (SRH)[9].The assessment of distinct components that are considered to be relevant for frailty could uncover important information about the specific domain in which a person is frail. Yang and Gu have studied the associations between distinct components of frailty and mortality and found that IADL and ADL limitations components played an important role in the association between frailty and mortality[10]. In a previous study on socioeconomic inequalities in frailty and frailty components by our team, we found consistent educational inequalities in overall frailty, number of morbidities and SRH[11].

American studies have found that older persons from ethnic minority groups are frailer compared with European Americans[12-14]. In Western Europe, large ethnic minority groups consist of immigrants settled during the decades after the Second World War. These immigrants are ageing, however little research on frailty has been conducted in this group. In the Netherlands, the number of immigrants aged 55 years or older increased threefold in the past 15 years[15]. The largest immigrant groups in the Netherlands have an Indonesian, Surinamese, Moroccan or Turkish ethnic background[16]. In the 1960s and early 1970s, many persons with a Moroccan or Turkish background came to the Netherlands as labour migrants[17]. Many Turkish or Moroccan 'first generation' immigrants have difficulties speaking and writing Dutch[17]. Many persons with a Surinamese background came to the Netherlands between 1970 and 1980, during the period of decolonisation of Suriname[17]. In general, persons with a Surinamese background are familiar with Dutch society and were taught Dutch language at school. Between 1945 and 1965, following the decolonisation of Indonesia, many persons migrated from Indonesia to the Netherlands[17]. Many of these persons have a Dutch or mixed Dutch and Indonesian ancestry and a similar socioeconomic status as native-born Dutch persons[16]. On average, older persons with a Turkish, Moroccan or Surinamese ethnic background have a lower socioeconomic status and more chronic health conditions compared with older persons with a Dutch background[18-21]. However, Dutch studies on the variation in frailty according to ethnic background are limited[22]. This

increases the urgency to study the frailty level among these older immigrant groups. The aim of this study was therefore to examine the association of ethnic background with frailty among older persons aged 55 years and older. In addition, we explored the associations of ethnic background with distinct components that are considered to be relevant for frailty (morbidities, ADL, IADL, health-related quality of life (HRQoL), psychosocial health and SRH).

METHODS

Study design

We applied a cross-sectional study design using data from The Older Persons and Informal Caregivers Survey Minimum DataSet (TOPICS-MDS). The development and design of TOPICS-MDS has been described in more detail[23]. TOPICS-MDS is a database designed to capture information on the well-being of older persons in the Netherlands. TOPICS-MDS was developed to collect uniform information from studies funded under the National Care for older citizens Programme[24]. Included survey items were based on the recommendations of experts from eight medical research centres in the Netherlands who identified key outcomes in older persons' health using validated instruments. Then, an independent multidisciplinary panel with expertise in gerontology, epidemiology, biostatistics and health services research evaluated and revised TOPICS-MDS. Dutch TOPICS-MDS questionnaires were piloted in four regions throughout the Netherlands. Misinterpretation of questions were identified and minor changes were made by a plain language expert. The Dutch version of TOPICS-MDS was translated into Turkish, the two Moroccan languages and the two Surinamese languages. Two independent translators, who were native speakers of the target language, translated all items and differences were reconciled in a consensus meeting. Another translator back translated the forward translation and discrepancies were discussed, which resulted in a final translation. Questionnaires were then cross-culturally validated by the three-step test-interview (TSTI)[25]. The translation and cross-cultural validation of TOPICS-MDS was done as part of the SYMBOL study and has been described in more detail[26]. Between 2010 and 2013, 50 studies were conducted in the Netherlands which applied the TOPICS-MDS questionnaire[23]. TOPICS-MDS consists of pooled data of these studies which differ across study design, sampling framework, and inclusion criteria. TOPICS-MDS is a fully anonymised dataset.

Patient and Public Involvement

The research proposal of this study was presented to a forum of older persons and informal caregivers who are part of the geriatric network of Southwest Netherlands and was adapted according to their suggestions. The study design was presented at the 'TOPICS Special Interest Group Diversity', who advised on design and subgroup analyses. This interest group consisted of researchers, older persons and a representative of the Network of Organisations of Older Migrants (NOOM) in the Netherlands. The results of this study will be disseminated

to participants on the TOPICS-MDS website https://topics-mds.eu/ and on the website of the Organisation of Health Research and Development (ZonMw) https://www.zonmw.nl/nl/.

Ethnic background

We defined ethnic background according to the classification of Statistics Netherlands[27]. The participant had a non-Dutch ethnic background if at least one of the parents was born in another country than the Netherlands. To determine the country of origin, the following was applied[27]. If the participant was also (as well as parent/parents) born outside of the Netherlands, the participants' country of birth determined the ethnic background. If the participant was born in the Netherlands but their mother was not, the country of birth of the mother determined the ethnic background. If the mother was born in the Netherlands but the father was not, the country of birth of the father determined the ethnic background. We categorised participants according to ethnic background; Dutch, Indonesian, Surinamese, Moroccan or Turkish ethnic background.

Population for analysis

We restricted our analysis to TOPICS-MDS data from studies on independently living persons aged 55 years and older with a Dutch, Indonesian, Surinamese, Moroccan or Turkish ethnic background. We included studies that recruited participants from the general population and from general practitioners' registries. We excluded studies among persons living in a nursing home, studies that recruited participants in a hospital setting (n=6136) and studies for persons with dementia (n=507). We excluded other ethnic groups due to small numbers (n=1718). We also excluded persons with more than 15 missing items for the TOPICS-Frailty Index (n=3662) and with missing country of birth (n=752). The final sample comprised data from 29 studies with data of 23 371 persons (see figure 1).

TOPICS-Frailty Index and components

Frailty was measured by the TOPICS-Frailty Index, which was developed and validated using data from the TOPICS-MDS questionnaire by Lutomski et al.[28]. As described previously[11], in our study we included the 45 item TOPICS-Frailty Index, after exclusion of the item measuring prostatism. Searle et al. showed that a Frailty Index with 30–40 items is accurate for predicting adverse outcomes[9 29]. The TOPICS-Frailty Index was calculated when at least 30 items were available. Binary items were scored 0 when the deficit was absent and 1 when the deficit was present. For items with multiple response categories, responses were coded so that they could be mapped on the interval 0–1, as proposed by Searle et al.[9]. For example, when the response categories were no/some/extreme, responses were coded 0/0.5/1 respectively. Then, the health deficits a person reported were added up and divided by the total health deficits measured for this person. This resulted in a score between 0-1. Persons were also grouped according to their TOPICS-Frailty Index score, we used a cut-off score ≥0.25 to indicate frailty as suggested by Rockwood et al.[30].

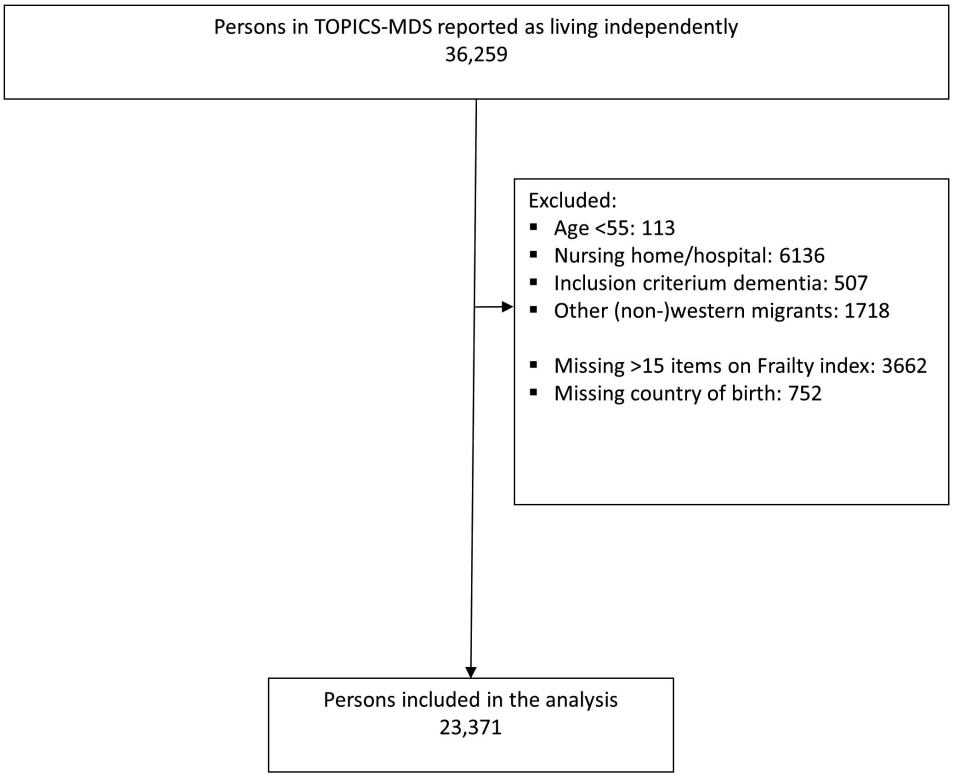

Figure 1: Population of analysis.

The TOPICS-Frailty Index consists of 45 items of the TOPICS-MDS questionnaire that belong to six components, each measured by validated instruments; morbidities, ADL, IADL, HRQoL, psychosocial health and SRH[9]. The component 'morbidities' was measured by 16 items regarding the self-reported presence (yes/no) of diabetes, stroke, heart failure, cancer, respiratory condition (asthma, chronic bronchitis, lung emphysema or Chronic obstructive pulmonary disease), incontinence, joint damage of hips or knees, osteoporosis, hip fracture, fractures other than hip, dizziness with falling, depression, anxiety/panic disorder, dementia, hearing problems, vision problems. The component 'ADL limitations' was measured by six items using a modified version of the Katz et al instrument[31 32]. Persons could indicate whether they needed help (yes/no) with the following activities: bathing, dressing, toileting, incontinence, sitting down, eating. The component 'IADL limitations' was measured by nine items using a modified version of the Katz et al instrument[31 32]. Persons could indicate whether they needed help (yes/no) with the following activities: using the telephone, travelling, shopping, preparing a meal, cleaning, taking medications, handling finance, brushing hair and walking. The component 'HRQoL' was measured by using the six

items of the EuroQol 5D+C[33]. Persons could indicate whether they had problems (no/some/extreme) with the following: mobility, self-care, usual activities, pain/discomfort, anxiety/depression and cognition. The component 'psychosocial health' was measured with five items of the RAND-36 [34]. Persons could indicate how much of the time in the past month (none/a little/ some/a good bit/most/all) they had been the following: nervous, calm, downhearted, happy and down in the dumps, and how much time (none/a little/some/most/all) health problems had interfered with social activities. The component 'SRH' was measured with two items of the RAND-36[34], one regarding perceived current health status (poor/fair/good/very good/excellent) and one regarding perceived changes in health in the past year (much worse/slightly worse/about the same/a little better/much better). The score for distinct components of the TOPICS-Frailty Index was calculated analogous to the TOPICS-Frailty Index, by adding up the health deficits within the component that a person had, divided by the total of possible health deficits included in the component[9]. Higher scores represent a higher proportion of health deficits for that component. We accepted no missing variables for the SRH component score and a maximum of one of three missing variables for the other frailty component scores.

Potential confounders

We incorporated the following potential confounders in this study: gender, age, living arrangement, marital status, generation of immigration, education level and socioeconomic status of the neighbourhood. Age in years was assessed by asking year of birth. Living arrangement was assessed by asking whether participants were living: independent alone or independent with others. We categorised answers into 'not alone' and 'alone'. Marital status was assessed by asking whether participants were: married, divorced, widowed, unmarried, long term cohabitation unmarried. We categorised answers into 'married/cohabitant partners', 'divorced', 'widowed' and 'single'. Generation of immigration was assessed by country of birth of participant and his/her parents. We categorized answers into 'first-generation' when the person was born in a country other than the Netherlands and 'second generation' if the person was born in the Netherlands and (one of) the parents were born in another country. Socioeconomic status was assessed with both education level and neighbourhood socioeconomic status. TOPICS-MDS uses the 1997 International Standard Classification of Education[35] to assess education level; participants were asked whether they had completed: fewer than 6 years of primary school; 6 years of primary school; primary school without further completed education; vocational school; secondary professional education or university entrance level or tertiary education. We categorised the level of education into 'primary education or less' and 'secondary education or higher'. For the neighbourhood socioeconomic status, the 2006 reference scores for area codes were used, as calculated by the Netherlands Institute for Social Research[36] based on the education level, income and labor market position of persons living in each area code. We categorized scores into quartiles: quartile 1 is the least deprived quartile and quartile 4 is the most deprived.

Statistical analysis

We calculated the statistical significance of differences in sociodemographic characteristics, frailty and frailty components (morbidities, ADL limitations, IADL limitations, psychosocial health, HRQoL and SRH) by ethnic background using chi-squared tests for categorical variables and one-way analysis of variance for continues variables.

To examine the association of ethnic background with frailty and with distinct frailty components, we estimated multilevel random-intercept models because data were clustered in studies[37]. As such dependency between the observations of participants of a study (because of sampling design and or inclusion criteria) was taken into account. We built one multilevel linear regression model for the continues TOPICS-Frailty Index outcome and one multilevel logistic regression model for the dichotomous outcome 'frailty', with ethnic background as independent variable. We furthermore built six separate multilevel linear regression models for the six frailty component outcomes with ethnic background as independent variable. Only potential confounders that led to a substantial change in effect estimates in the association between ethnic background and frailty (ie; ≥10% change) were included in all models: age, sex, living arrangement (alone/not alone) and education level[38]. Marital status was excluded due to multicollinearity with living arrangement. Interaction effects of ethnic background with age, sex, living arrangement and education level on frailty and the six frailty components were assessed.

Percentages of missing values in the covariates were 2% or less (table 1). Because the missing values were not completely at random, multiple imputation was used to deal with the missing values in the covariates. Five imputed datasets were created using a fully conditional specified model, thus taking into account the uncertainty of imputed values[39]. We used pooled estimates from these five imputed datasets to report regression coefficients and their 95% CIs. We considered a p value of .05 or lower to be statistically significant and used Bonferroni correction for testing explorative interactions (p value=.05/4)[40]. Descriptive analyses were performed using SPSS V.23.0 (IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp). Multilevel linear regression analyses were performed using R-V.3.3.2 using lme4 package.

Non-response analysis

A comparison of persons included in the study (n=23 371) with persons not included due to missing values for the TOPICS-Frailty Index and/or country of birth (n=4414) did not indicate significant differences in terms of age (p=.872), sex (p=.779), living arrangement (p=.444) and marital status (p=.166). However, excluded persons were more often living in rural areas and in deprived neighbourhoods (p<.001) than persons included in the study.

RESULTS

Table 1 presents the characteristics according to ethnic background. The mean age was 77.8 years (SD=7.0 years) and 58.9% were female. Four per cent of the sample had a non-Dutch ethnic background and the majority of these persons (90.4%) were first generation immigrants. Sex differed between the ethnic groups (p=.003), as did age, living arrangement, marital status, generation of immigration, education level and the socioeconomic status of the neighbourhood persons were living in (all p<.001).

Table 1: Sociodemographic characteristics by ethnic background of 23,371 persons of The Older Persons and Informal Caregivers Survey Minimum DataSet (TOPICS-MDS).

	Dutch N=22,360	Indonesian N=519	Surinamese N=214	Moroccan N=137	Turkish N=141	P-value*
Age in years (mean, SD)	78.0 (6.8)	78.7 (7.3)	72.0 (9.2)	67.4 (8.5)	65.9 (7.6)	<0.001
Sex, N (%)						0.003
Male	9251 (41.4)	193 (37.2)	85 (39.7)	45 (32.8)	41 (29.1)	
Female	13,109 (58.6)	326 (62.8)	129 (60.3)	92 (67.2)	100 (70.9)	
Living arrangement, N (%)						
Alone	9961 (44.5)	256 (49.3)	126 (58.9)	32 (23.4)	24 (17.0)	<0.001
With others	12,399 (55.5)	263 (50.7)	88 (41.1)	105 (76.6)	117 (83.0)	
Marital status, N (%)						
Married/Cohabitant partners	12,053 (53.9)	242 (46.6)	75 (35.0)	97 (70.8)	109 (77.3)	<0.001
Divorced	1371 (6.1)	50 (9.6)	45 (21.0)	13 (9.5)	7 (5.0)	
Widowed	7901 (35.3)	192 (37.0)	61 (28.5)	26 (19.0)	22 (15.6)	
Single	1035 (4.6)	35 (6.7)	33 (15.4)	1 (0.7)	3 (2.1)	
Generation of immigration						<0.001
First-generation	NA	432 (83.2)	206 (96.3)	135 (98.5)	141 (100.0)	
Second-generation	NA	87 (16.8)	8 (3.7)	2 (1.5)	0 (0.0)	
Education level, N (%)						<0.001
Secondary or higher	15,023 (67.2)	420 (80.8)	135 (63.1)	18 (13.1)	10 (7.3)	
Primary or less	7337 (32.8)	99 (19.2)	79 (36.9)	119 (86.9)	129 (92.7)	
SES neighbourhood, N (%)						
First quartile	6395 (28.6)	174 (33.5)	22 (10.3)	7 (5.1)	9 (6.4)	<0.001
Second quartile	6010 (26.9)	130 (25.0)	35 (16.4)	4 (2.9)	0 (0.0)	
Third quartile	4733 (21.2)	98 (18.9)	22 (10.3)	12 (8.8)	23 (16.3)	
Fourth quartile	5222 (23.3)	116 (22.5)	135 (63.1)	113 (82.5)	109 (77.3)	

* P-values are based on Chi-squared test for categorical variables and one-way ANOVA for continues variables. Missing N (%) for variables: Age=574 (2%); sex=9 (<1%); living arrangement=0 (0%); marital status=49 (<1%); Generation of immigration=0 (0%); education level=193 (1%); SES neighbourhood=386 (2%); NA=not applicable; SES=socioeconomic status.

Table 2: Frailty and frailty components by ethnic background of 23,371 persons of The Older Persons and Informal Caregivers Survey Minimum DataSet (TOPICS-MDS).

	Dutch N=22,360	Indonesian N=519	Surinamese N=214	Moroccan N=137	Turkish N=141	P-value*
Frailty Index, mean (SD)†	0.19 (0.12)	0.20 (0.12)	0.22 (0.16)	0.24 (0.12)	0.29 (0.15)	<0.001
Frailty, % (95% CI) ‡	28.0 (27.4-28.6)	32.2 (28.3-36.3)	36.9 (30.7-43.6)	43.1 (35.0-51.5)	58.2 (49.9-66.0)	<0.001
Morbidities, mean FI (SD)†	0.16 (0.12)	0.17 (0.13)	0.18 (0.15)	0.16 (0.09)	0.21 (0.14)	<0.001
Number morbidities, mean (SD)	2.51 (1.88)	2.68 (2.01)	2.75 (2.34)	2.50 (1.43)	3.28 (2.28)	<0.001
ADL limitations, mean FI (SD)†	0.09 (0.16)	0.09 (0.15)	0.10 (0.20)	0.09 (0.18)	0.14 (0.23)	0.002
Number ADL limitations, mean (SD)	0.52 (0.93)	0.51 (0.90)	0.63 (1.20)	0.52 (1.05)	0.83 (1.38)	0.002
IADL Limitations, mean FI (SD)†	0.20 (0.24)	0.24 (0.26)	0.25 (0.30)	0.36 (0.29)	0.40 (0.28)	<0.001
Number IADL limitations, mean (SD)	1.36 (1.63)	1.67 (1.78)	1.78 (2.08)	2.50 (2.06)	2.77 (1.94)	<0.001
HRQoL, mean FI (SD)†	0.21 (0.16)	0.21 (0.16)	0.24 (0.20)	0.26 (0.18)	0.35 (0.23)	<0.001
Psychosocial health, mean FI (SD)†	0.25 (0.18)	0.25 (0.17)	0.29 (0.21)	0.39 (0.15)	0.40 (0.16)	<0.001
Self-rated health, mean FI (SD)†	0.57 (0.17)	0.58 (0.18)	0.62 (0.18)	0.64 (0.17)	0.67 (0.19)	<0.001

* P-values are based on one-way ANOVA for continues variables and X^2 test for categorical variable. † Mean FI=mean number of health deficits reported/total health deficits measured in instrument; score between 0-1 where higher scores represent worse health. ‡ Scores ≥0.25 indicate frailty. Missing N (%) for variables: morbidities=542 (2%); ADL=43 (<1%); IADL=76 (<1%); psychosocial health=465 (2%); HRQoL=534 (2%); self-rated health=72 (<1%). (I)ADL= (instrumental) activities of daily living; FI=frailty index; HRQoL= health-related quality of life.

The proportion of persons who were frail differed according to ethnic background (p<.001; table 2). Mean TOPICS-Frailty Index scores varied from 0.19 (SD=0.12) among persons with a Dutch background to 0.29 (SD=0.15) in persons with a Turkish background. The distinct frailty component scores also differed according to ethnic background (p≤.002 or lower; table 2).

Multilevel regression analyses adjusted for age, sex, living arrangement and education level showed that persons with a Turkish, Moroccan or Surinamese background were frailer compared with persons with a Dutch background (p<.001 for all groups; table 3). There were no significant differences in frailty between persons with a Dutch background and persons with an Indonesian background.

Table 3. Association of ethnic background with frailty among 23,371 persons of The Older Persons and Informal Caregivers Survey Minimum DataSet (TOPICS-MDS).

		Frailty Index (score 0-1)	Frailty (yes)
	N	B (95% CI)†	OR (95% CI)‡
Dutch	22,360	ref	ref
Indonesian	519	0.003 (-0.006-0.012)	1.09 (0.89-1.34)
Surinamese	214	0.042*** (0.026-0.058)	1.98*** (1.42-2.78)
Moroccan	137	0.065*** (0.041-0.089)	2.86*** (1.73-4.72)
Turkish	141	0.121*** (0.098-0.143)	6.18*** (3.86-9.88)

† Values are derived from multilevel multivariable linear regression. ‡ Frailty Index score ≥ 0.25; values are derived from multilevel multivariable logistic regression. The models are adjusted for: age, sex, living arrangement (alone/not alone) and education level.

*** p<0.001. B=effect estimate; CI=confidence interval.

The associations of ethnic background with six distinct frailty component scores are presented in table 4. All groups with a non-Dutch background had higher IADL limitations scores compared with persons with a Dutch background (p<.05 or lower for all groups). Psychosocial and SRH scores were only higher among persons with a Moroccan or Turkish background compared with persons with a Dutch background (p<.001 for both groups). Out of all groups with a non-Dutch background, only persons with a Turkish background had higher scores for all frailty components compared with persons with a Dutch background (p<.001 for all components).

Table 4. Association of ethnic background with six distinct frailty components; among 23,371 persons of The Older Persons and Informal Caregivers Survey Minimum DataSet (TOPICS-MDS).

		Morbidities	ADL limitations	IADL limitations	Psychosocial health	Health-related quality of life	Self-rated health
	N	B (95% CI)	B (95% CI)	B (95% CI)	B (95% CI)	B (95% CI)	B (95% CI)
Dutch	22,360	ref	ref	ref	ref	ref	ref
Indonesian	519	0.002 (-0.008-0.012)	-0.007 (-0.020-0.006)	0.019* (0.001-0.036)	-0.003 (-0.018-0.011)	-0.001 (-0.014-0.013)	0.001 (-0.013-0.015)
Surinamese	214	0.020* (0.004-0.036)	0.046*** (0.024-0.067)	0.100*** (0.070-0.130)	0.017 (-0.012-0.046)	0.041*** (0.018-0.063)	0.013 (-0.010-0.037)
Moroccan	137	0.041*** (0.016-0.066)	0.010 (-0.021-0.042)	0.150*** (0.104-0.195)	0.078*** (0.025-0.130)	0.066*** (0.031-0.100)	0.070*** (0.034-0.106)
Turkish	141	0.098*** (0.075-0.122)	0.067*** (0.037-0.098)	0.203*** (0.159-0.247)	0.092*** (0.043-0.142)	0.161*** (0.129-0.194)	0.098*** (0.063-0.132)

Values are derived from multilevel multivariable linear regression. The models are adjusted for confounders: age, sex, living arrangement (alone/not alone) and education level.
* p<0.05; *** p<0.001. B=effect estimate; CI=confidence interval; (I)ADL=(instrumental) activities of daily living.

We found significant effect modification by education level and age in the association of ethnic background with frailty (p<.01 for both). We, therefore, present results stratified by education level in supplementary table S1 and stratified by age in supplementary table S2.

DISCUSSION

We found that older persons with a Turkish, Moroccan or Surinamese background were frailer compared with persons with a Dutch background. We did not find differences in frailty in persons with an Indonesian background compared with persons with a Dutch background. Studying distinct components of frailty separately showed that all groups with a non-Dutch background had more IADL limitations compared with persons with a Dutch background.

In our study, ethnic differences in frailty persisted after controlling for age, sex, living arrangement and education level. Van Assen et al., who used the Tilburg Frailty Index to measure frailty, also found that persons with a Surinamese, Moroccan or Turkish background were frailer compared with persons with a Dutch background[22]. A European study found that in Northern and Western Europe, immigrants who were born in low-income or middle-income countries demonstrated higher levels of frailty compared to native-born Europeans and immigrants born in high income countries[41]. However, while socioeconomic disadvantage among these immigrant groups plays an important role in the explanation of these differences, other factors such as poor healthcare experience and discrimination are also thought to be important[42-44]. Communication with healthcare providers can be challenging and care is often not adapted to specific needs of immigrant groups[45]. This high level of frailty among these older immigrants could therefore reflect the accumulation of health risks over the life course. A recent Dutch study found that cardiovascular and psychiatric diseases contributed most strongly to the disease burden among non-Western immigrants[18]. They estimated that their disease burden will increase stronger in the coming decades compared with persons with a Dutch background[18]. Targeted health interventions should therefore be developed in order to reach these immigrant groups, not only at older age, but also at younger ages in order to prevent frailty and reduce functional decline.

All groups with a non-Dutch ethnic background had higher IADL limitations component scores compared to persons with a Dutch background. A Swedish study found an increased risk of impaired IADL among older immigrants from low-income and middle-income countries compared with persons with a Swedish background[46]. In frailty instruments that do not take into account IADL limitations, such as the Fried phenotype or the Tilburg Frailty instrument, ethnic inequalities in frailty might be smaller. However, it is likely that help provided by the social network of an older person in performing instrumental activities differs culturally.

Van Assen et al. found that social frailty was higher in older persons with a Turkish or Surinamese, but lower in those with a Moroccan background compared with persons with a Dutch background[22]. Interventions should take into account whether additional support is needed for older immigrants to live independently and to what extent there is a burden for their caregivers.

This study also found important differences between immigrant groups. Psychosocial health component scores were higher among persons with a Turkish or Moroccan background but not among persons with a Surinamese background compared with those with a Dutch background. Other studies have found that both psychological frailty as well as psychiatric diseases are more common among Turkish and Moroccan immigrants than among Surinamese immigrants[18 20 22]. It has been suggested that a lower acculturation, higher discrimination and the distinct nature of the migration history of Turkish and Moroccan immigrants compared with Surinamese immigrants might be at the root of these differences[18 20 46]. These findings emphasise the importance of studying immigrant groups separately and developing intervention strategies targeted at specific needs of different immigrant groups.

The main strength of this study is that we were able to study frailty with a validated Frailty Index among an ethnically diverse group of older persons, as research on frailty among older immigrants is scarce. Furthermore, the TOPICS-MDS questionnaire was translated into the native languages of the main ethnic minority groups in the Netherlands as well as cross-culturally adapted. This study has some limitations. Although the TOPICS-MDS is a large database, there were relatively few persons with a Turkish or Moroccan background. Exploratory stratified analyses by education level and age therefore had less power, but could provide a starting point for future studies. Future studies among older persons should include more persons from ethnic minority groups to study ethnic differences in frailty in subgroups by sociodemographic characteristics such as age and education level. Second, although the operationalisation of the TOPICS-Frailty Index used in this study was validated, the operationalisation of the distinct frailty components as used in this study was not. These components consisted of validated tools such as the Katz et al instrument[31 32] and the EuroQol 5D+C[33], but were operationalised with an accumulation-of-deficits approach. The operationalisation of individual frailty components should therefore be validated in further research. Third, our study used data from 29 studies with samples that varied regarding sampling frame, inclusion criteria, study design, sample size, and data collection method. In the main analyses, we used meta-analyses techniques to correct for clustering between subjects in projects. However, we believe that these pooled data are likely to reflect reality better than data from a single project based on one non-random sample. Last, ethnic background was determined by country of birth, which is the standard in the Netherlands. This may be less reliable in some groups such as Surinamese who are ethnically diverse.

In conclusion, older persons with a Turkish, Moroccan or Surinamese background were frailer compared with persons with a Dutch background. Targeted intervention strategies should be developed for the prevention and reduction of frailty among these older immigrants. These strategies should also be targeted at the younger-old and meet the specific needs of different immigrant groups, such as psychosocial health among older persons with a Turkish or Moroccan background.

REFERENCES

1. Theou O, Brothers TD, Mitnitski A, et al. Operationalization of frailty using eight commonly used scales and comparison of their ability to predict all-cause mortality. *J Am Geriatr Soc* 2013;61(9):1537-51. doi: 10.1111/jgs.12420 [published Online First: 2013/09/14]
2. Clegg A, Young J, Iliffe S, et al. Frailty in elderly people. *Lancet* 2013;381(9868):752-62. doi: S0140-6736(12)62167-9 [pii]10.1016/S0140-6736(12)62167-9 [published Online First: 2013/02/12]
3. Morley JE, Vellas B, van Kan GA, et al. Frailty consensus: a call to action. *J Am Med Dir Assoc* 2013;14(6):392-7. doi: S1525-8610(13)00182-5 [pii]10.1016/j.jamda.2013.03.022 [published Online First: 2013/06/15]
4. Song X, Mitnitski A, Rockwood K. Prevalence and 10-year outcomes of frailty in older adults in relation to deficit accumulation. *J Am Geriatr Soc* 2010;58(4):681-7. doi: 10.1111/j.1532-5415.2010.02764.x
5. Theou O, Stathokostas L, Roland KP, et al. The effectiveness of exercise interventions for the management of frailty: a systematic review. *J Aging Res* 2011;2011:569194. doi: 10.4061/2011/569194 [published Online First: 2011/05/18]
6. Beswick AD, Rees K, Dieppe P, et al. Complex interventions to improve physical function and maintain independent living in elderly people: a systematic review and meta-analysis. *Lancet* 2008;371(9614):725-35. doi: S0140-6736(08)60342-6 [pii]10.1016/S0140-6736(08)60342-6 [published Online First: 2008/03/04]
7. Mitnitski AB, Mogilner AJ, Rockwood K. Accumulation of deficits as a proxy measure of aging. *ScientificWorldJournal* 2001;1:323-36. doi: 10.1100/tsw.2001.58
8. Rockwood K, Mitnitski A. Frailty in relation to the accumulation of deficits. *J Gerontol A Biol Sci Med Sci* 2007;62(7):722-7.
9. Searle SD, Mitnitski A, Gahbauer EA, et al. A standard procedure for creating a frailty index. *BMC Geriatr* 2008;8:24. doi: 1471-2318-8-24 [pii]10.1186/1471-2318-8-24 [published Online First: 2008/10/02]
10. Yang F, Gu D. Predictability of frailty index and its components on mortality in older adults in China. *BMC Geriatr* 2016;16:145. doi: 10.1186/s12877-016-0317-z
11. Franse CB, van Grieken A, Qin L, et al. Socioeconomic inequalities in frailty and frailty components among community-dwelling older citizens. *PLoS One* 2017;12(11):e0187946. doi: 10.1371/journal.pone.0187946
12. Hirsch C, Anderson ML, Newman A, et al. The association of race with frailty: the cardiovascular health study. *Ann Epidemiol* 2006;16(7):545-53. doi: 10.1016/j.annepidem.2005.10.003
13. Bandeen-Roche K, Seplaki CL, Huang J, et al. Frailty in Older Adults: A Nationally Representative Profile in the United States. *J Gerontol A Biol Sci Med Sci* 2015;70(11):1427-34. doi: 10.1093/gerona/glv133
14. Naharci MI, Engstrom G, Tappen R, et al. Frailty in Four Ethnic Groups in South Florida. *J Am Geriatr Soc* 2016;64(3):656-7. doi: 10.1111/jgs.14008

15. Statistics Netherlands (CBS). Statline: CBS, Den Haag/Heerlen; 2017 [Available from: http://statline.cbs.nl/Statweb accessed 23-3-2017.
16. Statistics Netherlands (CBS). Jaarrapport integratie 2016. Den Haag: CBS 2016.
17. Schellingerhout R. Gezondheid en welzijn van allochtone ouderen. Den Haag: Sociaal en Cultureel Planbureau 2004.
18. Ikram UZ, Kunst AE, Lamkaddem M, et al. The disease burden across different ethnic groups in Amsterdam, the Netherlands, 2011-2030. *Eur J Public Health* 2014;24(4):600-5. doi: 10.1093/eurpub/ckt136
19. Agyemang C, Snijder MB, Adjei DN, et al. Ethnic Disparities in CKD in the Netherlands: The Healthy Life in an Urban Setting (HELIUS) Study. *Am J Kidney Dis* 2016;67(3):391-9. doi: 10.1053/j.ajkd.2015.07.023
20. de Wit MA, Tuinebreijer WC, Dekker J, et al. Depressive and anxiety disorders in different ethnic groups: a population based study among native Dutch, and Turkish, Moroccan and Surinamese migrants in Amsterdam. *Soc Psychiatry Psychiatr Epidemiol* 2008;43(11):905-12. doi: 10.1007/s00127-008-0382-5
21. Parlevliet JL, Uysal-Bozkir O, Goudsmit M, et al. Prevalence of mild cognitive impairment and dementia in older non-western immigrants in the Netherlands: a cross-sectional study. *Int J Geriatr Psychiatry* 2016;31(9):1040-9. doi: 10.1002/gps.4417
22. van Assen MA, Pallast E, Fakiri FE, et al. Measuring frailty in Dutch community-dwelling older people: Reference values of the Tilburg Frailty Indicator (TFI). *Arch Gerontol Geriatr* 2016;67:120-9. doi: 10.1016/j.archger.2016.07.005
23. Lutomski JE, Baars MA, Schalk BW, et al. The development of the Older Persons and Informal Caregivers Survey Minimum DataSet (TOPICS-MDS): a large-scale data sharing initiative. *PLoS One* 2013;8(12):e81673. doi: 10.1371/journal.pone.0081673
24. BeterOud. Nationaal Programma Ouderenzorg 2017 [Available from: http://www.beteroud.nl/ouderen/nationaal-programma-ouderenzorg-npo.html.
25. Hak T, van der Veer K, Jansen H. The Three-Step Test-Interview (TSTI): An observational instrument for pretesting self-completion questionnaires 2004.
26. Parlevliet JL, Uysal-Bozkir Ö, Goudsmit M, et al. The SYMBOL Study: A Population-Based Study on Health and Cognition in Immigrant Older Adults in the Netherlands. *J Gerontol Geriat Res* 2014;3(4) doi: 10.4172/2167-7182.1000177
27. Statistics Netherlands (CBS). Jaarrapport integratie, 2010. Den Haag; Heerlen: Centraal Bureau voor de Statistiek 2010.
28. Lutomski JE, Baars MA, van Kempen JA, et al. Validation of a frailty index from the older persons and informal caregivers survey minimum data set. *J Am Geriatr Soc* 2013;61(9):1625-7. doi: 10.1111/jgs.12430
29. Mitnitski A, Song X, Skoog I, et al. Relative fitness and frailty of elderly men and women in developed countries and their relationship with mortality. *J Am Geriatr Soc* 2005;53(12):2184-9. doi: 10.1111/j.1532-5415.2005.00506.x

30. Rockwood K, Andrew M, Mitnitski A. A comparison of two approaches to measuring frailty in elderly people. *J Gerontol A Biol Sci Med Sci* 2007;62(7):738-43. [published Online First: 2007/07/20]
31. Katz S, Ford AB, Moskowitz RW, et al. Studies of Illness in the Aged. The Index of Adl: A Standardized Measure of Biological and Psychosocial Function. *JAMA* 1963;185:914-9.
32. Laan W, Zuithoff NP, Drubbel I, et al. Validity and reliability of the Katz-15 scale to measure unfavorable health outcomes in community-dwelling older people. *J Nutr Health Aging* 2014;18(9):848-54. doi: 10.1007/s12603-014-0479-3
33. Krabbe PF, Stouthard ME, Essink-Bot ML, et al. The effect of adding a cognitive dimension to the EuroQol multiattribute health-status classification system. *J Clin Epidemiol* 1999;52(4):293-301.
34. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;30(6):473-83.
35. Organisation for Economic Co-operation and Development. Classifying educational programmes : manual for ISCED-97 implementation in OECD countries. Paris: Organisation for Economic Co-operation and Development 1999.
36. Knol F. Van hoog naar laag; van laag naar hoog : de sociaal-ruimtelijke ontwikkeling van wijken tussen 1971-1995. Den Haag: Sociaal en Cultureel Planbureau 1998.
37. Snijders TAB, Bosker RJ. Multilevel analysis : an introduction to basic and advanced multilevel modeling. Los Angeles: SAGE 2012.
38. Mickey RM, Greenland S. The impact of confounder selection criteria on effect estimation. *Am J Epidemiol* 1989;129(1):125-37.
39. Greenland S, Finkle WD. A critical look at methods for handling missing covariates in epidemiologic regression analyses. *Am J Epidemiol* 1995;142(12):1255-64.
40. McDonald JH, University of D. Handbook of biological statistics. Baltimore, Maryland: Sparky House Publishing 2009.
41. Brothers TD, Theou O, Rockwood K. Frailty and migration in middle-aged and older Europeans. *Arch Gerontol Geriatr* 2014;58(1):63-8. doi: 10.1016/j.archger.2013.07.008
42. Evandrou M, Falkingham J, Feng Z, et al. Ethnic inequalities in limiting health and self-reported health in later life revisited. *J Epidemiol Community Health* 2016;70(7):653-62. doi: 10.1136/jech-2015-206074
43. Nazroo JY. The structuring of ethnic inequalities in health: economic position, racial discrimination, and racism. *Am J Public Health* 2003;93(2):277-84.
44. Hudson DL, Puterman E, Bibbins-Domingo K, et al. Race, life course socioeconomic position, racial discrimination, depressive symptoms and self-rated health. *Soc Sci Med* 2013;97:7-14. doi: 10.1016/j.socscimed.2013.07.031
45. Rechel B, Mladovsky P, Ingleby D, et al. Migration and health in an increasingly diverse Europe. *Lancet* 2013;381(9873):1235-45. doi: 10.1016/S0140-6736(12)62086-8
46. Pudaric S, Sundquist J, Johansson SE. Country of birth, instrumental activities of daily living, self-rated health and mortality: a Swedish population-based survey of people aged 55-74. *Soc Sci Med* 2003;56(12):2493-503.

SUPPLEMENTAL MATERIAL

Table S1. Association of ethnic background with Frailty Index scores and with six distinct frailty component scores; stratified by education level among 23,371 persons of The Older Persons and Informal Caregivers Survey Minimum DataSet (TOPICS-MDS).

		Frailty	Morbidities	ADL limitations	IADL limitations	Psychosocial health	Health-related quality of life	Self-rated health
	N	B (95% CI)	B (95% CI)	B (95% CI)	B (95% CI)	B (95% CI)	B (95% CI)	B (95% CI)
Persons with ≤ primary education								
Dutch	7,336	ref	ref	ref	ref	ref	ref	ref
Indonesian	100	0.008 (-0.015-0.030)	0.011 (-0.012-0.033)	-0.018 (-0.051-0.014)	0.047* (0.003-0.091)	-0.007 (-0.043-0.028)	0.004 (-0.028-0.036)	0.014 (-0.018-0.046)
Surinamese	79	0.083*** (0.055-0.110)	0.035* (0.007-0.063)	0.103*** (0.063-0.143)	0.198*** (0.144-0.252)	0.024 (-0.031-0.080)	0.080*** (0.041-0.120)	0.021 (-0.017-0.060)
Moroccan	119	0.071*** (0.039-0.102)	0.031 (-0.001-0.064)	0.035 (-0.006-0.076)	0.190*** (0.129-0.306)	0.086* (0.020-0.151)	0.066** (0.022-0.110)	0.057** (0.013-0.101)
Turkish	130	0.130*** (0.100-0.160)	0.089*** (0.059-0.120)	0.089*** (0.049-0.130)	0.248*** (0.191-0.306)	0.106*** (0.045-0.167)	0.168*** (0.127-0.209)	0.082*** (0.041-0.124)
Persons with ≥ secondary education								
Dutch	15,024	ref	ref	ref	ref	ref	ref	Ref
Indonesian	419	0.000 (-0.010-0.010)	-0.002 (-0.012-0.008)	-0.005 (-0.019-0.008)	0.010 (-0.009-028)	-0.005 (-0.021-0.011)	-0.005 (-0.019-0.010)	-0.005 (-0.020-0.011)
Surinamese	135	0.020* (0.000-0.039)	0.12 (-0.008-0.032)	0.011 (-0.016-0.037)	0.044* (0.008-0.080)	0.013 (-0.021-0.046)	0.019 (-0.009-0.047)	0.013 (-0.016-0.043)
Moroccan	18	0.080** (0.031-0.129)	0.054* (0.003-0.105)	0.021 (-0.046-0.088)	0.152*** (0.059-0.245)	0.125* (0.012-0.238)	0.101** (0.028-0.174)	0.064 (-0.013-0.140)
Turkish	11	0.087* (0.010-0.164)	0.082* (0.015-0.150)	0.108 (-0.035-0.251)	0.123 (-0.008-0.255)	-0.026 (-0.190-0.137)	0.100 (-0.006-0.205)	0.051 (-0.051-0.154)

Values are derived from multilevel multivariable linear regression, Dutch is the reference group. The models are adjusted for confounders: age, sex and living arrangement (alone/not alone). * p<0.05; ** p<0.01; ** p<0.001. B=effect estimate; CI=confidence interval; (I)ADL=(instrumental) activities of daily living.

Table S2. Association of ethnic background with Frailty Index scores and with six distinct frailty component scores; stratified by age category among 23,371 persons of The Older Persons and Informal Caregivers Survey Minimum DataSet (TOPICS-MDS).

		Frailty	Morbidities	ADL limitations	IADL limitations	Psychosocial health	Health-related quality of life	Self-rated health
	N	B (95% CI)	B (95% CI)	B (95% CI)	B (95% CI)	B (95% CI)	B (95% CI)	B (95% CI)
Persons aged 55-69 years								
Dutch	2,339	ref	ref	ref	ref	ref	ref	ref
Indonesian	59	-0.019 (-0.045-0.006)	-0.003 (-0.031- 0.023)	-0.016 (-0.047-0.015)	-0.021 (-0.067-0.024)	-0.026 (-0.073-0.022)	-0.044* (-0.086- -0.002)	-0.045* (-0.088- -0.002)
Surinamese	89	0.043** (0.018-0.068)	0.037* (0.011-0.063)	0.037* (0.005-0.068)	0.078*** (0.034-0.123)	0.005 (-0.058-0.069)	0.031 (-0.009-0.071)	0.024 (-0.018-0.066)
Moroccan	89	0.058*** (0.028-0.088)	0.030 (-0.001-0.062)	0.012 (-0.024-0.048)	0.150*** (0.096-0.203)	0.107*** (0.028-0.185)	0.056* (0.009-0.104)	0.062* (0.013-0.112)
Turkish	94	0.104*** (0.074-0.133)	0.084*** (0.053-0.115)	0.039* (0.003-0.074)	0.181*** (0.127-0.234)	0.147*** (0.070-0.225)	0.136*** (0.090-0.183)	0.082*** (0.034-0.131)
Persons aged 70+ years								
Dutch	20,021	ref	ref	ref	ref	ref	ref	Ref
Indonesian	460	0.006 (-0.004-0.016)	0.003 (-0.008-0.013)	-0.007 (-0.021-0.007)	0.022* (0.003-0.041)	0.000 (-0.015-0.016)	0.004 (-0.010-0.019)	0.008 (-0.007-0.023)
Surinamese	125	0.040** (0.020-0.059)	0.011 (-0.009-0.031)	0.044** (0.016-0.072)	0.102*** (0.065-0.140)	0.027 (-0.007-0.061)	0.043** (0.015-0.071)	0.006 (-0.022-0.035)
Moroccan	48	0.056* (0.019-0.094)	0.039 (-0.001-0.077)	-0.008 (-0.058-0.043)	0.141*** (0.070-0.212)	0.078* (0.000-0.155)	0.056* (0.004-0.107)	0.072** (0.017-0.127)
Turkish	47	0.139*** (0.105-0.173)	0.099*** (0.064-0.134)	0.127*** (0.079-0.174)	0.230*** (0.163-0.297)	0.046 (-0.023-0.115)	0.193*** (0.145-0.242)	0.119*** (0.067-0.170)

Values are derived from multilevel multivariable linear regression, Dutch is the reference group. The models are adjusted for confounders: age, sex, living arrangement (alone/ not alone) and education level. * p<0.05; ** p<0.01; ** p<0.001. B=effect estimate; CI=confidence interval; (I)ADL=(instrumental) activities of daily living.

Chapter 4

A prospective study on the variation in falling and fall risk among community-dwelling older citizens in 12 European countries

Carmen B. Franse, Judith A.C. Rietjens, Alex Burdorf, Amy van Grieken, Ida J. Korfage, Agnes van der Heide, Francesco Mattace Raso, Ed van Beeck, Hein Raat

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ABSTRACT

Objectives

The rate of falling among older citizens appears to vary across different countries, but the underlying aspects causing this variation are unexplained. We aim to describe between-country variation in falling and explore whether intrinsic fall risk factors can explain possible variation.

Design

Prospective study on data from the cross-national Survey of Health, Ageing and Retirement in Europe (SHARE).

Setting

Twelve European countries (Austria, Belgium, Czech Republic, Denmark, Estonia, France, Germany, Italy, The Netherlands, Spain, Sweden, Switzerland).

Participants

Community-dwelling persons aged ≥ 65 years (n=18 596).

Measurements

Socio-demographic factors (age, gender, education level and living situation) and intrinsic fall risk factors (less than good self-rated health (SRH), mobility limitations, limitations with activities of daily living (ADL), dizziness, impaired vision, depression and impaired cognition) were assessed in a baseline interview. Falling was assessed 2-years later by asking whether the participant had fallen within the 6 months prior to the follow-up interview.

Results

There was significant between-country variation in the rate of falling (varying from 7.9% in Switzerland to 16.2% in the Czech Republic). The prevalence of intrinsic fall risk factors varied twofold to fourfold between countries. Associations between factors age ≥80 years, less than good SRH, mobility limitations, ADL limitations, dizziness and depression, and falling were different between countries ($p<.05$). Between-country differences in falling largely persisted after adjusting for socio-demographic differences but strongly attenuated after adjusting for differences in intrinsic fall risk factors.

Conclusion

There is considerable variation in the rate of falling between European countries, which can largely be explained by between-country variation in the prevalence of intrinsic fall risk factors. There are also country-specific variations in the association between these intrinsic risk factors and falling. These findings emphasise the importance of addressing intrinsic fall risk in (inter)national fall-prevention strategies, while highlighting country-specific priorities.

INTRODUCTION

Every year around 30% of community-dwelling older citizens over age 65 fall [1-3]. Falling places a high burden on the health of older people and on public health resources [4]. Around 5-10% of all falls result in serious injury such as a head injury or fracture [5 6]. Around 90% of fractures of the hip, one of the most debilitating injuries among older people, are the result of a fall. In 2000, the combined costs in Europe for hip fractures were estimated at €24.4 billion[7], these costs are expected to double in 2050 due to the ageing population. Falling can also have negative psychosocial effects such as fear of falling, activity avoidance and social isolation [8 9]. Due to the burden caused by falling and positive results from fall prevention interventions, prevention of falling is a priority of health policy [3 10-12].

The rate of falling among older citizens appears to vary across countries and cultures [2 13 14]. However, few studies have investigated falling cross-nationally using uniform methodology to measure falling. A three-country study in community-dwelling men aged 65 years or above found that the proportion of fallers was highest in the US, intermediate in Sweden and lowest in Hong Kong [15]. Another study among persons aged 50-79 years in 36 European centres showed that the age-standardised incidence ranged between 1.7 and 75.1 falls/100 person years among men and between 3.0 and 52.5 falls/100 person years among women [13]. Differences in the incidence of falls explained 24%, 14%, and 6% of the between-centre variation in incidence of distal forearm and upper and lower limb fractures, respectively. The study provides little explanation on why they found such a wide variation in fall rates and speculated it is likely a complex pattern of varying intrinsic (patient-related) and external (environment related) factors.

What causes an individual person to fall is indeed a difficult question to answer as fall risk factors are multifold [1 10 16-19]. At the same time, risk factors have been well-described in the literature and studies have shown that intrinsic factors, in particular mobility and balance problems, are the strongest predictors of falling [1 19 20]. Between-country variation in the prevalence of intrinsic fall risk factors is therefore likely to contribute to between-country variation in falling, but this has not been documented so far. Furthermore, insight into regional differences of falls and fall risk factors can help (inter)national policy makers to prioritise the right fall prevention strategies or continue successful efforts. Exercise programmes, multifactorial fall prevention strategies and home safety interventions reduce falls,[3 11 21] the latter being more effective in persons with a higher intrinsic fall risk[3]. Therefore, the aim of this study is to describe the variation in falling across 12 European countries and to determine whether this variation can be explained by intrinsic fall risk factors. We sought to answer three questions:

1) How does the rate of falling vary for older citizens across 12 European countries?
2) Does the prevalence of intrinsic fall risk factors as well as the strength of the association with falling vary between the European countries?
3) To what extent does variation in prevalence of sociodemographic and intrinsic fall risk factors among European countries explain between-country variation in falling?

METHODS

Study design and population

This was a prospective study with a 2-year follow-up period. For this study we used data from the Survey of Health, Ageing and Retirement in Europe (SHARE). SHARE is a harmonised longitudinal survey of ageing processes in people aged 50 years and older across Europe that started in 2004. The study has been described in detail elsewhere [22]. Samples from different countries are based on probability household samples and respondents are interviewed using standardised computer assisted personal interviews (CAPI). SHARE has obtained ethical approval by the institutional review board at University of Mannheim, Germany.

We analysed data from community-dwelling persons aged ≥ 65 years at wave 4 (2010/2011) who also participated in wave 5 (2013)[23]. Data from 12 European countries (Sweden, Denmark, Austria, Germany, the Netherlands, Belgium, Switzerland, France, Italy, Spain, Czech Republic and Estonia) were included in this study. There were 28,344 persons aged 65 years and older from the 12 European countries in wave 4, of which 18,596 persons (74.3%) participated in wave 5 and were included in the study.

Measures

Falling

The outcome measure used in this study is the rate of falling, defined as the presence of one or more self-reported falls in the 6 months prior to wave 5. This was assessed by asking participants 'For the past 6 months at least, have you been bothered by any of the health conditions on this card?'. A showcard was presented to the participant with five health conditions among which was 'falling down'.

Socio-demographic factors

The following socio-demographic factors assessed at wave 4 were used: age, gender, education level and living situation. Year and month of birth of the respondent was assessed in the questionnaire, age was calculated and categorised in 5-year groups (65-69 years; 70-74 years; 75-79 years and ≥80 years) for stratification of rate of falling and categorised

into <80 years and ≥80 years for logistic regressions. Living situation was assessed by asking whether the respondent lived together with their spouse and whether anyone else was living in the household; the number of persons in the household was calculated and categorised into 'not alone' (>1 person) and 'alone' (one person). For international comparisons of education, SHARE uses the 1997 International Standard Classification of Education (ISCED-97). Education level was assessed by asking the highest level of education completed and categorised the level of education into 'low' (0-10 years) and 'high' (11-25 years).

Intrinsic fall risk factors

We used three systematic reviews to determine which risk factors were consistently and strongly associated with falling[1 20 24] and then used the risk factors which were present in the wave 4 data: self-rated health (SRH), mobility limitations, limitations with activities of daily living (ADL), dizziness, impaired vision, depression and impaired cognition. SRH is a common measure used in comparing population health and was assessed with the US global version of SRH[25], by asking: 'Would you say your health is…'; options were poor, fair, good, very good, excellent. Less than good SRH was defined as 'poor' or 'fair'[26]. Mobility limitations were assessed with three items from the extensively used and validated SF-36 instrument[27], by asking participants whether they had problems with one or more of the following activities: walking 100 metres, walking one set of stairs and walking several sets of stairs. Mobility limitations were defined as having problems with one or more of these activities. Six basic ADL limitations as developed by Katz et al[28] were assessed by asking participants whether they had difficulties with one or more of six ADLs (dressing, walking across a room, bathing, eating, getting in or out of bed, using toilet). ADL limitations were defined as having problems with one or more of these activities. Dizziness was assessed by asking: 'For the past 6 months at least, have you been bothered by any of the health conditions on this card?'. A showcard was presented to the participant with five conditions among which were 'dizziness, faints or blackouts'. Vision was assessed by asking: 'How good is your eyesight for seeing things at a distance, like recognising a friend across the street [using glasses or contact lenses as usual]? Would you say it is…'; options were poor, fair, good, very good, excellent. Impaired (diminished) vision was defined as 'poor' or 'fair'. Depression was assessed by the Euro-D scale, with 12 items: depression, pessimism, death wishes, guilt, sleep, interest, irritability, appetite, fatigue, concentration, enjoyment, and tearfulness. Each item is scored 0 (symptom not present) or 1 (symptom present). Scores ≥4 indicated depression. Euro-D was developed to compare symptoms of depression across Europe and validated in a European sample [29 30]. Cognitive function was assessed by five tests that assessed verbal fluency, immediate and delayed recall, orientation and numeracy[31 32]. A summary cognitive function score of averaged z-scores of the five tests was built for individuals who had valid values for at least three of the tests. Respondents were classified as being cognitively impaired if their score was in the lowest decile of the

summary indicator. Cognition impairment according to this definition is likely to reflect the lower range of statistically 'normal' cognitive function, not necessarily clinically diagnosable disorders[33].

Statistical analysis

The statistical significance of differences in socio-demographic characteristics and intrinsic fall risk factors among persons from different countries were calculated using chi-squared tests and independent samples t-test. Rate of falling was stratified by sex and different age categories to study differences between countries. To examine the association of socio-demographic and intrinsic risk factors with falling, multivariable logistic regression analyses were performed for each country separately. The multivariable models were conducted on the 17 575 persons (94.5%) with complete data. We tested for the significance of between-country differences in the strength of the association between predictors (socio-demographic and intrinsic risk factors) and falling by including data from all countries in one logistic regression model and adding an interaction term for country*predictor, for each predictor separately.

To examine whether differences in intrinsic fall risk could explain differences in rate of falling, we also performed logistic regression analyses with the dataset that contained all countries. Association between country of residence and falling was adjusted for socio-demographic and intrinsic fall risk factors. Country was entered as dummy variable with Switzerland as the reference category as it had the lowest rate of falling. Each logistic regression model was built up in several steps: we first tested the association between country of residence and falling (model 1), we subsequently added socio-demographic factors (model 2), mental health factors (model 3) and physical health factors (model 4). In the final model we added all socio-demographic and intrinsic fall risk factors together (model 5). All models were corrected for falling at baseline. We calculated change in ORs of models with predictors compared to model 1 with the formula: (OR *model 1*-OR *model with predictors*)/(OR *model 1*-1)*100%. Falling was assessed in the same way in wave 4 and entered as covariate in all multivariable models. In a sensitivity analysis we added interaction terms between predictors and country separately to the final model (model 5). We considered a p-value of .05 or lower to be statistically significant. All analyses were performed using SPSS version 21.0 (IBM SPSS Statistics for Windows, IBM Corp., Armonk, New York).

Non-response analysis and weights

SHARE has high contact rates (>95%) and a moderate cooperation rate (70-80%) between waves. Exact reasons for refusal to participate are unknown, for 2.6% of the sample death was reported as the reason. The mortality data are however not always reliable; SHARE aims to uncover this in the future[23]. A comparison of the persons included in this study (n=18 596) with the persons who were excluded due to non-participation at follow-up (n=9748)

indicated that these persons were older, had a higher intrinsic fall risk and more often reported a fall at baseline. Attrition was highest in Germany, France and the Czech Republic. To calculate descriptive statistics (table 1 and figure 1), we used calibrated sampling weights to account for the sampling design, non-response, and attrition. We report unweighted descriptive statistics in a supplementary table (see supplementary table S1). Weights were calibrated against the national populations by age group and sex, as well as for mortality between waves. We did not apply weights in regression models because weighting is unnecessary for consistency and potentially harmful for precision[34 35].

RESULTS

Socio-demographic and fall risk characteristics

Mean age at baseline for the overall weighted sample was 74.1 years (SD 6.8 years) and 55.8% were women. Participants in Spain and Italy had lower education levels compared with those from other countries and were less often living alone (p<.001; table 1).

The prevalence of all intrinsic fall risk factors varied between countries (p<.001; table 1). The prevalence of most intrinsic risk factors was on the lower end of the spectrum in Switzerland, Denmark, Sweden and The Netherlands and on the higher end of the spectrum in Italy, Estonia, Spain and Czech Republic. In France and Belgium the prevalence of ADL limitations, impaired vision and depression was on the higher end of the spectrum. Impaired cognition was highest in Spain (39.5%) and Italy (24.3%) and ranged from 4.0% to 13.5% in the other countries.

Falling

There was significant between-country variation in the proportion of persons reporting falling (p<.001; table 1). In Switzerland, Denmark, Sweden and Austria between 7.9% (95% CI 6.6% to 9.4%) and 9.5% (95% CI 8.3% to 10.9%) reported falling within the past 6 months. In Italy, The Netherlands, Germany and Belgium this varied between 11.0% (95% CI 9.5% to 12.8%) and 12.8% (95% CI 11.3% to 14.4%). In Estonia, France, Spain and Czech Republic this varied between 13.9% (95% CI 12.7% to 15.2%) and 16.2% (95% CI 14.7% to 17.9%).

The between-country variation in falling showed similar patterns for both men and women aged <80 years as well as among women aged ≥80 years (figure 1A and 1B). Among men aged ≥80 years, the between-country variation was smaller and distributed differently. Especially few men in Italy reported falling (figure 1A).

Table 1: Weighted baseline socio-demographic and intrinsic fall risk characteristics, and self-reported falling at the 2-year follow-up interview, of persons from 12 countries in The Survey of Health, Ageing and Retirement in Europe, 2010-2013.

	Switzerland	Denmark	Sweden	Austria	Italy	Netherlands	Germany	Belgium	Estonia	France	Spain	Czech Republic
	n=1386	n=873	n=1009	n=1983	n=1423	n=1092	n=591	n=1805	n=2917	n=1893	n=1559	n=2065
Age, mean ± SD[a]	73.9 ± 6.8	73.3 ± 6.9	73.9 ± 7.3	74.2 ± 6.9	74.4 ± 6.6	73.8 ± 6.9	74.6 ± 6.5	74.7 ± 6.9	74.0 ± 6.4	75.1 ± 7.1	74.7 ± 7.0	73.0 ± 6.6
Female, %[b]	55.8	54.2	53.6	57.5	57.3	55.3	55.2	58.3	67.9	58.3	58.0	59.0
Low education, %[bc]	28.2	23.8	51.2	29.9	81.4	56.7	17.9	51.3	41.8	57.3	90.1	46.6
Living alone, %[b]	36.6	38.8	42.7	38.0	27.4	41.0	38.4	34.1	43.0	38.6	26.0	32.3
Less than good SRH, %[bc]	19.8	24.4	33.6	35.1	53.5	32.1	45.5	33.7	78.6	44.7	56.4	48.8
Mobility limitation(s), %[bc]	18.3	24.7	26.3	42.5	52.8	26.2	37.2	37.5	43.6	40.3	49.6	47.6
ADL limitation(s), %[bc]	8.2	9.6	12.2	14.5	16.0	8.0	18.8	20.0	19.9	15.6	17.9	12.4
Dizziness, %[bc]	6.9	11.3	10.6	11.2	14.5	10.7	11.0	11.1	22.2	10.4	15.3	10.8
Impaired vision, %[bc]	10.6	9.5	8.3	9.6	27.7	10.6	10.2	14.2	32.0	16.4	34.4	14.8
Depression, %[bc]	17.9	13.7	19.4	21.6	37.7	18.3	24.1	29.9	43.6	34.0	41.0	25.9
Impaired cognition, %[bc]	4.4	7.0	6.7	9.2	28.1	9.9	9.4	13.0	10.2	13.6	38.7	8.0
Baseline falling, %[b,c,d]	3.1	4.5	5.6	7.0	5.1	4.5	4.9	6.5	7.3	7.7	9.8	6.6
Falling at follow-up, %[b,c,d]	7.9	9.1	9.4	9.5	11.0	11.5	11.8	12.8	13.9	14.9	16.2	16.2
95% CI	6.6-9.4	7.3-11.1	7.8-11.4	8.3-10.9	9.5-12.8	9.8-13.6	9.5-14.7	11.3-14.4	12.7-15.2	13.4-16.6	14.5-18.1	14.7-17.9

P-value <0.001, based on a) t-test and b)chi-squared test; c) missing N for variables: education=340; SRH=35; mobility=30; ADL=34; Dizziness=37; Vision=50; Depression=480; Cognition=397; Falling=55; d) Reporting one or more falls within the 6 months prior to the interview

ADL=Activities of daily living; CI=Confidence Interval; SD=Standard Deviation; SRH=Self-rated health

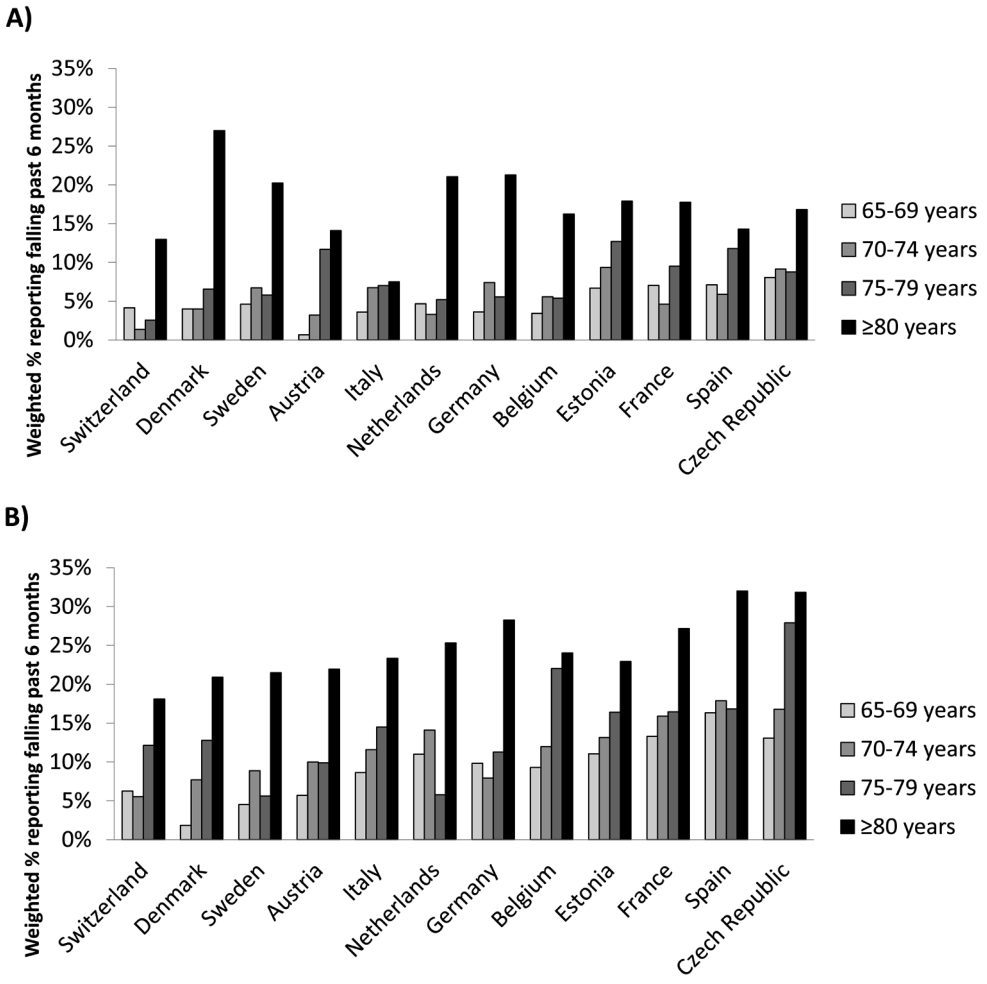

Figure 1: Rate of falling, by country and age group for (A) men and (B) women from 12 countries in the Survey of Health, Ageing and Retirement in Europe, 2010–2013.

Table 2: Multivariable binary logistic regression per country with associations (odds ratios and 95% confidence intervals) of socio-demographic and intrinsic fall risk factors with self-reported falling among persons from 12 countries in The Survey of Health, Ageing and Retirement in Europe, 2010-2013.

	Switzerland	Denmark	Sweden	Austria	Italy	Netherlands	Germany	Belgium	Estonia	France	Spain	Czech Republic	*P*[d]
	n=1345	n=840	n=946	n=1864	n=1364	n=1027	n=570	n=1747	n=2749	n=1771	n=1396	n=1956	n=17,575
Age ≥80 years	2.18[b] (1.33-3.57)	3.06[c] (1.69-5.55)	2.08[b] (1.20-3.59)	2.12[c] (1.44-3.11)	1.14 (0.70-1.87)	2.43[c] (1.49-3.97)	2.95[b] (1.47-5.92)	1.62[b] (1.16-2.61)	1.53[b] (1.17-2.00)	1.35 (0.98-1.87)	1.44[a] (1.01-2.04)	1.42[a] (1.02-1.99)	.004
Female gender	1.60 (0.96-2.66)	0.72 (0.39-1.33)	0.91 (0.55-1.53)	1.83[b] (1.21-2.77)	1.73[a] (1.13-2.65)	1.33 (0.81-2.19)	1.75 (0.92-3.35)	1.79[c] (1.27-2.54)	1.07 (0.82-1.40)	1.75[c] (1.27-2.43)	1.66[b] (1.17-2.36)	1.43[a] (1.07-1.91)	.086
Low education	1.23 (0.75-2.00)	1.06 (0.56-2.03)	0.70 (0.43-1.15)	0.74 (0.50-1.10)	0.69 (0.40-1.17)	1.37 (0.84-2.22)	0.92 (0.40-2.08)	1.00 (0.73-1.37)	0.82 (0.64-1.05)	1.32 (0.97-1.81)	0.85 (0.48-1.49)	1.18 (0.91-1.54)	.275
Living alone	1.24 (0.76-2.01)	1.46 (0.81-2.64)	0.90 (0.52-1.55)	1.49[a] (1.04-2.16)	0.99 (0.61-1.60)	1.53 (0.94-2.48)	1.30 (0.66-2.58)	1.40[a] (1.02-1.93)	1.27 (0.98-1.63)	1.21 (0.90-1.63)	1.39 (0.95-2.02)	1.35[a] (1.03-1.79)	.530
Less than good SRH	1.22 (0.70-2.11)	1.67 (0.89-3.13)	1.57 (0.92-2.68)	1.77[b] (1.19-2.65)	1.15 (0.71-1.85)	2.09[b] (1.27-3.43)	1.80 (0.89-3.63)	1.64[b] (1.17-2.32)	1.05 (0.73-1.51)	1.10 (0.80-1.50)	1.13 (0.77-1.64)	1.69[c] (1.26-2.27)	.001
Mobility limitation(s)	1.13 (0.63-2.03)	2.06[a] (1.06-3.99)	1.99[a] (1.13-3.51)	1.16 (0.76-1.75)	1.42 (0.87-2.31)	1.72[a] (1.05-2.83)	0.44[a] (0.19-0.98)	1.77[c] (1.25-2.50)	1.67[c] (1.27-2.21)	1.47[a] (1.06-2.03)	1.42 (0.97-2.07)	1.19 (0.90-1.59)	.002
ADL limitation(s)	1.36 (0.68-2.73)	1.98 (0.93-4.19)	1.45 (0.76-2.77)	2.02[b] (1.29-3.15)	1.41 (0.85-2.35)	1.59 (0.82-3.10)	2.43[a] (1.06-5.53)	1.33 (0.92-1.91)	1.51[b] (1.14-2.00)	1.60[a] (1.10-2.32)	1.17 (0.77-1.78)	1.20 (0.83-1.75)	.022
Dizziness	1.84 (0.95-3.57)	5.19[c] (2.76-9.77)	1.62 (0.85-3.08)	1.05 (0.66-1.69)	1.78[a] (1.10-2.87)	1.16 (0.61-2.19)	1.21 (0.52-2.78)	1.32 (0.87-1.99)	1.45[b] (1.11-1.89)	1.16 (0.77-1.77)	0.92 (0.61-1.39)	1.97[c] (1.38-2.81)	<.001
Impaired vision	1.77 (1.00-3.13)	1.07 (0.50-2.30)	1.61 (0.78-3.33)	1.25 (0.77-2.03)	1.03 (0.67-1.59)	1.12 (0.59-2.13)	1.05 (0.42-2.68)	0.88 (0.59-1.32)	1.50[c] (1.18-1.92)	0.97 (0.67-1.40)	1.27 (0.91-1.76)	1.10 (0.79-1.54)	.375
Depression	1.39 (0.82-2.36)	1.96[a] (1.02-3.79)	1.48 (0.86-2.56)	1.39 (0.93-2.07)	1.77[a] (1.13-2.76)	1.07 (0.63-1.82)	1.29 (0.64-2.58)	1.78[c] (1.29-2.45)	1.18 (0.92-1.52)	1.06 (0.78-1.44)	1.25 (0.87-1.79)	1.14 (0.85-1.54)	.025
Impaired cognition	1.76 (0.77-4.06)	1.28 (0.57-2.86)	2.24[a] (1.04-4.83)	1.38 (0.80-2.38)	2.02[b] (1.30-3.14)	2.24[b] (1.21-4.14)	1.13 (0.41-3.16)	1.33 (0.89-2.00)	1.47[a] (1.04-2.08)	1.11 (0.75-1.63)	1.42[a] (1.02-1.99)	1.54[c] (1.04-2.30)	.334

All Odds ratios are adjusted for other factors in the table and self-reported falling at baseline. a) p<0.05; b) p<0.01; c) p<0.001; d) We tested for the significance of between-country differences in the strength of the association between predictors (socio-demographic and intrinsic risk factors) and falling by including data from all countries in one logistic regression model and adding an interaction term for country(dummy)*predictor, for each predictor separately. ADL=Activities of daily living; SRH=self-rated health

Factors associated with falling in each country

When controlling for all factors in the model, older age (≥80 years) was associated with falling in almost all countries (ORs varying from 1.42 in the Czech Republic to 3.06 in Denmark). Female gender was associated with falling in six countries. Lower education level and living alone were not associated with falling in most countries (table 2).

Associations between the seven intrinsic factors and falling were in positive direction in almost all countries. The only exception was having at least one mobility limitation in Germany (OR=0.44; 95% CI 0.19 to 0.98), although this was in a positive direction (non-significant) in univariable analysis. Having at least one mobility limitation and impaired cognition were most often significantly associated with falling (ORs varying from 0.44 to 2.06 and from 1.42 to 2.24 respectively).

In countries where intrinsic fall risk factors were more prevalent (Estonia, Czech Republic, Spain, Italy, France and Belgium) the contribution of a specific fall risk factor was lower (ORs varying from 1.42 to 1.97) than in the other countries where fall risk factors were less prevalent (ORs varying from 1.72 to 5.19). These differences were significant for factors age ≥80 years, less than good SRH, mobility limitations, ADL limitations, dizziness and depression ($p<.05$; table 2, last column).

Country differences in falling

In the unadjusted model, differences in falling between Switzerland and six countries (The Netherlands, Belgium, France, Spain, Czech Republic and Estonia) were significant (table 3, model 1). After adjusting for socio-demographic factors, ORs changed -44.4% to 22.4% (model 2). In all countries attenuation of ORs was strongest when additionally adjusting for fall risk factors related to physical health (mobility limitations, ADL limitations, dizziness, SRH and vision) (model 4). In the final model (model 5), differences in falling between Switzerland and four countries (The Netherlands, Belgium, France and Czech Republic) remained significant. All ORs were strongly attenuated (varying from 21.9% for The Netherlands to 149.0% for Italy).

Table 3: Associations (odds ratios and 95% confidence intervals) between countries and self-reported falling adjusted for socio-demographic factors and intrinsic fall risk factors among persons from 12 countries in The Survey of Health, Ageing and Retirement in Europe, 2010-2013; N=17,575.

	Model 1: Univariate[1]	Model 2: Socio-demographic[2] adjusted	Model 3: Mental health[3] adjusted	Model 4: Physical health[4] adjusted	Model 5: Adjusted for all[5] variables
Switzerland	1	1	1	1	1
Denmark	1.28 (0.94-1.74)	1.24 (0.90-1.70)	1.25 (0.90-1.72)	1.09 (0.79-1.51)	1.12 (0.80-1.55)
Sweden	1.23 (0.91-1.66)	1.22 (0.90-1.67)	1.23 (0.90-1.69)	1.11 (0.81-1.51)	1.14 (0.83-1.57)
Austria	1.18 (0.91-1.52)	1.15 (0.88-1.50)	1.10 (0.84-1.44)	0.93 (0.71-1.21)	0.92 (0.70-1.22)
Italy	1.30 (0.99-1.71)	1.31 (0.99-1.74)	1.06 (0.79-1.42)	0.93 (0.69-1.24)	0.85 (0.63-1.15)
Netherlands	1.48[b] (1.11-1.97)	1.39[b] (1.04-1.88)	1.44[a] (1.07-1.95)	1.33 (0.98-1.79)	1.38[a] (1.02-1.86)
Germany	1.36 (0.96-1.91)	1.52[a] (1.07-2.17)	1.41 (0.98-2.02)	1.13 (0.79-1.62)	1.13 (0.78-1.63)
Belgium	1.78[c] (1.39-2.29)	1.65[c] (1.27-2.13)	1.47[b] (1.13-1.91)	1.34[a] (1.03-1.74)	1.31[a] (1.00-1.71)
Estonia	1.83[c] (1.45-2.32)	1.80[c] (1.42-2.29)	1.53[c] (1.19-1.95)	1.09 (0.85-1.40)	1.06 (0.82-1.37)
France	2.07[c] (1.62-2.63)	1.83[c] (1.42-2.36)	1.60[c] (1.23-2.07)	1.51[b] (1.17-1.95)	1.42[b] (1.09-1.84)
Spain	2.10[c] (1.64-2.70)	1.96[c] (1.50-2.55)	1.45[b] (1.10-1.91)	1.39[a] (1.06-1.83)	1.22 (0.92-1.62)
Czech Republic	2.30[c] (1.81-2.92)	2.35[c] (1.84-3.01)	2.23[c] (1.73-2.86)	1.78[c] (1.39-2.30)	1.79[c] (1.38-2.31)

a) p<0.05; b) p<0.01; c) p<0.001. 1)Adjusted for self-reported falling at baseline; 2)Adjusted for model 1 and socio-demographic factors (sex, age, education level and living situation); 3) Adjusted for model 2, depression and impaired cognition; 4) Adjusted for model 2, mobility limitations, activities of daily living (ADL) limitations, dizziness, less than good self-rated health (SRH) and impaired vision; 5) Adjusted for model 2, mobility limitations, ADL limitations, dizziness, less than good SRH, impaired vision, depression and impaired cognition.

DISCUSSION

Main study findings

The results of this study show considerable variation in the rate of falling and prevalence of intrinsic fall risk factors between European countries. Between-country differences in falling largely persisted after adjusting for socio-demographic differences, but were strongly attenuated after adjusting for differences in intrinsic fall risk factors.

Comparison with other findings

The rate of falling observed in the different countries (between 7.9% and 16.2% within 6 months) was on the low end of the rate reported in the literature, which is between 20% and 40% within 12 months [2 14 36-38]. In our study, falling was assessed retrospectively by asking whether a person was bothered by falling in the past 6 months. Preferably falls are measured prospectively on a weekly basis, as specificity of retrospective self-report is high but the sensitivity is lower (80-89%)[39], so there might have been a recall bias. Measuring falls prospectively is however a time intensive procedure and not feasible for larger surveys. However, we believe the reason for the lower rate is predominantly due to the specific

formulation of the question, as it assessed whether the person was bothered by the fall, this might have resulted in a tendency towards only reporting more serious falls.

Differences in wealth and expenditure on elderly care between countries play a role in the between-country variations in falling and intrinsic fall risk we found [40]. Older citizens in the original EU-15 countries are in better health compared with those in eastern European countries and within the EU-15 countries a north-south gradient for several health indicators at older age has been shown [40-43]. In our study, rate of falling and prevalence of fall risk was higher in Spain, Estonia and the Czech Republic and also Belgium and France, compared with the other countries. The Organisation for Economic Co-operation and Development (OECD) reports a lower proportion of institutionalised long term care recipients aged >65 years in southern and eastern European countries, but also in Belgium and France [44]. As our study only includes community-dwelling older citizens, this could partly explain a higher rate of falling and prevalence of intrinsic fall risk in these countries, where more persons in poor health are living independently.

Intrinsic risk factors, and mobility and balance problems in particular, have been shown to be most important in the aetiology of falling [1 19 20]. In our study, limitations in physical health factors explained the largest part of between-country differences, having one or more mobility limitations was significantly associated with falling in many countries and highly prevalent among most countries. The strength of the association of several intrinsic risk factors and older age with falling differed between countries. In countries where intrinsic fall risk factors were more prevalent, the impact of these intrinsic risk factors and older age on falling was smaller compared to the other countries. In these countries, we found a relatively high risk for falling in the group <80 years and the group who did not have these intrinsic risk factors, which could explain this finding. This could suggest that in these countries other conditions, such as frailty, contribute more to falling and occur at an earlier age [42].

Persons in Italy and especially men had a relatively low rate of falling and a high prevalence of intrinsic fall risk compared with other countries. Interestingly, an Australian study found a lower fall-rate among Italian-born immigrant men, which they also could not explain by established fall risk factors [45]. This contrasts our other findings, where we found a high intrinsic fall risk in countries with a high rate of falling. As we did not include environmental fall risk factors, it is possible that differences in extrinsic hazards such as floor coverings and home maintenance contribute to this finding. Additionally, it is possible that outdoor and indoor activity patterns associated with increased fall risk differ by culture (such as cycling, fast walking, housekeeping and taking stairs). Older persons in northern countries have been found to be more physically active compared with older persons living in southern countries [35 46]. In The Netherlands cycling is a common form of transportation and largely contributes to outdoor falls [47], this could clarify our finding that the prevalence of intrinsic

fall risk could to a smaller extent explain falling in The Netherlands. Future studies should investigate the impact of cultural differences in activity patterns and extrinsic risk factors on between-country differences in falling.

Strengths and weaknesses

To our knowledge, this is the first study comparing falling and fall risk among European countries. Previous studies have compared few countries or used centre-based data[13 15]. This study has the advantage of using standardised methods for data-collection and data from nationally representative samples of those aged 65 years and over from 12 European countries. By the use of survey data, we were able to capture many intrinsic fall risk factors. The longitudinal design ensured that the intrinsic fall risk factors preceded fall outcomes.

This study has some limitations. Between baseline and follow-up interviews, 25.7% of persons were lost to follow up. These persons were older, had a higher intrinsic fall risk and more often reported a fall at baseline. Attrition was highest in Germany, France and the Czech Republic, which might have resulted in an underestimation of the rate of falling, especially in these countries. This however, does not affect the overall trend seen between countries as the rate of falling in these countries was on the high end of the spectrum. Furthermore, we corrected for attrition and mortality using sampling weights calibrated against the national populations. Second, we did not have information on the number of falls (recurrent or first time fall) or place of fall. Studies suggest that indoor falls are more often due to intrinsic fall risk and outdoor falls due to environmental risk-factors [48 49]. Recurrent falls have been found to occur among persons with poorer health and higher intrinsic fall risk [50 51]. In an additional analysis we compared persons who reported falling in both wave 4 and 5, with persons who only reported falling in wave 5 and indeed found stronger associations between intrinsic risk factors and falling for the first group (table S2). Third, to minimise cross-cultural differences in translation of questions, SHARE uses the TRAPD method (translation, review, adjudication, pretesting, and documentation) developed for translation of cross cultural surveys [52 53]. However, it remains possible that cultural differences in the interpretation of a survey question might have caused some variation between countries. Finally, in the full model with all countries, we did not take into account the country-predictor interactions as all associations were consistent in the direction of the effect; pointing toward an increase in fall risk. In a sensitivity analysis we added interaction terms between predictors and country separately; the changes to our findings were marginal (data not shown).

Conclusion

In conclusion, there is considerable variation in rate of falling among citizens aged ≥65 years between European countries, which can largely be explained by between-country variation in the prevalence of intrinsic fall risk factors. There are also country-specific variations in the association between these intrinsic risk factors and falling. These findings emphasise the

importance of addressing intrinsic fall risk in (inter)national fall-prevention strategies, while highlighting country-specific priorities.

REFERENCES

1. Deandrea S, Lucenteforte E, Bravi F, et al. Risk factors for falls in community-dwelling older people: a systematic review and meta-analysis. *Epidemiology* 2010;21(5):658-68. doi: 10.1097/EDE.0b013e3181e89905 [published Online First: 2010/06/30]
2. Morrison A, Fan T, Sen SS, et al. Epidemiology of falls and osteoporotic fractures: a systematic review. *Clinicoecon Outcomes Res* 2013;5:9-18. doi: 10.2147/CEOR.S38721 ceor-5-009 [pii] [published Online First: 2013/01/10]
3. Gillespie LD, Robertson MC, Gillespie WJ, et al. Interventions for preventing falls in older people living in the community. *Cochrane Database Syst Rev* 2012;9:CD007146. doi: 10.1002/14651858.CD007146.pub3
4. Hartholt KA, van Beeck EF, Polinder S, et al. Societal consequences of falls in the older population: injuries, healthcare costs, and long-term reduced quality of life. *J Trauma* 2011;71(3):748-53. doi: 10.1097/TA.0b013e3181f6f5e5 [published Online First: 2010/11/04]
5. Tinetti ME, Williams CS. The effect of falls and fall injuries on functioning in community-dwelling older persons. *J Gerontol A Biol Sci Med Sci* 1998;53(2):M112-9. [published Online First: 1998/04/01]
6. Peeters G, van Schoor NM, Lips P. Fall risk: the clinical relevance of falls and how to integrate fall risk with fracture risk. *Best Practice & Research in Clinical Rheumatology* 2009;23(6):797-804. doi: DOI 10.1016/j.berh.2009.09.004
7. De Laet CE, van Hout BA, Burger H, et al. Incremental cost of medical care after hip fracture and first vertebral fracture: the Rotterdam study. *Osteoporos Int* 1999;10(1):66-72. doi: 90100066.198 [pii] 10.1007/s001980050196 [published Online First: 1999/09/29]
8. Tinetti ME, Mendes de Leon CF, Doucette JT, et al. Fear of falling and fall-related efficacy in relationship to functioning among community-living elders. *J Gerontol* 1994;49(3):M140-7. [published Online First: 1994/05/01]
9. Jorstad EC, Hauer K, Becker C, et al. Measuring the psychological outcomes of falling: a systematic review. *J Am Geriatr Soc* 2005;53(3):501-10.
10. Tinetti ME, Kumar C. The patient who falls: "It's always a trade-off". *JAMA* 2010;303(3):258-66. doi: 303/3/258 [pii] 10.1001/jama.2009.2024 [published Online First: 2010/01/21]
11. Gillespie LD, Robertson MC, Gillespie WJ, et al. Interventions for preventing falls in older people living in the community. *Cochrane Database Syst Rev* 2009(2):CD007146. doi: 10.1002/14651858.CD007146.pub2 [published Online First: 2009/04/17]
12. European Innovation Partnership on Active and Healthy Ageing. Specific Action on innovation in support of 'Personalized health management, starting with a Falls Prevention Initiative' Brussels: European Commision; 2013 [Available from: https://ec.europa.eu/eip/ageing/sites/eipaha/files/library/51a44f911f647_a2_action_plan.pdf.
13. Roy DK, Pye SR, Lunt M, et al. Falls explain between-center differences in the incidence of limb fracture across Europe. *Bone* 2002;31(6):712-7. doi: S8756328202009092 [pii] [published Online First: 2003/01/18]

14. Peel NM. Epidemiology of falls in older age. *Can J Aging* 2011;30(1):7-19. doi: S071498081000070X [pii] 10.1017/S071498081000070X [published Online First: 2011/03/16]
15. Karlsson MK, Ribom EL, Nilsson JA, et al. International and ethnic variability of falls in older men. *Scand J Public Health* 2014;42(2):194-200. doi: 1403494813510789 [pii] 10.1177/1403494813510789 [published Online First: 2013/11/22]
16. Ganz DA, Bao Y, Shekelle PG, et al. Will my patient fall? *JAMA* 2007;297(1):77-86. doi: 297/1/77 [pii] 10.1001/jama.297.1.77 [published Online First: 2007/01/04]
17. Leipzig RM, Cumming RG, Tinetti ME. Drugs and falls in older people: a systematic review and meta-analysis: II. Cardiac and analgesic drugs. *J Am Geriatr Soc* 1999;47(1):40-50. [published Online First: 1999/01/27]
18. Leipzig RM, Cumming RG, Tinetti ME. Drugs and falls in older people: a systematic review and meta-analysis: I. Psychotropic drugs. *J Am Geriatr Soc* 1999;47(1):30-9. [published Online First: 1999/01/27]
19. Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. *N Engl J Med* 1988;319(26):1701-7. doi: 10.1056/NEJM198812293192604 [published Online First: 1988/12/29]
20. National Institute for Clinical E. Clinical practice guideline for the assessment and prevention of falls in older people : guidelines commissioned by the National Institute for Clinical Excellence (NICE). London: Royal College of Nursing 2004.
21. Costello E, Edelstein JE. Update on falls prevention for community-dwelling older adults: review of single and multifactorial intervention programs. *J Rehabil Res Dev* 2008;45(8):1135-52. [published Online First: 2009/02/24]
22. Borsch-Supan A, Brandt M, Hunkler C, et al. Data Resource Profile: the Survey of Health, Ageing and Retirement in Europe (SHARE). *Int J Epidemiol* 2013;42(4):992-1001.
23. Malter F, Börsch-Supan A, Munich Center for the Economics of A. SHARE Wave 5 Innovations & Methodology. 2015
24. Perell KL, Nelson A, Goldman RL, et al. Fall risk assessment measures: an analytic review. *J Gerontol A Biol Sci Med Sci* 2001;56(12):M761-6. [published Online First: 2001/11/28]
25. Ware JE, Stewart AL. Measuring functioning and well-being : the medical outcomes study approach. Durham: Duke University Press 1993.
26. Hiel L, Beenackers MA, Renders CM, et al. Providing personal informal care to older European adults: should we care about the caregivers' health? *Prev Med* 2015;70:64-8. doi: 10.1016/j.ypmed.2014.10.028
27. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;30(6):473-83.
28. Katz S, Ford AB, Moskowitz RW, et al. Studies of Illness in the Aged. The Index of Adl: A Standardized Measure of Biological and Psychosocial Function. *JAMA* 1963;185:914-9.
29. Prince MJ, Reischies F, Beekman AT, et al. Development of the EURO-D scale--a European, Union initiative to compare symptoms of depression in 14 European centres. *Br J Psychiatry* 1999;174:330-8. [published Online First: 1999/10/26]

30. Castro-Costa E, Dewey M, Stewart R, et al. Ascertaining late-life depressive symptoms in Europe: an evaluation of the survey version of the EURO-D scale in 10 nations. The SHARE project. *Int J Methods Psychiatr Res* 2008;17(1):12-29. doi: 10.1002/mpr.236
31. Börsch-Supan A. First results from the survey of health, ageing and retirement in Europe (2004-2007) : starting the longitudinal dimension. Mannheim: Mannheim Research Institute for the Economicss of Aging (MEA) 2008.
32. Lee S, Kawachi I, Berkman LF, et al. Education, other socioeconomic indicators, and cognitive function. *Am J Epidemiol* 2003;157(8):712-20.
33. Leist AK, Glymour MM, Mackenbach JP, et al. Time away from work predicts later cognitive function: differences by activity during leave. *Ann Epidemiol* 2013;23(8):455-62. doi: S1047-2797(13)00142-7 [pii] 10.1016/j.annepidem.2013.05.014 [published Online First: 2013/07/31]
34. Solon G, Haider S, Wooldridge JM, et al. What are we weighting for? Cambridge, Mass.: National Bureau of Economic Research; 2013 [
35. Croezen S, Avendano M, Burdorf A, et al. Social participation and depression in old age: a fixed-effects analysis in 10 European countries. *Am J Epidemiol* 2015;182(2):168-76. doi: 10.1093/aje/kwv015
36. de Rekeneire N, Visser M, Peila R, et al. Is a fall just a fall: correlates of falling in healthy older persons. The Health, Aging and Body Composition Study. *J Am Geriatr Soc* 2003;51(6):841-6.
37. Bath PA, Morgan K. Differential risk factor profiles for indoor and outdoor falls in older people living at home in Nottingham, UK. *Eur J Epidemiol* 1999;15(1):65-73.
38. Tromp AM, Smit JH, Deeg DJ, et al. Predictors for falls and fractures in the Longitudinal Aging Study Amsterdam. *J Bone Miner Res* 1998;13(12):1932-9. doi: 10.1359/jbmr.1998.13.12.1932
39. Ganz DA, Higashi T, Rubenstein LZ. Monitoring falls in cohort studies of community-dwelling older people: effect of the recall interval. *J Am Geriatr Soc* 2005;53(12):2190-4. doi: JGS509 [pii] 10.1111/j.1532-5415.2005.00509.x [published Online First: 2006/01/10]
40. Jagger C, Gillies C, Moscone F, et al. Inequalities in healthy life years in the 25 countries of the European Union in 2005: a cross-national meta-regression analysis. *Lancet* 2008;372(9656):2124-31. doi: S0140-6736(08)61594-9 [pii] 10.1016/S0140-6736(08)61594-9 [published Online First: 2008/11/18]
41. Castro-Costa E, Dewey M, Stewart R, et al. Prevalence of depressive symptoms and syndromes in later life in ten European countries: the SHARE study. *Br J Psychiatry* 2007;191:393-401. doi: 191/5/393 [pii] 10.1192/bjp.bp.107.036772 [published Online First: 2007/11/06]
42. Etman A, Burdorf A, Van der Cammen TJ, et al. Socio-demographic determinants of worsening in frailty among community-dwelling older people in 11 European countries. *J Epidemiol Community Health* 2012;66(12):1116-21. doi: jech-2011-200027 [pii] 10.1136/jech-2011-200027 [published Online First: 2012/05/01]
43. Santos-Eggimann B, Cuenoud P, Spagnoli J, et al. Prevalence of frailty in middle-aged and older community-dwelling Europeans living in 10 countries. *J Gerontol A Biol Sci Med Sci* 2009;64(6):675-81. doi: glp012 [pii] 10.1093/gerona/glp012 [published Online First: 2009/03/12]

44. Organisation for Economic Co-operation and Development. OECD Health Statistics 2015 2015 [01/10/2015]. Available from: http://www.oecd.org/els/health-systems/health-data.htm.
45. Stanaway FF, Cumming RG, Naganathan V, et al. Ethnicity and falls in older men: low rate of falls in Italian-born men in Australia. *Age Ageing* 2011;40(5):595-601. doi: 10.1093/ageing/afr067
46. Schaap MM, van Agt HM, Kunst AE. Identification of socioeconomic groups at increased risk for smoking in European countries: looking beyond educational level. *Nicotine Tob Res* 2008;10(2):359-69. doi: 790125799 [pii] 10.1080/14622200701825098 [published Online First: 2008/02/01]
47. Boyé ND, Mattace-Raso FU, Van der Velde N, et al. Circumstances leading to injurious falls in older men and women in the Netherlands. *Injury* 2014;45(8):1224-30. doi: 10.1016/j.injury.2014.03.021 [published Online First: 2014/04/04]
48. Speechley M, Tinetti M. Falls and injuries in frail and vigorous community elderly persons. *J Am Geriatr Soc* 1991;39(1):46-52. [published Online First: 1991/01/01]
49. Kelsey JL, Procter-Gray E, Hannan MT, et al. Heterogeneity of falls among older adults: implications for public health prevention. *Am J Public Health* 2012;102(11):2149-56. doi: 10.2105/AJPH.2012.300677 [published Online First: 2012/09/22]
50. Boye ND, Mattace-Raso FU, Van Lieshout EM, et al. Physical performance and quality of life in single and recurrent fallers: data from the Improving Medication Prescribing to Reduce Risk of Falls study. *Geriatr Gerontol Int* 2015;15(3):350-5. doi: 10.1111/ggi.12287 [published Online First: 2014/04/16]
51. Pluijm SM, Smit JH, Tromp EA, et al. A risk profile for identifying community-dwelling elderly with a high risk of recurrent falling: results of a 3-year prospective study. *Osteoporos Int* 2006;17(3):417-25. doi: 10.1007/s00198-005-0002-0 [published Online First: 2006/01/18]
52. Börsch-Supan A, Alcser KH, Mannheim Research Institute for the Economics of A. The survey of health, aging [ageing], and retirement in Europe methodology ; [SHARE, survey of health, ageing and retirement in Europe]. Mannheim: MEA 2005.
53. Harkness JA, Vijver FJRvd, Mohler PP. Cross-cultural survey methods. Hoboken, N.J.: J. Wiley 2003.

SUPPLEMENTAL MATERIAL

Table S1: Unweighted baseline socio-demographic and intrinsic fall risk characteristics, and self-reported falling at the 2-year follow-up interview, of persons from 12 countries in The Survey of Health, Ageing and Retirement in Europe, 2010-2013.

	Switzerland	Austria	Sweden	Denmark	Italy	Germany	Netherlands	Belgium	Estonia	France	Spain	Czech Republic
	n=1386	n=1983	n=1009	n=873	n=1423	n=591	n=1092	n=1805	n=2917	n=1893	n=1559	n=2065
Age, mean ± SD[a]	73.3 ± 6.5	73.5 ± 6.5	73.6 ± 6.8	73.6 ± 7.0	73.3 ± 6.1	73.2 ± 5.8	73.2 ± 6.7	74.5 ± 7.0	73.9 ± 6.0	74.9 ± 7.0	75.1 ± 6.9	72.6 ± 6.2
Female, %[b]	52.3	57.3	52.3	54.0	51.3	47.2	54.4	56.8	63.4	57.5	55.1	58.6
Low education, %[bc]	26.0	29.8	50.8	24.2	80.2	14.9	55.8	50.5	40.6	58.0	90.6	48.2
Living alone, %[b]	28.2	36.0	29.3	34.1	16.3	22.8	28.4	34.0	30.5	37.5	16.9	31.7
Less than good SRH, %[bc]	18.4	34.2	32.8	24.5	50.4	43.8	30.7	33.8	79.2	44.8	56.8	50.6
Mobility limitation(s), %[bc]	17.1	41.0	24.2	24.9	49.3	32.5	24.5	37.8	43.1	39.7	50.1	48.2
ADL limitation(s), %[bc]	7.3	13.3	11.4	9.6	13.3	15.7	7.6	20.1	19.7	15.3	18.4	11.6
Dizziness, %[bc]	6.3	10.5	10.2	11.6	13.4	11.0	10.6	11.1	22.0	10.1	15.1	10.8
Impaired vision, %[bc]	10.0	9.1	7.7	9.9	25.9	8.8	10.3	14.3	31.7	16.5	34.7	15.2
Depression, %[bc]	17.0	21.1	19.1	13.6	35.1	23.2	17.3	30.4	42.4	33.9	40.1	26.0
Impaired cognition, %[bc]	4.0	8.3	6.0	7.1	24.3	8.7	8.9	12.8	9.9	13.5	39.5	8.6
Falling at baseline, %[b,c,d]	2.7	6.5	5.0	4.5	4.9	3.9	3.9	6.7	6.8	7.8	9.6	7.4
Falling at follow-up, %[b,c,d]	7.2	9.0	9.0	9.3	9.6	9.7	10.5	13.0	13.4	15.1	15.7	16.3
95% CI	5.9-8.6	7.8-10.3	7.4-10.9	7.5-11.4	8.1-11.2	7.5-12.3	8.8-12.4	11.5-14.6	12.1-14.6	13.5-16.7	13.9-17.5	14.7-17.9

P-value <0.001, based on a) t-test and b)chi-squared test; c) missing N for variables: education=340; SRH=35; mobility=30; ADL=34; Dizziness=37; Vision=50; Depression=480; Cognition=397; Falling=55; d) Reporting one or more falls within the 6 months prior to the interview.

ADL=Activities of daily living; CI=Confidence Interval; SD=Standard Deviation; SRH=Self-rated health.

Table S2: Multivariable binary logistic regression with associations (odds ratios and 95% confidence intervals) of socio-demographic and intrinsic fall risk factors with self-reported falling in wave 5 and wave 4 & 5, among persons from 12 countries in The Survey of Health, Ageing and Retirement in Europe, 2010-2013.

	Falling < 6 months of wave 5 N=2068/17,575	Falling < 6 months of both wave 4 & wave 5 N=376/17,575
Age ≥80 years	1.68[c] (1.50-1.88)	1.68[c] (1.33-2.11)
Female gender	1.43[c] (1.28-1.60)	1.62[c] (1.25-2.12)
Low education	1.00 (0.89-1.11)	0.77[a] (0.60-0.98)
Living alone	1.31[c] (1.18-1.46)	1.46[b] (1.16-1.84)
Less than good SRH	1.43[c] (1.27-1.60)	1.81[c] (1.35-2.43)
Mobility limitation(s)	1.44[c] (1.29-1.62)	2.75[c] (2.03-3.73)
ADL limitation(s)	1.46[c] (1.28-1.66)	2.10[c] (1.65-2.66)
Dizziness	1.44[c] (1.26-1.63)	2.59[c] (2.06-3.26)
Impaired vision	1.18[b] (1.05-1.34)	1.53[c] (1.21-1.94)
Depression	1.30[c] (1.16-1.45)	1.69[c] (1.33-2.16)
Impaired cognition	1.43[c] (1.25-1.64)	1.09 (0.83-1.43)

All Odds ratios are adjusted for other factors in the table and country, the outcome 'falling < 6 months of wave 5' is additionally adjusted for self-reported falling at baseline. a) $p<0.05$; b) $p<0.01$; c) $p<0.001$

ADL=Activities of daily living; SRH=self-rated health

Part 2

Promotion of healthy ageing among older persons in Europe

Chapter 5

Evaluation design of Urban Health Centres Europe (UHCE): preventive integrated health and social care for community-dwelling older persons in five European cities

Carmen B. Franse, Antonius J.J. Voorham, Rob van Staveren, Elin Koppelaar, Rens Martijn, Elisa Valía-Cotanda, Tamara Alhambra-Borrás, Tasos Rentoumis, Lovorka Bilajac, Vanja V. Marchesi, Tomislav Rukavina, Arpana Verma, Greg Williams, Gary Clough, Jorge Garcés-Ferrer, Francesco Mattace Raso, Hein Raat

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ABSTRACT

Background

Older persons often have interacting physical and social problems and complex care needs. An integrated care approach in the local context with collaborations between community-, social-, and health-focused organisations can contribute to the promotion of independent living and quality of life. In the Urban Health Centres Europe (UHCE) project, five European cities (Greater Manchester, United Kingdom; Pallini (in Greater Athens Area), Greece; Rijeka, Croatia; Rotterdam, the Netherlands; and Valencia, Spain) develop and implement a care template that integrates health and social care and includes a preventive approach. The UHCE project includes an effect and process evaluation.

Methods

In a one-year pre-post controlled trial, in each city 250 participants aged 75+ years are recruited to receive the UHCE approach and are compared with 250 participants who receive 'care as usual'. Benefits of UHCE approach in terms of healthy life styles, fall risk, appropriate medication use, loneliness level and frailty, and in terms of level of independence and health-related quality of life and health care use are assessed. A multilevel modeling approach is used for the analyses. The process evaluation is used to provide insight into the reach of the target population, the extent to which elements of the UHCE approach are executed as planned and the satisfaction of the participants.

Discussion

The UHCE project will provide new insight into the feasibility and effectiveness of an integrated care approach for older persons in different European settings.

Trial registration

ISRCTN registry number is ISRCTN52788952. Date of registration is 13/03/2017.

BACKGROUND

By 2040, Europeans over 65 years old will account for 27% of the EU-28's population, compared with 18% in 2013, according to Eurostat predictions [1]. This will be associated with a steep increase in demand for care. Health professionals, including physicians, will have an increasing workload and have limited time for prevention. Adding to this, older persons often have multiple, interacting social and health problems [2-4]. However, care is currently often characterised by a monodisciplinary approach, where health and social care are isolated from each other [5 6].

A preventive integrated care approach in the local context where informal and formal infrastructures can be connected, and where community-, social-, and health-focused organisations are collaborating can contribute to the promotion of independent living and quality of life [7 8]. A care coordinator, typically a nurse practitioner or physician assistant, may play a key role in assessing physical and social problems among older people and coordinate follow-up care [9-12]. This promotes collaboration and communication between community-, social-, and health-focused professionals. However, more insight is still needed in ways to combine health and social care and the content of effective care pathways [7]. Previous research efforts on integrated care have had mixed results and best practices are needed [13 14]. Although there is evidence that physical exercise programs contribute to better health and prevent falls in older populations [15-17], less is known about the effects of social care programs when integrated in health care [18-20]. Integration between social and health care can be organized in different ways according to availability and organizational structures in the local context, therefore it is valuable to evaluate the effectiveness of integrated care approaches in different (international) settings.

The UHCE project

In the Urban Health Centres Europe (UHCE) project, a consortium of twelve European partners was set up to respond to the call of the European Commission Executive Agency for Health and Consumers to improve and evaluate community action in the field of health, in particular the improvement of management of multi-morbidity of older persons using integrated care pathways that focus on adherence to treatment and prevention of falls and frailty. (www.uhce.eu). UHCE aims to address three pertinent issues among older persons; (a) appropriate medication prescription and adherence, (b) falls prevention, (c) prevention of functional decline and frailty. In this project, five European cities (Greater Manchester, United Kingdom; Pallini, Greece; Rijeka, Croatia; Rotterdam, the Netherlands; and Valencia, Spain) will develop and implement a care template that integrates health and social care and includes a population oriented, preventive approach. In UHCE, a general care template is adapted to the local context of the five cities. The main objective of the evaluation study is to evaluate the UHCE approach in a pre-post controlled design in terms of benefits for older

persons (75 years and older) involved and process performance. The following research questions will be answered:

1. What are the benefits of the UHCE approach for older persons in terms of healthy life styles, fall risk, appropriate medication use, loneliness and frailty, as well as the benefits in terms of level of independence and health-related quality of life?
2. What are the benefits of the UHCE approach in terms of reducing the use of ambulatory and residential health- and social care among older persons?
2. What is the reach of the target population by the UHCE approach, to what extent are the elements of the UHCE template executed as planned and are the main stakeholders satisfied?

The UHCE approach is applied in an intervention group, which is compared with a control group. We hypothesize that intervention group participants, compared to those in the control group have more favourable life styles (physical activity, smoking, alcohol use) less fall risk and higher appropriate medication use, less loneliness, less frailty, higher level of independence and more favourable health-related quality of life. We furthermore hypothesize that participants in the intervention group, compared to the control group use less ambulatory, residential and social care. We aim towards a reach of participants in the intervention group of 70% or higher, and an appreciation of 7 or higher on a 1-10 scale.

METHODS/DESIGN

The intervention: The UHCE approach

A general template of the UHCE approach was developed by systematically reviewing the literature to identify evidence based interventions and validated assessment instruments for frailty, fall risk and polypharmacy (see www.uhce.eu). Furthermore, focus groups and interviews with main stakeholders (older persons, health and social care professionals, caregivers and policy makers) were held to identify their demands and preferences regarding the UHCE template, which led to the decision to address loneliness as a separate health problem, in addition to frailty, fall risk and polypharmacy.

UHCE starts with a frailty assessment and an assessment of fall risks, polypharmacy and loneliness in order to identify priorities for prevention and care of the older persons participating (figure 1). We use validated instruments that are practical and commonly used in a primary care setting. Fall risk is measured following a validated protocol developed by the Dutch safety research institute [21]. Polypharmacy is measured following the common definition of using of five or more different medicines[22], in addition we measure whether persons have difficulty to take the medicines as prescribed[23]. Loneliness is measured with the social subscale of the Tilburg Frailty Indicator[24]. Frailty is measured with the Tilburg

Frailty indicator, which was made and validated for use in primary care and has been extensively researched [24 25].

The results of the assessments are discussed with the older person, a person in charge of care coordination (nurse practitioner or other) and a physician (figure 1). As a result of this shared decision-making process, a decision on a care plan is made and each participant is referred to evidence based "care pathways" (interventions) that are described in the UHCE template and adapted to the context of each of the five participating cities. The main UHCE care pathways are: multifactorial fall prevention actions (which include physical exercise groups, home hazard identification or other actions based on the judgement of a physician), actions addressing polypharmacy (which include appropriate prescribing and adherence action or other actions based on the judgement of a physician), actions addressing loneliness (which include support groups, social activities, or other actions based on the judgement of a physician) and frailty action (which include group based exercise programs or other actions based on the judgement of a physician).

The care coordinator (a nurse, social worker or trained physician assistant) coordinates and monitors the progress of each individual care plan under the supervision of the physician (figure 1). Follow-up visits are scheduled if needed. The care coordinator monitors the compliance to the care plan. The general UHCE template is adjusted in accordance with national standards and the local setting of the five participating cities.

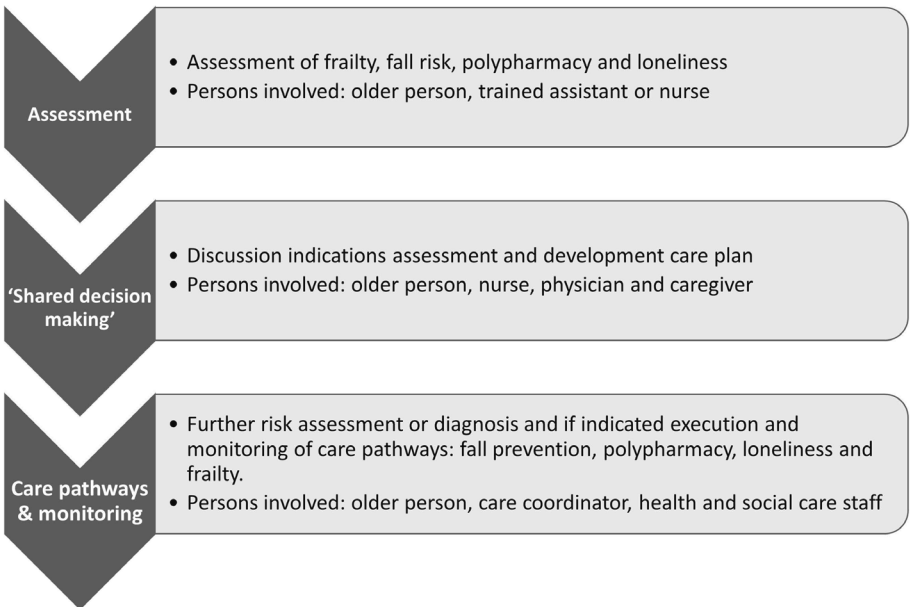

Figure 1: The UHCE approach

Design, setting and procedures

The evaluation of UHCE has a specific pre-post controlled design [26]. Intervention and control sites (general practitioner; GP practices or primary health centres; PHC) are chosen based on their location in distinct neighbourhoods in the participating cities. Older persons in the catchment area of an intervention site receive an invitation by their physician to join the study in the area where the UHCE approach is applied. Older persons in the catchment area of a control site receive an invitation by their physician to join the study in the area where 'usual care' is applied. The study is performed in accordance with the capacity, organizational and contextual factors of each of the five participating cities, as described below.

Greater Manchester is a metropolitan county in North West England, with a population of 2.7 million persons[27]. Participants are recruited through GPs of individual GP practices, the intervention practices are located in Tameside and Glossop districts and the control practices are located in South Manchester. Assessments are taken at the participant's home by a trained assistant. The results are assessed by researchers and clinicians before being provided to the participant's GP. The participant's GP is responsible for decisions on care in collaboration with health and social care staff at the GP practice.

Pallini is a suburban town and a municipality situated in the eastern part of the greater Athens area, with a population of 54,415 persons [28]. Participants are recruited through the Municipal Health and Social Services. In Pallini, as only city, participants are randomized (by using a random numbers table) into the intervention group (UHCE approach) and the control group ('usual care'). Assessments are taken at three community centres and the Municipal Health Centre by trained health staff. A health professional or a social worker is the care coordinator, and a physician is responsible for decisions on care in collaboration with the nurse.

Rijeka is a port city located at the most western part of the Republic of Croatia and has a population of 128,384 persons [29]. Participants are recruited through individual GP practices, intervention practices are located in the Western part of Rijeka and control practices are located in the Eastern part of Rijeka. Assessments are taken at the participant's home by community nurses, who act as care coordinators. The participant's GP, supported by the nurse is responsible for decisions on care.

Rotterdam is a port city in the Netherlands province of South Holland, with a population of 638,714 persons[30]. Participants are recruited through their GP based in PHC, the intervention PHC is located in Ommoord neighbourhood and the control PHCs are located in the Oosterflank and Zevenkamp neighbourhoods. Assessments are taken at the participant's home by a trained assistant. Results are then provided to a geriatric nurse, who is the care

coordinator, in collaboration with the GP. The participant's GP, supported by the nurse is responsible for decisions on care.

Valencia is a port city located on the Southeastern coast of Spain, it has a population of 800,666 persons [31]. Participants are recruited through the GPs of the intervention PHC in the Nou Moles neighbourhood and the control PHC in the El Botanic neighbourhood. Assessments are taken at the participant's home by a trained assistant who supports case management by the GP. The participant's GP is responsible for decisions on care supported by the nurse and social workers of the health centres.

Study population and eligibility to participate in the study

We aim to include 250 participants in both the intervention group and 250 participants in the control group in each city. In total, 1250 participants are included in the intervention group and 1250 participants in the control group. In each city, the target population consists of persons living independently, aged 75 years or more, who are, according to their GP, expected to be able to participate in the study for at least 6 months. Persons are not eligible to participate if they are not able to comprehend the information provided in the local language or if they are not able to cognitively evaluate the risks and benefits of participation and are not expected to be able to make an informed decision regarding participation in the study, according to their GP or physician. If possible, the participant is invited to designate an informal caregiver to support him or her, such as the partner, a child, sibling, friend or neighbour.

Data-collection and measures

Data collection is done with the use of a questionnaire; which includes the UHCE assessment (described above), outcome and other measures. Two non-invasive measurements (hand-grip strength and mid-upper arm circumference) are additionally performed and written down in the questionnaire. These data are collected at both baseline (T0) and after 12 months (T1). The instruments used for the outcome measures are described in the measurements section. The instruments and items for which no validated translations are available are translated forward and backward by translators. Forward- and back-translations are discussed by the study team and translation is adapted when needed.

Outcome measures

Both general outcome health measures and specific outcome health measures applicable to each care pathway are applied: healthy life styles, fall risk, appropriate medication use, loneliness, frailty, level of independence and health-related quality of life. Healthy life style is measured with one item on physical activity, two items on smoking, and three items of the AUDIT-C[32] on high-risk alcohol use. Fall risk is measured by two items on (the number of) falls in the previous year, a single item asking whether or not the person is afraid of falling,

and fear of falling while performing several daily activities as measured by the 7-item Falls Efficacy Scale International (FES-I) short version[33]. Appropriate medication use is measured with 10 items of the Medication risk questionnaire (MRQ-10)[23], a tool developed for use by older persons to identify who is at increased risk of potentially experiencing a medication-related problem. Loneliness is measured with the short 6-item version of the Jong Gierveld loneliness scale[34], which measures the degree of what one wants and what one has in terms of interpersonal affection and intimacy. Frailty is measured with the 15-item Tilburg Frailty indicator[24 25], that includes questions on physical, psychological and social components of frailty. Physical frailty is additionally measured with the SHARE-Frailty instrument which is an instrument that was developed and validated in a European population[35 36], SHARE-frailty includes hand-grip strength measurement, and physical frailty is also measured with a measurement of the mid-upper arm circumference[37], a measure for malnutrition. Level of independence is measured with the Groningen activity restriction scale[38], that includes 18 items on independence of activities of daily living (ADL) and instrumental activities of daily living (IADL) and additionally with the one-item Global Activity Limitation Index (GALI)[39 40]. Health-related quality of life is measured with the 12-item short-form (SF-12)[41 42] and the full 5-item mental health scale of the SF-36[43].

Additionally to health measures, use of care is measured with four questions regarding the use of doctor appointments, household work, help caring (such as washing or dressing) and hospital admissions.

Other measures

Various socio-demographic characteristics are measured: age, gender, country of birth, educational level, income, marital status, employment situation, household composition and religion. Additionally, several questions on the participant's general health are asked: self-reported height and weight, use of walking or other aids, whether they ever have been diagnosed with any of fifteen listed health conditions. Any additional remarks can be left in an open box at the end of the questionnaire.

Process evaluation

A process evaluation is used to monitor program implementation and help to understand the relationship between the delivery of specific UHCE approach elements and program outcomes. We based our design of the process evaluation on the theoretical framework for public health interventions as developed by Steckler and Linnan [44 45]. The following elements are included and outlined below: reach, dose delivered and received, fidelity, satisfaction, and context.

Reach

This process element aims at measuring the proportion of the intended target population that is reached by the care approach. In UHCE we calculate which proportion of the participants that we contacted participate in the UHCE approach. If possible reasons for refusal are reported.

Dose delivered and received

Dose delivered measures whether the anticipated care is offered to the participant and dose received measures the extent in which participants actively engage in the care that is offered. For this purpose, data on the delivery of the UHCE approach and reasons for non-participation in care are recorded by the care coordinator. A 1-page logbook is kept for each participant that includes the different stages of the UHCE approach: 1. assessment, 2 shared decision making, and 3. care pathways and monitoring. At least after 6 months, the care coordinator records (if needed telephone contact with the participant or responsible health care provider is sought) whether key elements of the UHCE approach are delivered. In case of loss to follow- up at the T1 measurement, reasons are recorded by the research staff, given they are provided by the participant.

Fidelity and satisfaction

We aim to measure the extent to which the UHCE approach is implemented as planned (fidelity) and the satisfaction of main stakeholders with the UHCE approach. In the T1 questionnaire, three items measure the general satisfaction with professional, social and self-care in the past 12 months, 4 items measure the satisfaction with specific UHCE elements (assessment, shared-decision making and care-pathways) and a final question rates the whole UHCE approach on a scale from 1 to 10. To gain more in-depth knowledge on how the UHCE approach is carried out and which barriers are encountered, focus groups and semi-structured interviews with older persons, caregivers, and social and health professionals involved in UHCE are held 12 months after inclusion of the last group of participants. In each city we organize 1 focus group with 6-8 older persons and caregivers (e.g. family, friends) and 1 group with 6-8 social and health care professionals. All professionals involved with UHCE are invited to participate in the focus groups. The focus group discussions are recorded and translated in English.

Context

As the UHCE approach is implemented in five diverse settings its' success depends on the context in which it is implemented. With the use of structured forms we make an inventory of relevant contextual factors of each city in which the UHCE approach is embedded; type and experience of health staff, setting, resources and interventions available or newly developed.

Power considerations

In each of the five cities, 250 participants are included in the intervention group and 250 participants in the control group. Assuming a 20% loss to follow-up between T0 and T1 due to mortality, rehousing or impossibility to participate, we expect to receive complete data of 2000 participants at follow up, equally divided over the intervention group and the control group. We assume equal standard deviations in the intervention group and the control group, alpha of 0.05 and power of 0.80. Given 5 participating cities with each an intervention and control group, we applied a correction factor to account for the cluster design, assuming an average cluster size of 200 older citizens (2000/10) and an intra-class correlation coefficient of 0.02. For this expected sample size and assumptions, with regard to the continuous outcome measures, a difference of 0.25 SD (standard deviation) between the intervention and the control group can be detected at follow-up. For example, regarding the health-related quality of life as measured by the Physical and Mental Component Summary Scale scores of the SF-12, a difference of 2.9 points can be detected for the Physical Component Summary Scale (SD=11.4) and 3.0 points for the Mental Component Summary Scale (SD=11.9)[46].

Data management and analysis

Data from all cities is combined and data-management and analysis is done at Erasmus MC. Paper questionnaires are scanned and automatically transferred into electronic files. Paper participant logbooks are entered into an electronic data-entry form by research staff. Electronic data is checked for missing or incorrect data. If an error is present in the electronic data, scans of the paper questionnaires and logbooks are consulted. If needed responsible staff are contacted for clarification.

Descriptive statistics are used to summarize characteristics of participants in each city and in the total study population. Participant socio-demographic characteristics (age, gender, income, educational level) are compared at baseline between the intervention and control group of each city and in the total study population. A multilevel modelling approach is used to examine differences in the outcome measures between the intervention and control group, taking into account the clustering effects at the city-level. Multilevel linear regression analyses are conducted for the continuous outcome variables with group (intervention or control) as independent variable and baseline values and potential confounders as covariates. Multilevel logistic regression is performed for dichotomous outcome variables. Subgroup analyses are conducted by means of formal interaction tests for intervention and those variables which are likely to influence the effect of the intervention itself: gender, age and educational level. In addition, subgroup analyses are done for subgroups of individuals with an indication for specific care pathways (frailty, fall risk, polypharmacy and loneliness), comparing participants with this indication in control and intervention groups. In addition, the above mentioned analyses are repeated for each city separately.

All qualitative data (interviews and focus groups) are recorded, transcribed and translated to English. Thematic analysis of data is done using a pre-defined coding framework which is developed through discussion and consensus among the research team[47].

Dissemination

We have set up an Advisory Board with experts from six EU countries. The role of the Advisory Board is to provide a critical perspective throughout the project. The scientific project results are disseminated by the project team through publications in scientific journals and conferences. To further disseminate the knowledge to all stakeholders we use the project website (www.uhce.eu). The European Local Inclusion and Social Action Network (ELISAN) is one of the partners of the UHCE project and aids the dissemination of project results to all stakeholders via social media.

DISCUSSION

This study aims to evaluate the potential benefits of the UHCE approach on healthy lifestyle, fall risks, appropriate medication use, loneliness, frailty, level of independence and quality of life in older European persons. This is done using a pre-post controlled design in five European cities: (Greater Manchester, United Kingdom; Pallini (in Greater Athens Area), Greece; Rijeka, Croatia; Rotterdam, the Netherlands; and Valencia, Spain). This study has several strengths. To our knowledge this is one of the first European studies that aims to implement an integrated care approach in different European settings. Carrying out an integrated care approach in different settings will provide information on the generalizability of the care approach in various European settings. This could also help facilitate future implementation into routine primary care practice. The development of the UHCE approach was based on the experiences and preferences of a diverse group of stakeholders (older persons, their caregivers, medical and social care providers), which supported the co-creation of the intervention for the end-user and could generate a wider acceptance of the intervention.

The proposed study has some limitations and we expect to encounter some challenges. Participation of older persons may be a problem; that may affect the cities differently. To increase participation, requests to participate are sent through their personal GP, where possible. Because our target group consists of older persons, we also expect persons to move to another place (e.g. nursing home), pass away during the follow-up period, or not be fit enough to participate. We apply a non-randomized design, which makes results subject to confounding variables. Randomization was not desirable for cities that worked with GP practices as it is not feasible for GPs to give ‘usual care’ and care according to UHCE at

the same time. In our questionnaire we tried to capture the most important confounding variables; however it remains possible that we missed other relevant variables.

As the growth of the European older population will pose a challenge for the European Union, new ways of providing care are necessary. Integrating social and health care and providing a preventive care approach may provide better outcomes. The UHCE project will further elucidate whether such an approach could be effective and feasible for an older population in different settings and identify potential effective elements of integrated preventive care.

REFERENCES

1. Eurostat. Population structure and ageing: European Union, 1995-2013; 2014 [Available from: http://ec.europa.eu/eurostat/statistics-explained/index.php/Population_structure_and_ageing accessed 05/01/2017.
2. Andrew MK, Mitnitski A, Kirkland SA, et al. The impact of social vulnerability on the survival of the fittest older adults. *Age Ageing* 2012;41(2):161-65.
3. Fratiglioni L, Wang HX, Ericsson K, et al. Influence of social network on occurrence of dementia: a community-based longitudinal study. *Lancet* 2000;355(9212):1315-9. doi: 10.1016/S0140-6736(00)02113-9
4. Mendes de Leon CF, Glass TA, Berkman LF. Social engagement and disability in a community population of older adults: the New Haven EPESE. *Am J Epidemiol* 2003;157(7):633-42.
5. Hunt L. Test and learn: Working towards integrated services. *Nurs Older People* 2014;26(7):16-20. doi: 10.7748/nop.26.7.16.e624
6. Glasby J. The holy grail of health and social care integration. *BMJ* 2017;356:j801. doi: 10.1136/bmj.j801
7. Eklund K, Wilhelmson K. Outcomes of coordinated and integrated interventions targeting frail elderly people: a systematic review of randomised controlled trials. *Health Soc Care Community* 2009;17(5):447-58. doi: HSC844 [pii]10.1111/j.1365-2524.2009.00844.x [published Online First: 2009/02/28]
8. van Leeuwen KM, Bosmans JE, Jansen AP, et al. Cost-Effectiveness of a Chronic Care Model for Frail Older Adults in Primary Care: Economic Evaluation Alongside a Stepped-Wedge Cluster-Randomized Trial. *J Am Geriatr Soc* 2015;63(12):2494-504. doi: 10.1111/jgs.13834
9. Frich LM. Nursing interventions for patients with chronic conditions. *J Adv Nurs* 2003;44(2):137-53. doi: 2779 [pii] [published Online First: 2003/10/03]
10. Markle-Reid M, Browne G, Weir R, et al. The effectiveness and efficiency of home-based nursing health promotion for older people: a review of the literature. *Med Care Res Rev* 2006;63(5):531-69. doi: 63/5/531 [pii]10.1177/1077558706290941 [published Online First: 2006/09/07]
11. Markle-Reid M, Browne G, Gafni A. Nurse-led health promotion interventions improve quality of life in frail older home care clients: Lessons learned from three randomized trials in Ontario, Canada. *J Eval Clin Pract* 2013;19(1):118-31.
12. Liebel DV, Friedman B, Watson NM, et al. Review of nurse home visiting interventions for community-dwelling older persons with existing disability. *Med Care Res Rev* 2009;66(2):119-46. doi: 1077558708328815 [pii]10.1177/1077558708328815 [published Online First: 2008/12/31]
13. Metzelthin SF, van Rossum E, de Witte LP, et al. Effectiveness of interdisciplinary primary care approach to reduce disability in community dwelling frail older people: cluster randomised controlled trial. *BMJ* 2013;347:f5264. [published Online First: 2013/09/12]
14. Janse B, Huijsman R, de Kuyper RD, et al. The effects of an integrated care intervention for the frail elderly on informal caregivers: a quasi-experimental study. *BMC Geriatr* 2014;14:58. doi: 1471-2318-14-58 [pii]10.1186/1471-2318-14-58 [published Online First: 2014/06/03]

15. El-Khoury F, Cassou B, Charles MA, et al. The effect of fall prevention exercise programmes on fall induced injuries in community dwelling older adults: systematic review and meta-analysis of randomised controlled trials. *BMJ* 2013;347:f6234. [published Online First: 2013/10/31]
16. Gillespie LD, Robertson MC, Gillespie WJ, et al. Interventions for preventing falls in older people living in the community. *Cochrane Database Syst Rev* 2009(2):CD007146. doi: 10.1002/14651858.CD007146.pub2 [published Online First: 2009/04/17]
17. Howe TE, Rochester L, Neil F, et al. Exercise for improving balance in older people. *Cochrane Database Syst Rev* 2011(11):CD004963. doi: 10.1002/14651858.CD004963.pub3 [published Online First: 2011/11/11]
18. Cattan M, White M, Bond J, et al. Preventing social isolation and loneliness among older people: a systematic review of health promotion interventions. *Ageing Soc* 2005;25:41-67. doi: DOI 10.1017/Soi44686X04002594
19. Hagan R, Manktelow R, Taylor BJ, et al. Reducing loneliness amongst older people: a systematic search and narrative review. *Aging Ment Health* 2014;18(6):683-93. doi: 10.1080/13607863.2013.875122 [published Online First: 2014/01/21]
20. Dickens AP, Richards SH, Greaves CJ, et al. Interventions targeting social isolation in older people: a systematic review. *BMC Public Health* 2011;11:647. doi: 1471-2458-11-647 [pii]10.1186/1471-2458-11-647 [published Online First: 2011/08/17]
21. Veiligheid.nl. Fall risk test Veiligheid.nl; [Available from: http://www.veiligheid.nl/voorlichtingsmateriaal/valanalyse-inventarisatie-valrisico-65-door-de-eerstelijnszorg accessed 7 july 2014.
22. Maher RL, Hanlon J, Hajjar ER. Clinical consequences of polypharmacy in elderly. *Expert Opin Drug Saf* 2014;13(1):57-65. doi: 10.1517/14740338.2013.827660
23. Barenholtz Levy H. Self-administered medication-risk questionnaire in an elderly population. *Annals of Pharmacotherapy* 2003;37(7-8):982-7.
24. Gobbens RJ, van Assen MA, Luijkx KG, et al. The Tilburg Frailty Indicator: psychometric properties. *J Am Med Dir Assoc* 2010;11(5):344-55. doi: 10.1016/j.jamda.2009.11.003
25. Gobbens RJ, Luijkx KG, Wijnen-Sponselee MT, et al. Towards an integral conceptual model of frailty. *J Nutr Health Aging* 2010;14(3):175-81.
26. Miller JN, Colditz GA, Mosteller F. How study design affects outcomes in comparisons of therapy. II: Surgical. *Stat Med* 1989;8(4):455-66.
27. Office for National Statistics. Population Estimates for UK, England and Wales, Scotland and Northern Ireland, mid-2014 population estimates Newport, South Wales, UK: Office for National Statistics; 2015 [Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/datasets/populationestimatesforukenglandandwalesscotlandandnorthernireland accessed 21-04-2017.
28. Hellenic Statistical Authority. 2011 Population-Housing Census: Hellenic Statistical Authority, Athens, Greece; 2011 [Available from: http://www.statistics.gr/en/2011-census-pop-hous.

29. Croatian Bureau of Statistics. Census of Population, Households and Dwellings 2011: Croatian Bureau of Statistics, Zagreb; 2011 [Available from: http://www.dzs.hr/default_e.htm accessed 07/04/2017.
30. Statistics Netherlands (CBS). Statline Dutch Statistics, Den Haag/Heerlen2017 [Available from: http://statline.cbs.nl/Statweb/publication accessed 27/03/2017.
31. Statistics office Valencia. Statistics Summary of the city of Valencia: Statistics office Valencia, Valencia, Spain; 2016 [Available from: http://www.valencia.es/ayuntamiento/webs/estadistica/Recull/RECULL2016_Ingles.pdf.
32. Bush K, Kivlahan DR, McDonell MB, et al. The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking. Ambulatory Care Quality Improvement Project (ACQUIP). Alcohol Use Disorders Identification Test. *Arch Intern Med* 1998;158(16):1789-95.
33. Yardley L, Beyer N, Hauer K, et al. Development and initial validation of the Falls Efficacy Scale-International (FES-I). *Age Ageing* 2005;34(6):614-9.
34. De Jong Gierveld J, Van Tilburg T. The De Jong Gierveld short scales for emotional and social loneliness: tested on data from 7 countries in the UN generations and gender surveys. *Eur J Ageing* 2010;7(2):121-30. doi: 10.1007/s10433-010-0144-6
35. Romero-Ortuno R, Walsh CD, Lawlor BA, et al. A frailty instrument for primary care: findings from the Survey of Health, Ageing and Retirement in Europe (SHARE). *BMC Geriatr* 2010;10:57. doi: 1471-2318-10-57 [pii]10.1186/1471-2318-10-57 [published Online First: 2010/08/25]
36. Romero-Ortuno R. The Frailty Instrument for primary care of the Survey of Health, Ageing and Retirement in Europe predicts mortality similarly to a frailty index based on comprehensive geriatric assessment. *Geriatr Gerontol Int* 2013;13(2):497-504. doi: 10.1111/j.1447-0594.2012.00948.x [published Online First: 2012/09/22]
37. Wijnhoven HA, Schilp J, van Bokhorst-de van der Schueren MA, et al. Development and validation of criteria for determining undernutrition in community-dwelling older men and women: The Short Nutritional Assessment Questionnaire 65+. *Clinical Nutrition* 2012;31(3):351-8.
38. Suurmeijer TP, Doeglas DM, Moum T, et al. The Groningen Activity Restriction Scale for measuring disability: its utility in international comparisons. *Am J Public Health* 1994;84(8):1270-3.
39. van Oyen H, Van der Heyden J, Perenboom R, et al. Monitoring population disability: evaluation of a new Global Activity Limitation Indicator (GALI). *Soz Praventivmed* 2006;51(3):153-61.
40. Berger N, Van Oyen H, Cambois E, et al. Assessing the validity of the Global Activity Limitation Indicator in fourteen European countries. *BMC Med Res Methodol* 2015;15:1. doi: 10.1186/1471-2288-15-1
41. Haywood KL, Garratt AM, Fitzpatrick R. Quality of life in older people: a structured review of generic self-assessed health instruments. *Qual Life Res* 2005;14(7):1651-68. [published Online First: 2005/08/27]
42. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996;34(3):220-33. [published Online First: 1996/03/01]

43. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;30(6):473-83.
44. Steckler A., Linnan L., Process evaluation for public health interventions and research. San Francisco, Calif.: Jossey-Bass 2002.
45. Saunders RP, Evans MH, Joshi P. Developing a process-evaluation plan for assessing health promotion program implementation: a how-to guide. *Health Promot Pract* 2005;6(2):134-47. doi: 6/2/134 [pii]10.1177/1524839904273387 [published Online First: 2005/04/28]
46. Aaronson NK, Muller M, Cohen PD, et al. Translation, validation, and norming of the Dutch language version of the SF-36 Health Survey in community and chronic disease populations. *J Clin Epidemiol* 1998;51(11):1055-68.
47. Boyatzis RE. Transforming qualitative information : thematic analysis and code development. Thousand Oaks [u.a.]: Sage 2009.

Chapter 6

The effectiveness of a coordinated preventive care approach for healthy ageing (UHCE) among older persons in five European cities: A pre-post controlled trial

Carmen B. Franse, Amy van Grieken, Tamara Alhambra-Borrás, Elisa Valía-Cotanda, Rob van Staveren, Tasos Rentoumis, Athina Markaki, Lovorka Bilajac, Vanja V. Marchesi, Tomislav Rukavina, Arpana Verma, Greg Williams, Elin Koppelaar, Rens Martijn, Antonius J.J. Voorham, Francesco Mattace Raso, Jorge Garcés-Ferrer, Hein Raat

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ABSTRACT

Background

Older persons often have multiple health and social problems and need a variety of health services. A coordinated preventive approach that integrates the provision of health and social care services could promote healthy ageing. Such an approach can be organised differently, depending on the availability and organizational structures in the local context. Therefore, it is important to evaluate the effectiveness of a coordinated preventive care approach in various European settings.

Objectives

This study explored the effects of a coordinated preventive health and social care approach on the lifestyle, health and quality of life of community-dwelling older persons in five European cities.

Design

International multi-center pre-post controlled trial.

Setting

Community settings in cities in the United Kingdom, Greece, Croatia, the Netherlands and Spain.

Participants

1844 community-dwelling older persons (mean age=79.5; SD=5.6).

Methods

The Urban Health Centres Europe (UHCE) approach consisted of a preventive multidimensional health assessment and, if a person was at-risk, coordinated care-pathways targeted at fall risk, appropriate medication use, loneliness and frailty. Intervention and control sites were chosen based on their location in distinct neighbourhoods in the participating cities. Persons in the catchment area of the intervention sites 'the intervention group' received the UHCE approach and persons in catchment areas of the control sites 'the control group' received care as usual. A questionnaire and two measurements were taken at baseline and at one-year follow-up to assess healthy lifestyle, fall risk, appropriate medication use, loneliness level, frailty, level of independence, health-related quality of life and care use. To evaluate differences in outcomes between intervention group and control group for the total study population, for those who received follow-up care-pathways and for each city separately (multilevel) logistic and linear regression analyses were used.

Results

Persons in the intervention group had less recurrent falls (OR= 0.65, 95% CI = 0.48; 0.88) and lower frailty (B=-0.43, 95% CI= -0.65 to -0.22) at follow-up compared with persons in the control group. Physical health-related quality of life and mental well-being was better (B=0.95; 95% CI= 0.14-1.76; and B=1.50; 95% CI=0.15-2.84 respectively). The effects of the UHCE approach were stronger in the subgroup of persons (53.6%) enrolled in care-pathways.

Conclusions

Our study found promising but minor effects for the use of a coordinated preventive health and social care approach for the promotion of healthy ageing of older persons. Future studies should further evaluate effects of coordinated preventive health and social care aimed at healthy ageing.

BACKGROUND

It is estimated that by 2040, Europeans over 65 years old will account for 27% of the population, compared with 19% in 2015[1]. This will be associated with a sharp increase in demand for care. Promotion of healthy ageing is therefore a priority of European policy[2]. Older persons often have multiple health and social problems and need a variety of health services[3 4]. However, care in Europe is characterised by a curative and monodisciplinary approach focussed on one illness or disease[5 6]. In addition, a focus on prevention and health promotion could increase healthy life years and reduce the burden on health care resources[6]. As a result of this, the demand is growing for a preventive approach in which both health and social care services are provided[6 7].

A typical coordinated preventive care approach for older persons includes a multidimensional assessment of health and social risks and multidisciplinary coordinated follow-up care[8-11]. In many European countries, general practitioners (GPs) are the gatekeepers to specialised care and have a central role in community care[12]. A nurse practitioner or physician assistant could alleviate the burden of the GP and act as care coordinator. Evidence for preventive interventions with multidisciplinary coordinated follow-up care is mixed and more research is needed[13-15]. Most of these studies have been conducted in Northwest European or American settings, studies in Southern and Eastern European settings are lacking[16-19].

Aspects such as accessibility of primary care, availability of prevention and treatment services and continuity of care vary considerably between European countries[6 20]. A striking example is the difference between European countries in the importance and accessibility of GPs in community care[12]. This has an impact on the role a GP could play and the organization of care. Therefore, it is important to evaluate the effectiveness of coordinated preventive care approaches in various European settings. Coordinated preventive health and social care can be organised in many ways depending on the availability and organizational structures in the local context.

Objective

The Urban Health Centres Europe (UHCE) approach was developed to promote healthy ageing of older persons. The UHCE approach included a preventive multidimensional assessment of health risks and, if indicated, coordinated follow-up health and social care. The UHCE approach was specifically targeted at fall risk, appropriate medication use, loneliness and frailty. This study evaluates the UHCE approach, which we hypothesized had a positive effect on lifestyle, fall risk, appropriate medication use, loneliness, frailty, level of independence, health-related quality of life and care use among community-dwelling older persons.

METHODS

Study design and setting

The effect evaluation of the UHCE approach was conducted in primary care and community settings in five European cities (Greater Manchester, United Kingdom; Pallini, Greece; Rijeka, Croatia; Rotterdam, the Netherlands; and Valencia, Spain) between May 2015 and June 2017. In Manchester, Rijeka, Rotterdam and Valencia a specific pre-post controlled design was applied [21]. Randomization was not desirable for these cities that worked with existing GP practices as it was not feasible for GPs to give 'usual care' and care according to UHCE at the same time. In these cities, intervention and control sites (GP practices or primary health centres; PHC) were chosen based on their location in distinct neighbourhoods in the participating cities. Older persons in the catchment area of an intervention site receive an invitation by their physician to join the study in the area where the UHCE approach is applied. Older persons in the catchment area of a control site receive an invitation by their physician to join the study in the area where 'usual care' is applied (table 1). In Pallini, participants from municipality registers were first randomised by the use of a random numbers table into the intervention group and the control group (table 1). Participants were afterwards invited to participate in the study by a health team of the municipality employed for this study. Ethical committee procedures have been followed in all cities and approval has been provided. Written informed consent was obtained from all participants. The study was registered as ISRCTN52788952.

Participants

In each city, the initial target population consisted of persons living independently, aged 75 years or older, who were, according to their physician, able to participate in the study for at least 6 months. Persons were not eligible to participate if they were not able to comprehend the information provided in the local language or if they were not able to cognitively evaluate the risks and benefits of participation and were not expected to be able to make an informed decision regarding participation in the study, according to their physician. In two cities; Pallini and Valencia, the age of the target population was lowered to 70 years or older due to difficulties encountered during the inclusion. Persons were invited to participate in the study by their health care provider (table 1).

Intervention

In the intervention group, persons received care according to the UHCE approach. We used the CREDICI II criteria for complex interventions as a reporting guideline[22], see supplementary text S1. The development of the UHCE approach followed an intervention mapping approach[23]. A general template for the UHCE approach was developed by systematically reviewing the literature to identify evidence based interventions and validated assessment instruments for fall risk, polypharmacy, loneliness and frailty (see www.uhce.eu). Additionally, focus groups

and interviews with main stakeholders (older persons, health and social care professionals, caregivers and policy makers) were held to identify their needs and preferences regarding healthy and active ageing. This led to the decision to address loneliness as a separate health problem, in addition to frailty, fall risk and polypharmacy[24] as well as any medical problems which were identified during the assessment that did not belong to the previously mentioned categories. We furthermore decided to apply an integral conceptual model of frailty, which includes physical as well as social and psychological components and is geared towards a multidisciplinary approach[25].

The general template of the UHCE approach consisted of three stages. In the first stage of the UHCE approach, the older person received a health assessment of fall risk, polypharmacy, loneliness and frailty in order to identify whether the person had an indication of a need for a follow-up care-pathway. A short standardized assessment form was developed for all cities, which consisted of validated instruments. For assessment of fall risk, a validated protocol developed by the Dutch safety research institute was applied[26]. Assessment of polypharmacy followed the common definition of using of five or more different medicines[27], in addition difficulty in taking medications as prescribed was assessed[28]. Assessment of loneliness made use of the social subscale of the Tilburg Frailty Indicator[29] and if loneliness was indicated further assessment with the Jong-Gierveld loneliness scale[30]. The assessment of frailty followed the Tilburg Frailty indicator for indication of frailty[29]. In the second stage of the UHCE approach, shared-decision making took place; the results of the assessments (the indications for care-pathways) were discussed with the older person, a person in charge of care coordination and a physician. Staff encouraged the older person to involve an informal caregiver in the shared-decision making process. Shared-decision making was included in order to develop a care plan which was adapted to the preferences of the older person, which was thought to promote involvement in care-pathways. In the third stage, as a result of the shared decision-making process, a decision on a care plan was made and each participant was referred to care-pathways. The care-pathways aimed to promote healthy ageing among the older persons by reducing fall risk, inappropriate medication use, loneliness and frailty. Specific interventions were recommended: 1) fall prevention actions; recommended evidence-based interventions were home-based exercise programmes, group exercise programmes and multifactorial assessment and intervention programmes, 2) actions addressing polypharmacy (adherence and/or appropriate prescribing actions); recommended evidence-based interventions focused on self-monitoring programmes to improve adherence and/or multifaceted pharmaceutical care for appropriate prescribing, 3) actions addressing loneliness; recommended evidence-based interventions were social activities and/or support within a group format, and 4) frailty/medical action; recommended evidence-based interventions included group exercise programmes and multidisciplinary care. Additionally in this care-pathway, other medical care which did not fall under care-pathways 1-3 could be given when the healthcare provider deemed this necessary. The

care coordinator was asked to monitor the progress of each individual care plan under the supervision of a physician. Follow-up visits could be scheduled if needed. For this purpose, a uniform logbook was developed for all cities which was kept for each older person who received the UHCE approach. In this logbook the care coordinator recorded the outcomes and involvement of the older person and health staff in the three stages (assessment, shared-decision and care-pathways) of the UHCE approach. The results of this logbook, along with the evaluation of other process indicators, were part of the evaluation of process components of the UHCE approach, following the Steckler and Linnan framework[31]. This evaluation has previously been described in more detail[24].

The general template of the UHCE approach was then adapted to the national standards and context of each of the five participating cities. Specific information for each city; on the place and staff involved in the assessment, staff who acted as care coordinator, type of care and health staff involved in the care-pathways, is reported in table 1. Initially, the UHCE project aimed to make use of or improve existing care available in the communities. However, in Pallini, Rijeka and Valencia, the availability of existing care was limited or the referral to existing care proved to be difficult. In these cases new care provisions were developed. No additional monetary incentives were provided to health staff involved in existing care. In the settings where new care was developed, staff was hired on a voluntary bases or compensated. No monetary incentives were provided to participants. For some of the interventions participants could borrow materials needed for the intervention (e.g. tablets). Persons in the control group received their usual care. Participants in the control group had access to existing care services delivered in the care-pathways, but not to newly developed services. No coordinated preventive referral to existing care services nor coordinated preventive monitoring of health was in place. In all cities except for Pallini, GPs were the first point of contact and had a gatekeeper function towards existing care services. In Pallini, GPs were scarce and specialist care was directly accessible upon appointment.

Table 1. Study design, procedures and interventions of all cities in UHCE

	Manchester, UK	Pallini, Greece	Rijeka, Croatia	Rotterdam, NL	Valencia, Spain
Source study population	GP list	Municipality/senior centres registers	GP list	GP list	GP list
Method invitation	Letter from GP	Phone calls municipality team	In person by community nurse	Letter from GP	In person by nurse or GP
Age inclusion	≥75 years	≥70 years	≥75 years	≥75 years	≥70 years
Intervention and control group	IG: GP practices in Tameside and Glossop districts. CG: GP practices in South Manchester	Individual randomization of participants from Pallini Municipality/ senior centres	IG: GP practices in Western Rijeka. CG: GP practices in Eastern Rijeka	IG: PHC in Ommoord neighbourhood. CG: PHCs in Oosterflank and Zevenkamp neighbourhoods	IG: PHC in Nou Moles neighbourhood. CG: PHC in El Botanic neighbourhood
Assessment	At home by trained assistant	At senior/health centre by HP	At home by community nurse	At home by trained assistant	At home by trained assistant
Care coordinator	Trained assistant supervised by GP	HP or social worker	Community nurse	Geriatric nurse practitioner	Trained assistant supervised by GP
Type of care in care-pathways	Multiple per pathway; e.g. home adjustment by OT, walking group by volunteers (falls); medication review by GP (polypharmacy); buddying services by volunteers (loneliness); further care by GP (frailty).	Group based endurance and balance training by PE (falls); self-managed medication adherence App (polypharmacy); support groups by psychologist (loneliness); further care by physician (frailty).	Group based balance and strength training by PT (falls and frailty); self-managed medication adherence App (polypharmacy); social group activities (loneliness).	Multiple per pathway; e.g. physiotherapy by PT (falls); medication review by pharmacist (polypharmacy); social activities (loneliness); further care by GP (frailty).	Group based balance and strength training by PT (falls and frailty), medication review according to national protocol by GP (polypharmacy), social support group led by social worker (loneliness).
Care existing or newly developed	All existing; offered by local charity organization and according to practice GP	All newly developed	Falls, frailty and polypharmacy newly developed. Loneliness existing services	All existing, medical care according to practice GP and social care by local organizations	Falls, frailty and loneliness newly developed. Polypharmacy existing protocol

Abbreviations: CG=control group; GP=General practitioner; HP=health professional; IG=intervention group; NL=The Netherlands; OT=occupational therapist; PE=physical educator; PHC=primary care center; PT=physical therapist; UK=United Kingdom.

Measures

Because the UHCE approach acted upon general health outcomes reported in the literature [16-19] as well as health outcomes specific to care-pathways (depending on the care-pathway persons were involved in), we explored the effect of the UHCE approach on various primary outcomes[24]. We hypothesized that the UHCE approach would have positive effects on both general outcome measures of healthy lifestyle, level of independence and quality of life as well as specific outcome measures to each care-pathway: fall risk, appropriate medication use, loneliness and frailty. Data was collected at baseline and after 12 months by using a self-report questionnaire and two physical measurements. The instruments and items for which no validated translation was available were translated forward and backward. Forward- and back-translations were discussed by the study team and translation was adapted when needed. In each city, the questionnaire and assessment was piloted in at least five older persons. Misinterpretation of questions were identified and minor changes were made. Measures used are described below. Details of measurement of these measures are described in the supplementary text S2.

General health outcome measures

Healthy lifestyle was measured with one item on physical activity, two items on smoking, and three items of The Alcohol Use Disorders Identification Test (AUDIT-C)[32]. Frailty was measured with the 15-item Tilburg Frailty indicator (TFI); scores range from 0 to 15 with higher scores indicating higher levels of frailty[25 29]. Physical frailty was additionally measured with the SHARE-Frailty instrument[33 34]. Malnutrition, a component of physical frailty, was measured with the validated Short Nutritional Assessment Questionnaire 65+ (SNAQ-65+)[35]. Level of independence was measured with the 18-item Groningen activity restriction scale (GARS); scores range from 18 to 72 with higher scores indicating lower levels of independence[36]. Severely limited function was measured with the one-item Global Activity Limitation Index (GALI)[37 38]. Health-related quality of life was measured with the 12-item short-form (SF-12v2), which consists of physical and mental component summary (PCS/MCS) scores [39 40], and the full 5-item mental well-being scale of the SF-36[41]. Scores for SF-12v2 and SF36 range from 0 to 100 with higher scores indicating higher levels of quality of life or well-being.

Specific health outcomes care-pathways

Fall risk was measured by an item on any falls and an item on recurrent falls in the previous year, an item on fear of falling, and fear of falling while performing several daily activities as measured by the 7-item Falls Efficacy Scale International (FES-I) short version; scores range from 7 to 28 with higher scores indicating higher levels of fear of falling [42]. Appropriate medication use was measured with 10 items of the Medication risk questionnaire (MRQ-10); scores range from 0-10 with higher scores indicating lower levels of appropriate medication

use [28]. Loneliness was measured with the 6-item version of the Jong Gierveld loneliness scale[30]; scores range from 6-18 with higher scores indicating higher levels of loneliness.

Care use

As secondary outcome measures, use of health and social care was measured in the questionnaire. Four items measured, within the past 12 months: the number of visits to a medical doctor, the number of days admitted to a hospital, the hours per week receiving help in household work due to health problems and the hours per week receiving help in caring for oneself.

Socio-demographic factors

Age (in years), gender, living situation (alone/not alone) and education level were assessed in the baseline questionnaire. Education level was measured by asking the highest level of education completed and categorised according to the 2011 International Standard Classification of Education (ISCED) into 'lower' (ISCED 0-2) and 'higher' (ISCED 3-8)[43].

Analysis

Participant socio-demographic characteristics and health outcomes were evaluated at baseline between the intervention and control group in the total study population and in each city separately by means of chi-square tests for categorical variables and one-way ANOVA for continuous variables.

Main effects at follow-up were evaluated for the total study population, as per "intention to treat", using a multilevel modelling approach. Clustering effects at city-level were taken into account. Multilevel linear regression analyses were conducted for continuous outcome variables with group (intervention or control) as independent variable. Multilevel logistic regression was performed for dichotomous outcome variables. We corrected effect estimates of multilevel analyses for covariates, based on literature [44]; age, sex, living situation, education level and the baseline status of the outcome variable. Subgroup "per-protocol" analyses were done for persons with an indication for specific care-pathways. We compared persons in the control group who had an indication with persons in the intervention group who had an indication and enrolled in a care-pathway. Persons who received other types of medical care or did not have an indication but received care, were analysed in a separate 'frailty/medical care-pathway'. We compared persons in the frailty/medical care-pathway with all persons in the control group. We assessed interactions between intervention condition and city, gender, age and education level in the association between intervention condition and all outcomes[24]. We applied Bonferroni correction for testing interactions[45] (P=0.05/45=0.001). We found significant interaction for 'city', and performed linear and logistic regression analyses per city separately with the same variables as in the main analyses. We considered a P-value of 0.05 or lower to be statistically significant for all other

analyses. Multilevel logistic regression analyses and interaction testing were performed using R-3.3.2. All other analyses were performed using SPSS version 23.0 (IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp).

A power calculation has been previously described[24]. The target sample size was 1250 participants in both the intervention group and the control group[24]. Accounting for a 20% loss to follow-up, we expected to receive complete data of 1000 participants in both groups at follow up. We assumed an alpha of 0.05 and power of 0.80 and applied a correction factor to account for the cluster design by city, assuming an average cluster size of 200 older citizens (2000/10) and an intra-class correlation coefficient of 0.02. On this basis, a treatment difference of 0.25 standard deviation (SD) for continues outcomes such as the SF12 could be detected at follow-up.

RESULTS

Overall, 1215 persons were included in the intervention group and 1110 persons in the control group at baseline (figure 1). At the 12-month follow-up, 986 persons in the intervention group (81.2%) completed the questionnaire and 858 persons in the control group (77.3%) completed the questionnaire (figure 1). Reasons for drop-out at follow-up were unwillingness to participate, feeling too ill to participate, mortality and relocation. Persons who dropped out of the intervention group after baseline were older (P<0.001), lower educated (P<0.001) and had a lower level of independence (GARS, P<0.001) than persons included in the intervention group at follow-up. Persons who dropped out of the control group only had a lower level of independence (GARS, P=0.003) than persons included in the control group at follow-up. Of the 986 persons in the intervention group, information of 15 persons on enrolment in care-pathways was missing or could not be linked to study data. Of those with information, 520 (53.6%) enrolled in any care-pathway during the UHCE study, this differed by city (figure 1).

At baseline, the average age of persons in this study was 79.5 years (SD=5.6), 60.8% of the sample consisted of women, 38.1% were living alone and 51.1% had a lower education level (table 2). The fear of falling score measured with the short FES-I and loss of independence score were lower and mental health-related quality of life and mental well-being were higher among persons in the intervention group compared to the control group (P<0.05). All other characteristics were similar between the groups at baseline. Characteristics by city are presented in table S1.

Table 2: Socio-demographic, lifestyle and health characteristics by intervention and control group among persons in the UHCE study (N=1844).

	Total	Control group	Intervention group	P value
	N=1844	N=858	N=986	
Age in years, mean (SD)	79.5 (5.6)	79.7 (5.5)	79.3 (5.7)	0.188
Female gender, N (%)	1122 (60.8)	527 (61.4)	595 (60.3)	0.636
Living alone, N (%)	703 (38.1)	323 (37.7)	380 (38.5)	0.708
Lower education, N (%)	935 (51.1)	429 (50.6)	506 (51.5)	0.705
Healthy lifestyle, N (%)	1265 (69.1)	569 (67.3)	696 (70.7)	0.109
Fear of falling, N (%)	867 (47.0)	410 (47.8)	457 (46.3)	0.538
Fall past year, N (%)	552 (30.2)	267 (31.4)	285 (29.1)	0.278
Recurrent falls past year, N (%)	255 (13.9)	118 (13.9)	137 (14.0)	0.953
Physical frailty (SHARE-FI)	367 (20.2)	180 (21.5)	187 (19.1)	0.204
Severely limited function (GALI), N (%)	319 (17.4)	158 (18.5)	161 (16.4)	0.222
Malnutrition (SNAQ-65+), N (%)	273 (15.4)	112 (13.8)	161 (16.7)	0.093
Fear of falling (short FES-I) , mean (SD)	10.5 (4.7)	10.7 (5.0)	10.3 (4.5)	0.038
Medication risk (MRQ-10), mean (SD)	4.4 (1.6)	4.4 (1.6)	4.4 (1.7)	0.358
Loneliness (short JG), mean (SD)	0.6 (0.7)	0.6 (0.7)	0.6 (0.7)	0.165
Frailty (TFI), mean (SD)	5.1 (3.2)	5.2 (3.2)	5.1 (3.1)	0.632
Loss independence (GARS), mean (SD)	25.0 (9.4)	25.5 (10.2)	24.5 (8.7)	0.022
HRQoL PCS (SF-12), mean (SD)	42.1 (12.0)	41.8 (12.1)	42.3 (11.9)	0.469
HRQoL MCS (SF-12), mean (SD)	50.3 (10.6)	49.3 (10.7)	51.2 (10.4)	<0.001
Mental well-being (SF-36), mean (SD)	74.2 (20.4)	73.0 (20.9)	75.2 (20.0)	0.022

Missing items: Age=1, Gender=0, Living situation=1, Education=13, Healthy lifestyle=14, Fear of falling=0; Fall=16, Recurrent falls=16; SHARE-FI=26; GALI=9; SNAQ-65+=71; short FES-I=18, MRQ-10=22, short JG=23, TFI=8, GARS=3, SF-12=92, SF-36=18. Lower education=ISCED 0-2; Healthy lifestyle= no smoking, no drinking and exercise>1 times a week. For short FES-I (range 7-28); MRQ-10 (range 0-10); short JG (range 6-18); TFI (range 0-15); GARS (range 18-72); higher scores mean worse health or more health risk. SF-12 and SF-36 scores range 0-100 and higher scores means a higher quality of life or better mental well-being. Abbreviations: FES-I= Falls Efficacy Scale International; GALI= Global Activity Limitation Index; GARS=Groningen activity restriction scale; ISCED=International Standard Classification of Education; JG=Jong-Gierveld; MRQ-10=Medication Risk Questionnaire 10; SF-12=short form 12; SF-36=short form 36; SHARE-FI= Survey of Health, Ageing and Retirement in Europe-Frailty Instrument; SNAQ-65+= Short Nutritional Assessment Questionnaire 65+; TFI=Tilburg Frailty Index.

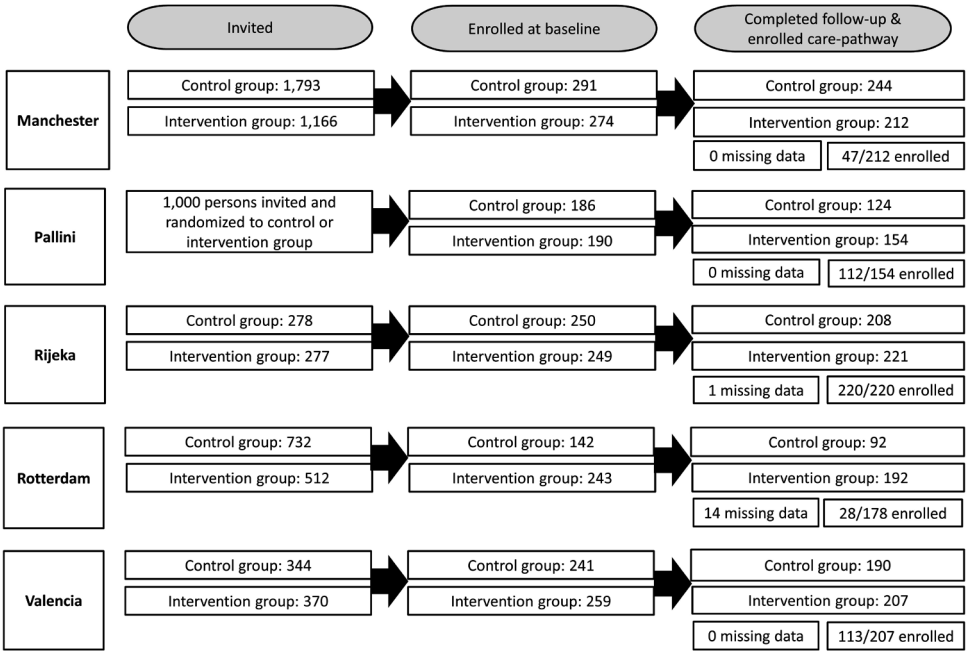

Figure 1: Flowchart of participants through trial.

At follow-up, persons in the intervention group had significantly less recurrent falls compared to persons in the control group (10.5% vs. 14.8%; OR= 0.65, 95% CI = 0.48-0.88; table 3). Frailty was lower among persons in the intervention group compared to persons in the control group (mean=4.9, SD=3.3 vs mean=5.5, SD=3.4; B=-0.43, 95% CI= -0.65 to -0.22; table 3). Physical health-related quality of life was significantly better among persons in the intervention group compared to persons in the control group (mean=41.8, SD=12.1 vs 40.4, SD=11.5, B=0.95; 95% CI= 0.14-1.76; table 3). Finally, mental well-being was significantly better among persons in the intervention group compared to persons in the control group (mean=74.9, SD=20.5 vs mean=71.8, SD=21.3, B=1.50; 95% CI=0.15-2.84; table 3). No other effects of the UHCE approach on lifestyle, health or quality of life were found. Results by city are presented in table S2 and S3. In Rijeka, significant positive effects were found for nine outcomes. In Valencia, significant positive effects were found for three outcomes and in Rotterdam for one outcome. In Manchester, significant positive effects were found for one outcome and negative effects for one outcome. No effects were found in Pallini.

Table 3: Prevalence and mean of outcomes at follow-up and effects of the UHCE approach with the control group as reference (N=1844).

	Control group N=858	Intervention group N=986	Adjusted effect estimates	P value
	N (%)	N (%)	OR (95% CI)[a]	
Healthy lifestyle	555 (65.4)	678 (68.9)	0.96 (0.68; 1.34)	0.790
Fear of falling	441 (51.6)	472 (48.1)	0.86 (0.68; 1.08)	0.188
Fall past year	267 (31.3)	280 (28.9)	0.92 (0.74; 1.14)	0.441
Recurrent falls past year	126 (14.8)	102 (10.5)	0.65 (0.48; 0.88)	0.005
Physical frailty (SHARE-FI)	245 (29.4)	236 (24.8)	0.78 (0.60; 1.02)	0.065
Severely limited function (GALI)	176 (20.7)	192 (19.7)	1.09 (0.83; 1.43)	0.539
Malnutrition (SNAQ-65+)	135 (17.1)	145 (15.3)	0.82 (0.62; 1.09)	0.181
	Mean (SD)	Mean (SD)	B (95% CI)[b]	
Fear of falling (short FES-I)	11.5 (5.4)	10.8 (5.2)	-0.25 (-0.60;0.10)	0.167
Medication risk (MRQ-10)	4.4 (1.6)	4.4 (1.6)	0.03 (-0.09;0.15)	0.653
Loneliness (short-JG)	0.7 (0.7)	0.6 (0.7)	-0.10 (-0.24;0.03)	0.128
Frailty (TFI)	5.5 (3.4)	4.9 (3.3)	-0.43 (-0.65;-0.22)	<0.001
Loss independence (GARS)	27.4 (11.9)	26.4 (10.8)	-0.11 (-0.73;0.52)	0.742
HRQoL PCS (SF-12)	40.4 (11.5)	41.8 (12.1)	0.95 (0.14;1.76)	0.022
HRQoL MCS (SF-12)	48.8 (11.3)	50.6 (11.2)	0.52 (-0.32;1.37)	0.224
Mental well-being (SF-36)	71.8 (21.3)	74.9 (20.5)	1.50 (0.15;2.84)	0.029

a) Values are derived from random-intercept multilevel logistic regression models adjusted for clustering by city and adjusted for age, gender, education, living situation and baseline status of the outcome measure.

b) Values are derived from random-intercept multilevel linear regression models adjusted for clustering by city and adjusted for age, gender, education, living situation and baseline status of the outcome measure. Healthy lifestyle= no smoking, no drinking and exercise>1 times a week. For short FES-I (range 7-28); MRQ-10 (range 0-10); short JG (range 6-18); TFI (range 0-15); GARS (range 18-72); higher scores mean worse health or more health risk. SF-12 and SF-36 scores range 0-100 and higher scores means a higher quality of life or better mental well-being. Abbreviations: B=Beta coefficient; FES-I= Falls Efficacy Scale International; JG=Jong-Gierveld; MRQ-10=Medication Risk Questionnaire 10; OR=Odds ratio; SF-12=short form 12; SF-36=short form 36; SHARE-FI= Survey of Health, Ageing and Retirement in Europe-Frailty Instrument; SNAQ-65+= Short Nutritional Assessment Questionnaire 65+; TFI=Tilburg Frailty Index.

When comparing persons who enrolled in any type of care-pathway with all persons in the control group (table 4), adjusted significant effects were stronger compared to the whole intervention group for recurrent falls (OR=0.58, 95% CI=0.40-0.85), frailty (B=-0.44, 95% CI=-0.71 to -0.17) and physical health-related quality of life (B=1.22, 95% CI=0.24-2.21). Additionally there was a positive effect on loneliness (B=-0.18, 95% CI=-0.35 to -0.02). The positive effect on mental well-being was no longer significant.

For persons in the falls, loneliness and frailty/medical care-pathways, significant positive effects were found on frailty and physical health-related quality of life (table S4). For persons in the falls care-pathway, additional positive effects were found on recurrent falls and loneliness. For persons in the loneliness care-pathway additional positive effects were found on fear of falling measured as single item and recurrent falls. For persons in the frailty/ medical care-pathway, additional positive effects were found on fear of falling measured as single item and loneliness. For persons in the polypharmacy care-pathway no positive effects were found.

Table 4: Prevalence and mean of outcomes at follow-up and effects of the UHCE approach for persons enrolled in any care-pathway with the control group as reference (N=1378).

	Control group N=858	Intervention group N=520	Adjusted effect estimates	P value
	N (%)	N (%)	OR (95% CI)[a]	
Healthy lifestyle	555 (65.4)	334 (64.5)	1.04 (0.67; 1.62)	0.848
Fear of falling	441 (51.6)	302 (58.2)	0.83 (0.63; 1.11)	0.215
Fall past year	267 (31.3)	142 (27.6)	0.82 (0.63; 1.06)	0.129
Recurrent falls past year	126 (14.8)	51 (9.9)	0.58 (0.40; 0.85)	0.005
Physical frailty (SHARE-FI)	245 (29.4)	154 (31.0)	0.87 (0.64; 1.18)	0.360
Severely limited function (GALI)	176 (20.7)	126 (24.6)	1.19 (0.86; 1.64)	0.303
Malnutrition (SNAQ-65+)	135 (17.1)	103 (20.6)	1.05 (0.76; 1.46)	0.755
	Mean (SD)	Mean (SD)	B (95% CI)[b]	
Fear of falling (short FES-I)	11.5 (5.4)	12.3 (5.7)	-0.24 (-0.68;0.21)	0.299
Medication risk (MRQ-10)	4.4 (1.6)	4.5 (1.7)	0.08 (-0.07;0.23)	0.312
Loneliness (short-JG)	0.7 (0.7)	0.7 (0.7)	-0.18 (-0.35;-0.02)	0.033
Frailty (TFI)	5.5 (3.4)	5.9 (3.3)	-0.44 (-0.71;-0.17)	0.001
Loss independence (GARS)	27.4 (11.9)	28.3 (12.0)	0.06 (-0.75;0.87)	0.886
HRQoL PCS (SF-12)	40.4 (11.5)	40.3 (11.8)	1.22 (0.24;2.21)	0.015
HRQoL MCS (SF-12)	48.8 (11.3)	46.7 (11.8)	-0.31 (-1.39;0.76)	0.568
Mental well-being (SF-36)	71.8 (21.3)	67.2 (20.6)	0.68 (-1.06;2.41)	0.444

a) Values are derived from random-intercept multilevel logistic regression models adjusted for clustering by city and adjusted for age, gender, education, living situation and baseline status of the outcome measure.

b) Values are derived from random-intercept multilevel linear regression models adjusted for clustering by city and adjusted for age, gender, education, living situation and baseline status of the outcome measure. Healthy lifestyle= no smoking, no drinking and exercise>1 times a week. For short FES-I (range 7-28); MRQ-10 (range 0-10); short JG (range 6-18); TFI (range 0-15); GARS (range 18-72); higher scores mean worse health or more health risk. SF-12 and SF-36 scores range 0-100 and higher scores means a higher quality of life or better mental well-being. Abbreviations: B=Beta coefficient; FES-I= Falls Efficacy Scale International; JG=Jong-Gierveld; MRQ-10=Medication Risk Questionnaire 10; OR=Odds ratio; SF-12=short form 12; SF-36=short form 36; SHARE-FI= Survey of Health, Ageing and Retirement in Europe-Frailty Instrument; SNAQ-65+= Short Nutritional Assessment Questionnaire 65+; TFI=Tilburg Frailty Index.

Regarding care use, the number of hours per week needing household help due to health problems was reduced among persons in the intervention group compared to persons in the control group (table S5). There were no effects on the use of doctor visits, hospital admissions and help in self-care.

DISCUSSION

Principal findings

Using a pre-post controlled design, we explored the effects of the UHCE approach on multiple outcomes of the lifestyle, health and quality of life among older persons in five European cities. The UHCE approach showed minor positive effects in tackling recurrent falls and frailty and promoting physical health-related quality of life and mental well-being compared to care as usual. Effects were stronger in the subgroup of persons who enrolled in care-pathways.

Interpretation

It is promising that we found positive effects of the UHCE approach on tackling recurrent falls and frailty and promoting physical health-related quality of life and mental well-being. However, the effect sizes of these outcomes were minor for the whole intervention group and minor or small for the subgroup of persons who enrolled in care-pathways. Furthermore, our study was exploratory in the sense that we measured effects on multiple outcomes which increases the chances of finding false positive results due to chance alone. Several systematic reviews report favourable effects of similar interventions on falls, functional decline, nursing home admissions and mortality[16 18 19], but others do not[17 46]. Effects on quality of life are less studied and evidence is of low quality[17]. A possible reason for the small effects found in our study is that only around half of the persons in the intervention group enrolled in care-pathways. The dose in which older persons take-up complex care interventions is rarely studied and could impact on the effectiveness of interventions[19 31]. For professionals, parts of the intervention might be time consuming or difficult to apply[44 47]. For older persons, health and mobility problems can be barriers to engagement in interventions[47 48]. The effects of the UHCE approach on health and quality of life were stronger when evaluating the subsample of persons enrolled in care-pathways. When analysing care-pathways separately, positive effects on fall outcomes, frailty and quality of life were found in persons who followed the falls prevention, frailty and/or loneliness care-pathways. As part of the falls prevention and frailty care-pathways most persons received physical exercise programmes. There is ample evidence on the benefits of physical exercise programmes for the prevention of falls and risk of falling in older populations[49-51] and to a lesser extent frailty[52], mental health and quality of life[53 54]. The polypharmacy care-pathway did not decrease inappropriate medication

use for persons enrolled in this care-pathway. The MRQ-10 instrument used to measure inappropriate medication use might have not been sensitive enough to detect a change.

To our knowledge this was the first coordinated preventive care study conducted in multiple European settings. Most of the studies on coordinated preventive health and social care have been conducted in the US, Canada or Northwest Europe[16-19]. In these settings, care for older persons was greatly improved during the 1980s to 1990s and care interventions after that time might have been of little extra benefit[19]. This could explain the low uptake of care in the Northwest European cities Manchester and Rotterdam. In these cities, qualitative analyses of logbooks revealed that many older persons reported that they did not enrol in a care-pathway because they were already involved in other care. Most positive effects of the UHCE approach were found in Rijeka, where all persons in the intervention group enrolled in a care-pathway. Possible explanations for the high uptake of care in Rijeka were a high morale to engage in activities among participants and regular monitoring of the care process by community nurses who had a personal relationship with the participants and acted as care coordinator in this study. Establishment of a trusted relationship is important for improvement of uptake and adherence to care interventions among older persons[48]. This therefore could be a key component of future studies. These studies could quantitatively explore to what extent the bond between patient and care provider impacts on effectiveness.

In our study, not using additional inclusion criteria such as frailty or multi-morbidity might also have impacted on enrolment in care-pathways as participants could have been too healthy to need care. However, frail persons might in turn not be fit and willing enough to engage in preventive care. Evidence on effective intervention components of coordinated care interventions and target populations has been mixed[16 19]. In a meta-analysis, Beswick et al. found reductions in nursing home admissions for populations with increased death rates and no benefits for any specific type of intervention among multifactorial interventions[19]. Though, Stuck et al. found that only interventions with a multidimensional geriatric assessment, regular follow-up visits and targeted at persons at lower risk for death were effective in reducing functional decline[16]. More research is needed to uncover the effective elements and target groups of complex coordinated preventive care interventions for older persons. In order to identify these elements, reporting of the development and evaluation of these complex interventions should be streamlined[22 55]. It could also be possible that structured and preventive monitoring and promotion of the health of older persons could result in stronger health benefits within a longer time span, as our study only measured effects in one year. Future studies should investigate the long-term effects of a coordinated preventive care approach for older persons.

Strengths and limitations

The main strength of our study is that we implemented the UHCE approach in five diverse European cities. This provides information on the effectiveness and generalisability of a coordinated preventive care approach in various European settings. With the use of a uniform questionnaire and measurements we were able to apply the same evaluation design in all cities and there were few missing data. There were also some limitations. First, although we almost reached our targeted sample size for the intervention group, we did not for the control group. Especially in Pallini and Rotterdam there were difficulties including persons in the control group despite attempts to boost participation. Selective inclusion cannot be excluded, although differences between control group and intervention group at baseline were small. To account for differences in sample size between cities, we used a multilevel modelling approach in analyses. Persons lost to follow-up in the intervention group were older and had a lower level of independence compared to persons in the intervention group included in the analyses. Therefore, the UHCE approach might have reached a relatively healthy group of older persons. Secondly, we applied a non-randomised design, which makes results subject to confounding variables. However, differences between persons in the control and intervention group at baseline were small. Third, whereas the UHCE project initially aimed to make use of existing care provisions, this was not always possible in all settings. This may have impacted the acceptability of the UHCE approach, especially in cases where health staff was newly employed, who were unfamiliar to the older participants.

Conclusions

Our study found promising but minor effects for the use of a coordinated preventive health and social care approach for the promotion of healthy ageing of older persons. Future studies should further evaluate the effects of coordinated preventive health and social care aimed at healthy ageing in diverse European settings. The main challenge is participation in care of this vulnerable older population. Therefore, effective strategies are needed to promote engagement in care, tailored to the needs of older persons. More research is needed to determine the specific effective components of coordinated preventive health and social care that contribute to health improvements of older persons.

REFERENCES

1. Eurostat. Population structure and ageing: European Union, 1995-2013; 2014 [Available from: http://ec.europa.eu/eurostat/statistics-explained/index.php/Population_structure_and_ageing accessed 05/01/2017.
2. European Innovation Partnership on Active and Healthy Ageing. Specific Action on innovation in support of 'Personalized health management, starting with a Falls Prevention Initiative' Brussels: European Commision; 2013 [Available from: https://ec.europa.eu/eip/ageing/sites/eipaha/files/library/51a44f911f647_a2_action_plan.pdf.
3. Andrew MK, Mitnitski A, Kirkland SA, et al. The impact of social vulnerability on the survival of the fittest older adults. *Age Ageing* 2012;41(2):161-65.
4. Mendes de Leon CF, Glass TA, Berkman LF. Social engagement and disability in a community population of older adults: the New Haven EPESE. *Am J Epidemiol* 2003;157(7):633-42.
5. Glasby J. The holy grail of health and social care integration. *BMJ* 2017;356:j801. doi: 10.1136/bmj.j801
6. Kringos DS, Boerma WGW, Hutchinson A, et al. Building primary care in a changing Europe2015.
7. Nolte E, Knai C, McKee M, et al. Managing chronic conditions : experience in eight countries. Copenhagen: World Health Organization on behalf of the European Observatory on Health Systems and Policies 2009.
8. Frich LM. Nursing interventions for patients with chronic conditions. *J Adv Nurs* 2003;44(2):137-53. doi: 2779 [pii] [published Online First: 2003/10/03]
9. Markle-Reid M, Browne G, Weir R, et al. The effectiveness and efficiency of home-based nursing health promotion for older people: a review of the literature. *Med Care Res Rev* 2006;63(5):531-69. doi: 63/5/531 [pii]10.1177/1077558706290941 [published Online First: 2006/09/07]
10. Markle-Reid M, Browne G, Gafni A. Nurse-led health promotion interventions improve quality of life in frail older home care clients: Lessons learned from three randomized trials in Ontario, Canada. *J Eval Clin Pract* 2013;19(1):118-31.
11. Liebel DV, Friedman B, Watson NM, et al. Review of nurse home visiting interventions for community-dwelling older persons with existing disability. *Med Care Res Rev* 2009;66(2):119-46. doi: 1077558708328815 [pii]10.1177/1077558708328815 [published Online First: 2008/12/31]
12. Eurostat. Healthcare personnel statistics - physicians: European Commission; 2017 [Available from: http://ec.europa.eu/eurostat/statistics-explained/index.php/Healthcare_personnel_statistics_-_physicians#Further_Eurostat_information accessed 17/11/2017 2017.
13. Cattan M, White M, Bond J, et al. Preventing social isolation and loneliness among older people: a systematic review of health promotion interventions. *Ageing Soc* 2005;25:41-67. doi: DOI 10.1017/Soi44686X04002594
14. Hagan R, Manktelow R, Taylor BJ, et al. Reducing loneliness amongst older people: a systematic search and narrative review. *Aging Ment Health* 2014;18(6):683-93. doi: 10.1080/13607863.2013.875122 [published Online First: 2014/01/21]

15. Dickens AP, Richards SH, Greaves CJ, et al. Interventions targeting social isolation in older people: a systematic review. *BMC Public Health* 2011;11:647. doi: 1471-2458-11-647 [pii]10.1186/1471-2458-11-647 [published Online First: 2011/08/17]
16. Stuck AE, Egger M, Hammer A, et al. Home visits to prevent nursing home admission and functional decline in elderly people: systematic review and meta-regression analysis. *JAMA* 2002;287(8):1022-8. doi: jma10044 [pii] [published Online First: 2002/02/28]
17. Mayo-Wilson E, Grant S, Burton J, et al. Preventive home visits for mortality, morbidity, and institutionalization in older adults: a systematic review and meta-analysis. *PLoS One* 2014;9(3):e89257. doi: 10.1371/journal.pone.0089257 PONE-D-13-47215 [pii] [published Online First: 2014/03/14]
18. Huss A, Stuck AE, Rubenstein LZ, et al. Multidimensional preventive home visit programs for community-dwelling older adults: a systematic review and meta-analysis of randomized controlled trials. *J Gerontol A Biol Sci Med Sci* 2008;63(3):298-307. doi: 63/3/298 [pii] [published Online First: 2008/04/01]
19. Beswick AD, Rees K, Dieppe P, et al. Complex interventions to improve physical function and maintain independent living in elderly people: a systematic review and meta-analysis. *Lancet* 2008;371(9614):725-35. doi: S0140-6736(08)60342-6 [pii]10.1016/S0140-6736(08)60342-6 [published Online First: 2008/03/04]
20. World Health Organization. Primary health care : now more than ever2008.
21. Miller JN, Colditz GA, Mosteller F. How study design affects outcomes in comparisons of therapy. II: Surgical. *Stat Med* 1989;8(4):455-66.
22. Mohler R, Kopke S, Meyer G. Criteria for Reporting the Development and Evaluation of Complex Interventions in healthcare: revised guideline (CReDECI 2). *Trials* 2015;16:204. doi: 10.1186/s13063-015-0709-y
23. Bartholomew LK, Parcel GS, Kok G. Intervention mapping: a process for developing theory- and evidence-based health education programs. *Health Educ Behav* 1998;25(5):545-63. [published Online First: 1998/10/13]
24. Franse CB, Voorham AJJ, van Staveren R, et al. Evaluation design of Urban Health Centres Europe (UHCE): preventive integrated health and social care for community-dwelling older persons in five European cities. *BMC Geriatr* 2017;17(1):209. doi: 10.1186/s12877-017-0606-1
25. Gobbens RJ, Luijkx KG, Wijnen-Sponselee MT, et al. Towards an integral conceptual model of frailty. *J Nutr Health Aging* 2010;14(3):175-81.
26. Veiligheid.nl. Fall risk test Veiligheid.nl; [Available from: http://www.veiligheid.nl/voorlichtingsmateriaal/valanalyse-inventarisatie-valrisico-65-door-de-eerstelijnszorg accessed 7 july 2014.
27. Maher RL, Hanlon J, Hajjar ER. Clinical consequences of polypharmacy in elderly. *Expert Opin Drug Saf* 2014;13(1):57-65. doi: 10.1517/14740338.2013.827660
28. Barenholtz Levy H. Self-administered medication-risk questionnaire in an elderly population. *Annals of Pharmacotherapy* 2003;37(7-8):982-7.

29. Gobbens RJ, van Assen MA, Luijkx KG, et al. The Tilburg Frailty Indicator: psychometric properties. *J Am Med Dir Assoc* 2010;11(5):344-55. doi: 10.1016/j.jamda.2009.11.003
30. De Jong Gierveld J, Van Tilburg T. The De Jong Gierveld short scales for emotional and social loneliness: tested on data from 7 countries in the UN generations and gender surveys. *Eur J Ageing* 2010;7(2):121-30. doi: 10.1007/s10433-010-0144-6
31. Steckler A., Linnan L., Process evaluation for public health interventions and research. San Francisco, Calif.: Jossey-Bass 2002.
32. Bush K, Kivlahan DR, McDonell MB, et al. The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking. Ambulatory Care Quality Improvement Project (ACQUIP). Alcohol Use Disorders Identification Test. *Arch Intern Med* 1998;158(16):1789-95.
33. Romero-Ortuno R, Walsh CD, Lawlor BA, et al. A frailty instrument for primary care: findings from the Survey of Health, Ageing and Retirement in Europe (SHARE). *BMC Geriatr* 2010;10:57. doi: 1471-2318-10-57 [pii]10.1186/1471-2318-10-57 [published Online First: 2010/08/25]
34. Romero-Ortuno R. The Frailty Instrument for primary care of the Survey of Health, Ageing and Retirement in Europe predicts mortality similarly to a frailty index based on comprehensive geriatric assessment. *Geriatr Gerontol Int* 2013;13(2):497-504. doi: 10.1111/j.1447-0594.2012.00948.x [published Online First: 2012/09/22]
35. Wijnhoven HA, Schilp J, van Bokhorst-de van der Schueren MA, et al. Development and validation of criteria for determining undernutrition in community-dwelling older men and women: The Short Nutritional Assessment Questionnaire 65+. *Clinical Nutrition* 2012;31(3):351-8.
36. Suurmeijer TP, Doeglas DM, Moum T, et al. The Groningen Activity Restriction Scale for measuring disability: its utility in international comparisons. *Am J Public Health* 1994;84(8):1270-3.
37. van Oyen H, Van der Heyden J, Perenboom R, et al. Monitoring population disability: evaluation of a new Global Activity Limitation Indicator (GALI). *Soz Praventivmed* 2006;51(3):153-61.
38. Berger N, Van Oyen H, Cambois E, et al. Assessing the validity of the Global Activity Limitation Indicator in fourteen European countries. *BMC Med Res Methodol* 2015;15:1. doi: 10.1186/1471-2288-15-1
39. Haywood KL, Garratt AM, Fitzpatrick R. Quality of life in older people: a structured review of generic self-assessed health instruments. *Qual Life Res* 2005;14(7):1651-68. [published Online First: 2005/08/27]
40. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996;34(3):220-33. [published Online First: 1996/03/01]
41. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;30(6):473-83.
42. Yardley L, Beyer N, Hauer K, et al. Development and initial validation of the Falls Efficacy Scale-International (FES-I). *Age Ageing* 2005;34(6):614-9.
43. Organisation for Economic Co-operation and Development. Classifying educational programmes : manual for ISCED-97 implementation in OECD countries. Paris: Organisation for Economic Co-operation and Development 1999.

44. Metzelthin SF, van Rossum E, de Witte LP, et al. Effectiveness of interdisciplinary primary care approach to reduce disability in community dwelling frail older people: cluster randomised controlled trial. *BMJ* 2013;347:f5264. [published Online First: 2013/09/12]
45. McDonald JH, University of D. Handbook of biological statistics. Baltimore, Maryland: Sparky House Publishing 2009.
46. Bouman A, van Rossum E, Nelemans P, et al. Effects of intensive home visiting programs for older people with poor health status: a systematic review. *BMC Health Serv Res* 2008;8:74. doi: 1472-6963-8-74 [pii]10.1186/1472-6963-8-74 [published Online First: 2008/04/05]
47. Metzelthin SF, Daniels R, van Rossum E, et al. A nurse-led interdisciplinary primary care approach to prevent disability among community-dwelling frail older people: a large-scale process evaluation. *Int J Nurs Stud* 2013;50(9):1184-96. doi: S0020-7489(12)00458-0 [pii]10.1016/j.ijnurstu.2012.12.016 [published Online First: 2013/02/07]
48. Provencher V, Mortenson WB, Tanguay-Garneau L, et al. Challenges and strategies pertaining to recruitment and retention of frail elderly in research studies: a systematic review. *Arch Gerontol Geriatr* 2014;59(1):18-24. doi: 10.1016/j.archger.2014.03.006
49. El-Khoury F, Cassou B, Charles MA, et al. The effect of fall prevention exercise programmes on fall induced injuries in community dwelling older adults: systematic review and meta-analysis of randomised controlled trials. *BMJ* 2013;347:f6234. [published Online First: 2013/10/31]
50. Gillespie LD, Robertson MC, Gillespie WJ, et al. Interventions for preventing falls in older people living in the community. *Cochrane Database Syst Rev* 2009(2):CD007146. doi: 10.1002/14651858.CD007146.pub2 [published Online First: 2009/04/17]
51. Howe TE, Rochester L, Neil F, et al. Exercise for improving balance in older people. *Cochrane Database Syst Rev* 2011(11):CD004963. doi: 10.1002/14651858.CD004963.pub3 [published Online First: 2011/11/11]
52. Theou O, Stathokostas L, Roland KP, et al. The effectiveness of exercise interventions for the management of frailty: a systematic review. *J Aging Res* 2011;2011:569194. doi: 10.4061/2011/569194 [published Online First: 2011/05/18]
53. Bridle C, Spanjers K, Patel S, et al. Effect of exercise on depression severity in older people: systematic review and meta-analysis of randomised controlled trials. *Br J Psychiatry* 2012;201(3):180-5.
54. Park SH, Han KS, Kang CB. Effects of exercise programs on depressive symptoms, quality of life, and self-esteem in older people: a systematic review of randomized controlled trials. *Appl Nurs Res* 2014;27(4):219-26. doi: 10.1016/j.apnr.2014.01.004
55. Campbell M, Fitzpatrick R, Haines A, et al. Framework for design and evaluation of complex interventions to improve health. *BMJ* 2000;321(7262):694-6. [published Online First: 2000/09/15]

SUPPLEMENTAL MATERIAL

Table S1: Socio-demographic, lifestyle and health characteristics by intervention and control group of each city among persons in the UHCE study at baseline (N=1844).

	Manchester, UK			Pallini, GR			Rijeka, HR			Rotterdam, NL			Valencia, ES		
	CG N=244	IG N=212	*	CG N=124	IG N=154	*	CG N=208	IG N=221	*	CG N=92	IG N=192	*	CG N=190	IG N=207	*
Age in years, mean (SD)	81.9 (4.8)	81.4 (5.0)		75.3 (5.6)	75.1 (5.4)		81.4 (4.4)	80.8 (4.5)		80.8 (4.7)	81.8 (5.2)		77.3 (5.1)	76.6 (5.1)	
Female gender, N (%)	57.4	53.3		54.8	54.5		71.2	66.5		59.8	60.9		61.1	64.7	
Living alone, N (%)	49.2	51.9		22.6	20.1		44.2	34.8	a	36.3	50.5	a	26.3	31.4	
Lower education, N (%)	28.4	25.0		67.2	54.5	a	43.8	42.1		78.4	61.4	b	63.2	77.3	b
Healthy lifestyle, N (%)	69.3	70.8		59.7	62.7		54.4	63.6		70.0	71.9		82.0	83.1	
Fear of falling, N (%)	36.1	41.5		53.2	48.1		65.4	54.8	a	38.0	30.7		44.7	55.6	a
Fall past year, N (%)	35.8	32.5		31.1	22.7		32.0	31.3		25.3	34.4		27.9	23.2	
Recurrent falls past year, N (%)	17.3	17.9		14.3	12.3		17.0	12.6		9.9	15.1		7.9	11.6	
Physical frailty (SHARE-FI)	28.2	25.1		17.8	19.1		24.8	13.6	b	22.5	22.5		11.2	15.5	
Severely limited functioning (GALI), N (%)	19.7	17.9		17.6	21.1		31.4	22.2	a	16.3	14.7		4.7	6.8	
Malnutrition (SNAQ-65+), N (%)	13.1	15.2		16.5	13.2		19.5	24.5		12.2	16.3		8.1	12.7	
Fear of falling (short FES-I), mean (SD)	9.2 (3.9)	9.6 (4.2)		11.0 (4.5)	10.8 (4.3)		14.4 (6.2)	12.6 (5.6)	b	9.6 (3.5)	8.8 (3.2)		8.9 (2.9)	9.4 (3.5)	
Medication risk (MRQ-10), mean (SD)	4.7 (1.6)	4.7 (1.5)		4.2 (1.8)	4.6 (1.7)		4.3 (1.6)	4.2 (1.7)		4.4 (1.7)	4.4 (1.7)		4.1 (1.5)	4.3 (1.6)	
Loneliness (short JG), mean (SD)	0.4 (0.5)	0.3 (0.5)		0.7 (0.7)	0.7 (0.7)		1.1 (0.7)	0.9 (0.7)	c	0.5 (0.7)	0.5 (0.7)		0.4 (0.6)	0.5 (0.6)	
Frailty (TFI), mean (SD)	4.1 (2.9)	4.5 (2.9)		5.4 (3.1)	5.9 (3.0)		7.6 (3.1)	6.1 (3.1)	c	4.4 (3.1)	4.1 (3.0)		4.2 (2.5)	5.0 (3.1)	b
Loss independence (GARS), mean (SD)	24.1 (8.4)	24.3 (8.5)		24.0 (8.9)	22.8 (7.0)		31.7 (13.2)	27.4 (10.9)	c	25.3 (8.1)	25.5 (8.6)		21.7 (7.1)	21.9 (5.7)	
HRQoL PCS (SF-12), mean (SD)	40.6 (12.4)	41.7 (11.6)		45.5 (11.6)	43.4 (12.1)		36.9 (10.7)	39.8 (11.7)	b	40.8 (12.4)	41.9 (12.5)		47.0 (10.6)	44.9 (11.0)	
HRQoL MCS (SF-12), mean (SD)	52.2 (8.6)	52.0 (8.6)		48.4 (9.8)	49.5 (10.2)		42.0 (10.3)	47.9 (10.9)	c	53.6 (9.4)	54.1 (9.7)		52.2 (10.9)	52.6 (11.2)	
Mental well-being (SF-36), mean (SD)	83.8 (16.0)	84.4 (14.6)		62.1 (19.9)	66.6 (18.2)		59.2 (19.1)	68.2 (19.6)	c	81.9 (16.1)	81.4 (16.8)		76.8 (19.4)	73.8 (23.1)	

Lower education= ISCED level 0-2. Healthy lifestyle= no smoking, no drinking and exercise>1 times a week. . For short FES-I (range 7-28); MRQ-10 (range 0-10); short JG (range 6-18); TFI (range 0-15); GARS (range 18-72); higher scores mean worse health or more health risk. SF-12 and SF-36 scores range 0-100 and higher scores means a higher quality of life or better mental well-being. Abbreviations: CG= Control Group; ES=Spain; FES-I= Falls Efficacy Scale International; GALI=; GARS=; GR=Greece; HR=Croatia; IG=Intervention Group; ISCED=International Standard Classification of Education; JG=Jong-Gierveld; MRQ-10=Medication Risk Questionnaire 10; NL=The Netherlands; P=P-value; SF-12=short form 12; SF-36=short form 36; SNAQ-65+=Short Nutritional Assessment Questionnaire 65+; TFI=Tilburg Frailty Index; UK=United Kingdom.

* P-value; a=P-value <.05; b=P-value <.01; c=P-value <.001

Table S2: Lifestyle and health outcomes by intervention and control group of each city among persons in the UHCE study at follow-up (N=1844).

	Manchester, UK		Pallini, GR		Rijeka, HR		Rotterdam, NL		Valencia, ES	
	CG N=244	IG N=212	CG N=124	IG N=154	CG N=208	IG N=221	CG N=92	IG N=192	CG N=190	IG N=207
Healthy lifestyle, N (%)	68.0	73.6	61.2	62.1	52.2	61.4	70.0	69.3	76.7	76.8
Fear of falling, N (%)	36.1	44.3	55.4	46.4	74.0	54.8	39.1	31.9	50.8	60.9
Fall past year, N (%)	32.4	41.2	26.1	21.0	30.8	25.3	32.6	30.3	33.2	24.3
Recurrent falls past year, N (%)	16.4	19.0	10.9	7.7	18.3	8.1	17.4	10.6	10.0	6.3
Physical frailty (SHARE-FI)	31.0	25.4	21.2	24.6	48.1	38.0	22.5	25.4	14.7	9.7
Severely limited functioning (GALI), N (%)	18.9	25.0	15.0	22.9	41.8	28.5	14.4	15.3	6.3	6.8
Malnutrition (SNAQ-65+), N (%)	15.3	10.5	26.2	14.5	26.0	26.7	16.3	12.8	10.2	10.6
Fear of falling (short FES-I), mean (SD)	9.5 (4.1)	9.9 (4.8)	12.7 (5.0)	12.3 (5.7)	15.8 (6.3)	13.2 (6.0)	9.9 (4.0)	9.2 (3.7)	9.2 (3.5)	9.7 (4.2)
Medication risk (MRQ-10), mean (SD)	4.7 (1.5)	4.9 (1.5)	4.3 (1.9)	4.5 (2.0)	4.1 (1.6)	4.0 (1.5)	4.2 (1.5)	4.2 (1.5)	4.5 (1.6)	4.6 (1.5)
Loneliness (short JG), mean (SD)	0.4 (0.6)	0.3 (0.5)	0.9 (0.8)	0.8 (0.8)	1.2 (0.7)	0.9 (0.7)	0.4 (0.6)	0.5 (0.6)	0.3 (0.6)	0.5 (0.6)
Frailty (TFI), mean (SD)	4.2 (2.9)	3.9 (2.8)	5.3 (3.3)	5.7 (3.9)	8.2 (3.0)	6.2 (3.4)	4.2 (3.0)	4.3 (3.0)	4.7 (2.8)	4.7 (3.0)
Loss independence (GARS), mean (SD)	25.2 (9.7)	25.3 (10.2)	25.2 (10.5)	24.8 (10.1)	36.3 (13.8)	30.9 (13.0)	26.9 (9.1)	27.2 (9.3)	22.3 (8.5)	23.2 (8.7)
HRQoL PCS (SF-12), mean (SD)	41.6 (11.6)	40.1 (12.6)	42.9 (10.4)	42.5 (12.6)	34.5 (10.1)	40.2 (11.0)	40.5 (11.8)	42.4 (12.2)	43.9 (11.0)	44.3 (11.7)
HRQoL MCS (SF-12), mean (SD)	53.3 (9.2)	53.7 (8.7)	46.1 (9.6)	47.8 (10.3)	39.9 (9.9)	43.6 (11.8)	54.5 (8.7)	55.6 (8.9)	51.8 (10.7)	52.2 (11.4)
Mental well-being (SF-36), mean (SD)	84.3 (16.6)	85.7 (14.6)	61.2 (17.8)	63.4 (18.0)	54.7 (16.6)	64.8 (20.0)	82.5 (14.9)	83.1 (16.2)	76.0 (20.3)	74.9 (22.3)

Healthy lifestyle= no smoking, no drinking and exercise>1 times a week. For short FES-I (range 7-28); MRQ-10 (range 0-10); short JG (range 6-18); TFI (range 0-15); GARS (range 18-72); higher scores mean worse health or more health risk. SF-12 and SF-36 scores range 0-100 and higher scores means a higher quality of life or better mental well-being. Abbreviations: CG= Control Group; ES=Spain; FES-I= Falls Efficacy Scale International; GALI=; GARS=; GR=Greece; HR=Croatia; IG=Intervention Group; JG=Jong-Gierveld; MRQ-10=Medication Risk Questionnaire 10; NL=The Netherlands; P=P-value; SF-12=short form 12; SF-36=short form 36; SNAQ-65+=Short Nutritional Assessment Questionnaire 65+; TFI=Tilburg Frailty Index; UK=United Kingdom.

Table S3: Effect of the UHCE approach on outcomes for each city separately.

	Manchester, UK (N=456)	‡	Pallini, GR (N=279)	‡	Rijeka, HR (N=429)	‡	Rotterdam, NL (N=284)	‡	Valencia, ES (N=397)	‡
	OR (95% CI)*		OR (95% CI)*		OR (95% CI)*		OR (95% CI)*		OR (95% CI)*	
Healthy lifestyle	0.59 (0.29; 1.22)		1.22 (0.59; 2.56)		0.91 (0.38; 2.22)		1.13 (0.45; 2.84)		1.10 (0.49; 2.43)	
Fear of falling	1.38 (0.87; 2.19)		0.67 (0.37; 1.21)		0.44 (0.27; 0.71)	b	0.69 (0.36; 1.32)		1.30 (0.80; 2.12)	
Fall past year	1.60 (1.05; 2.42)	a	0.82 (0.43; 1.58)		0.84 (0.54; 1.31)		0.69 (0.38; 1.28)		0.63 (0.40; 1.00)	
Recurrent falls past year	1.17 (0.69; 1.96)		0.65 (0.27; 1.54)		0.45 (0.24; 0.84)	a	0.40 (0.17; 0.93)	a	0.42 (0.18; 0.95)	a
Physical frailty (SHARE-FI)	1.06 (0.62; 1.84)		1.15 (0.49; 2.73)		0.58 (0.32; 1.05)		0.95 (0.45; 2.03)		1.87 (0.95; 3.67)	
Severely limited function (GALI)	1.65 (0.99; 2.74)		1.53 (0.71; 3.31)		0.59 (0.37; 0.94)	a	1.20 (0.52; 2.82)		0.79 (0.31; 2.02)	
Malnutrition (SNAQ-65+)	0.56 (0.30; 1.05)		0.96 (0.38; 2.42)		0.98 (0.62; 1.56)		0.66 (0.29; 1.51)		1.17 (0.59; 2.33)	
	B (95% CI)†	P	B (95% CI)†	P	B (95% CI)†	P	B (95% CI)†	P	B (95% CI)†	P
Fear of falling (short FES-I)	0.31 (-0.33; 0.96)		-0.07 (-1.05; 0.91)		-1.27 (-2.11; -0.43)	a	-0.49 (-1.31; 0.33)		0.22 (-0.47; 0.92)	
Medication risk (MRQ-10)	0.20 (-0.03; 0.43)		-0.09 (-0.47; 0.30)		-0.12 (-0.38; 0.13)		0.11 (-0.18; 0.41)		-0.08 (-0.34; 0.19)	
Loneliness (short-JG)	-0.04 (-0.25; 0.18)		-0.18 (-0.66; 0.30)		-0.57 (-0.88; -0.27)	c	0.08 (-0.28; 0.44)		0.16 (-0.08; 0.41)	
Frailty (TFI)	-0.57 (-0.93; -0.21)	b	0.14 (-0.55; 0.82)		-1.12 (-1.62; -0.61)	c	0.23 (-0.29; 0.74)		-0.50 (-0.94; -0.06)	a
Loss independence (GARS)	-0.11 (-1.27; 1.05)		0.80 (-0.90; 2.51)		-1.83 (-3.40; -0.25)	a	0.06 (-1.24; 1.36)		0.54 (-0.75; 1.82)	
HRQoL PCS (SF-12)	-2.38 (-4.04; -0.72)	a	-0.19 (-2.56; 2.18)		3.78 (2.36; 5.20)	c	2.17 (-0.13; 4.47)		2.00 (0.20; 3.80)	a
HRQoL MCS (SF-12)	0.89 (-0.63; 2.40)		-0.14 (-2.64; 2.37)		0.96 (-0.85; 2.77)		0.69 (-1.49; 2.87)		0.32 (-1.62; 2.25)	
Mental well-being (SF-36)	0.96 (-1.27; 3.20)		-0.28 (-4.16; 3.61)		5.25 (2.36; 8.14)	c	0.35 (-2.90; 3.60)		1.65 (-1.69; 4.99)	

* Values are derived from logistic regression models adjusted for age, gender, education, living situation and baseline status of the outcome measure. †Values are derived from linear regression models adjusted for age, gender, education, living situation and baseline status of the outcome measure. Healthy lifestyle= no smoking, no drinking and exercise>1 times a week. For short FES-I (range 7-28); MRQ-10 (range 0-10); short JG (range 6-18); TFI (range 0-15); GARS (range 18-72); higher scores mean worse health or more health risk. SF-12 and SF-36 scores range 0-100 and higher scores means a higher quality of life or better mental well-being. Abbreviations: B=Beta coefficient; FES-I= Falls Efficacy Scale International; JG=Jong-Gierveld; MRQ-10=Medication Risk Questionnaire 10; OR=Odds ratio; SF-12=short form 12; SF-36=short form 36; SHARE-FI= Survey of Health, Ageing and Retirement in Europe-Frailty Instrument; SNAQ-65+=Short Nutritional Assessment Questionnaire 65+; TFI=Tilburg Frailty Index.

‡ P-value; a=P-value <.05; b=P-value <.01; c=P-value <.001

Table S4: Effect of each UHCE care-pathway on outcomes for at-risk persons in the intervention group who enrolled in a specific care-pathway compared to at-risk persons in the control group.

	Falls pathway CG=437 IG=211	**Polypharmacy pathway CG=415 IG=118**	**Loneliness pathway CG=797 IG=199**	**Frailty/medical pathway CG=858 IG=182**
	Adjusted effect estimates	Adjusted effect estimates	Adjusted effect estimates	Adjusted effect estimates
	OR (95% CI); P*	OR (95% CI); P*	OR (95% CI); P*	OR (95% CI); P*
Healthy lifestyle	1.13 (0.53; 2.39); 0.710	0.94 (0.36; 2.43); 0.890	1.11 (0.59; 2.10); 0.737	1.21 (0.66; 2.23); 0.540
Fear of falling	0.69 (0.44; 1.09); 0.092	1.02 (0.56; 1.84); 0.949	0.60 (0.39; 0.92); 0.021	0.60 (0.40; 0.91); 0.016
Fall past year	0.70 (0.48; 1.02); 0.056	0.84 (0.50; 1.39); 0.491	0.75 (0.51; 1.08); 0.120	0.90 (0.61; 1.33); 0.610
Recurrent falls past year	0.45 (0.26; 0.76); 0.002	0.58 (0.28; 1.19); 0.138	0.41 (0.22; 0.77); 0.006	0.74 (0.43; 1.28); 0.285
Physical frailty (SHARE-FI)	0.89 (0.58;1.36); 0.570	0.68 (0.37; 1.24); 0.210	0.68 (0.44; 1.06); 0.089	0.74 (0.46; 1.18); 0.210
Severely limited function GALI)	0.93 (0.59;1.48); 0.761	1.37 (0.72; 2.59); 0.338	0.83 (0.51; 1.33); 0.437	1.34 (0.84; 2.14); 0.222
Malnutrition (SNAQ-65+)	0.71 (0.31;1.61); 0.165	1.03 (0.54; 1.97); 0.920	1.11 (0.70; 1.78); 0.657	1.28 (0.80; 2.05); 0.306
	B (95% CI); P†	B (95% CI); P†	B (95% CI); P†	B (95% CI); P†
Fear of falling (short FES-I)	-0.65 (-1.40; 0.11); 0.092	0.16 (-0.79; 1.12); 0.737	-0.58 (-1.20; 0.04); 0.069	-0.46 (-1.07; -0.14); 0.130
Medication risk (MRQ-10)	-0.02 (-0.25; 0.20); 0.833	0.27 (-0.04; 0.59); 0.086	-0.02 (-0.24; 0.20); 0.831	0.10 (-0.12; 0.33); 0.369
Loneliness (short-JG)	-0.26 (-0.52; -0.01); 0.043	-0.23 (-0.56; 0.10); 0.173	-0.22 (-0.46; 0.03); 0.079	-0.27 (-0.51; -0.03); 0.028
Frailty (TFI)	-0.84 (-1.26; -0.42); <0.001	-0.26 (-0.79; 0.28); 0.343	-0.75 (-1.12; -0.37); <0.001	-0.44 (-0.81; -0.08); 0.018
Loss independence (GARS)	-0.76 (-2.15; 0.63); 0.282	0.75 (-1.04; 2.54); 0.409	-1.00 (-2.17; 0.16); 0.091	0.00 (-1.09; 1.08); 0.995
HRQoL PCS (SF-12)	1.81 (0.39; 3.23); 0.013	1.33 (-0.64; 3.31); 0.184	3.05 (1.67; 4.44); <0.001	1.86 (0.40; 3.32); 0.013
HRQoL MCS (SF-12)	0.09 (-1.54; 1.72); 0.911	0.06 (-2.10; 2.23); 0.955	0.61 (-0.91; 2.14); 0.430	-0.07 (-1.60; 1.45); 0.924
Mental well-being (SF-36)	2.00 (-0.72; 4.71); 0.149	2.31 (-1.06; 5.69); 0.179	2.14 (-0.31; 4.58); 0.087	1.36 (-1.06; 3.78); 0.269

* Values are derived from random-intercept multilevel logistic regression models adjusted for clustering by city and adjusted for age, gender, education, living situation and baseline status of the outcome measure. †Values are derived from random-intercept multilevel linear regression models adjusted for clustering by city and adjusted for age, gender, education, living situation and baseline status of the outcome measure. Healthy lifestyle= no smoking, no drinking and exercise>1 times a week. For short FES-I (range 7-28); MRQ-10 (range 0-10); short JG (range 6-18); TFI (range 0-15); GARS (range 18-72); higher scores mean worse health or more health risk. SF-12 and SF-36 scores range 0-100 and higher scores means a higher quality of life or better mental well-being. Abbreviations: B=Beta coefficient; FES-I= Falls Efficacy Scale International; JG=Jong-Gierveld; MRQ-10=Medication Risk Questionnaire 10; OR=Odds ratio; SF-12=short form 12; SF-36=short form 36; SHARE-FI= Survey of Health, Ageing and Retirement in Europe-Frailty Instrument; SNAQ-65+=Short Nutritional Assessment Questionnaire 65+; TFI=Tilburg Frailty Index.

Table S5: Mean social and health care use in past 12 months at follow-up and effects of the UHCE approach with the control group as reference (N=1844).

	Control group N=858	Intervention group N=986	Adjusted effect estimates	P value
	Mean (SD)	Mean (SD)	B (95% CI)[a]	
Number visits medical doctor	6.5 (6.5)	6.0 (7.7)	-0.25 (-0.90;0.41)	0.463
Days admitted to hospital	1.3 (5.3)	1.5 (6.1)	0.24 (-0.30;0.77)	0.390
Hours/week help household due to health	1.5 (5.3)	1.0 (3.3)	-0.39 (-0.75;-0.04)	0.030
Hours/week help self-care	0.4 (2.7)	0.3 (2.6)	-0.01 (-0.23;0.20)	0.904

a) Values are derived from random-intercept multilevel linear regression models adjusted for clustering by city and adjusted for age, gender, education, living situation and baseline status of the outcome measure.

Supplementary Text S1: CREDICI II criteria

First stage: Development

1 **Description of the intervention's underlying theoretical basis**

The development of the UHCE approach followed an intervention mapping approach. An integral conceptual model of frailty was applied, which includes physical as well as social and psychological components and is geared towards a multidisciplinary approach.

2 **Description of all intervention components, including the reasons for their selection as well as their aims / essential functions**

The general template of the UHCE approach consisted of three stages. In the first stage of the UHCE approach, the older person received a health assessment consisting of validated instruments in order to identify whether the person had an indication of a need for a follow-up care-pathway. In the second stage of the UHCE approach, shared-decision making took place; the results of the assessments (the indications for care-pathways) were discussed with the older person, a person in charge of care coordination and a physician. Shared-decision making was included in order to develop a care plan which was adapted to the preferences of the older person, which was thought to promote involvement in care-pathways. In the third stage, as a result of the shared decision-making process, a decision on a care plan was made and each participant was referred to care-pathways. The care-pathways aimed to promote healthy ageing among the older persons by reducing fall risk, inappropriate medication use, loneliness and frailty.

3 **Illustration of any intended interactions between different components**

Interaction stage 1 (indication for care-pathway as a result of the assessment) and stage 3 (care-pathways) by stage 2 (shared decision-making and fine-tuning care-plan to the needs of the older person). Results of the assessments (the indications for care-pathways) were discussed with the older person, a person in charge of care coordination and a physician. Staff encouraged the older person to involve an informal caregiver in the shared-decision making process. Shared-decision making was included in order to develop a care plan which was adapted to the preferences of the older person, which was thought to promote involvement in care-pathways.

4 **Description and consideration of the context's characteristics in intervention modelling**

The general template of the UHCE approach was adapted to the national standards and context of each of the five participating cities. Specific information for each city; on the place and staff involved in the assessment, staff who acted as care coordinator, type of care and health staff involved in the care-pathways, is reported in Table 1.

Second Stage: Feasibility and piloting

5 **Description of the pilot test and its impact on the definite intervention**

Focus groups and interviews with main stakeholders (older persons, health and social care professionals, caregivers and policy makers) were held to identify their needs and preferences regarding healthy and active ageing. This led to the decision to address loneliness as a separate health problem, in addition to frailty, fall risk and polypharmacy. In each city, the assessment was piloted in at least five older persons. Misinterpretation of questions were identified and minor changes were made.

Third stage: Evaluation

6 **Description of the control condition (comparator) and reasons for the selection**

Persons in the control group received their usual care. Participants in the control group had access to existing care services delivered in the care-pathways, but not to newly developed services. No coordinated preventive referral to existing care services and monitoring of health was in place. In all cities except for Pallini, GPs were the first point of contact and had a gatekeeper function towards existing care services. In Pallini, GPs were scarce and specialist care was directly accessible upon appointment.

7 **Description of the strategy for delivering the intervention within the study context**

A short standardized assessment form was developed for all cities, which consisted of validated instruments. In addition, a uniform logbook was developed for all cities which was kept for each older person who received the UHCE approach. In this logbook the care coordinator recorded the outcomes and involvement of the older person and health staff in the three stages (assessment, shared-decision and care-pathways) of the UHCE approach.

8 **Description of all materials or tools used delivery the intervention**

A short standardized assessment form was developed for all cities, which consisted of validated instruments. In addition, a uniform logbook was developed for all cities which was kept for each older person who received the UHCE approach. In this logbook the care coordinator recorded the outcomes and involvement of the older person and health staff in the three stages (assessment, shared-decision and care-pathways) of the UHCE approach.

9 **Description of fidelity of the delivery process compared the study protocol**

Initially, the UHCE project aimed to make use of or improve existing care available in the communities. However, in Pallini, Rijeka and Valencia, the availability of existing care was limited or the referral to existing care proved to be difficult. In these cases new care provisions were developed. In two cities; Pallini and Valencia, the age of the target population was lowered to 70 years or older due to difficulties encountered during the inclusion.

10 **Description of a process evaluation and its underlying theoretical basis**

A uniform logbook was developed for all cities which was kept for each older person who received the UHCE approach. In this logbook the care coordinator recorded the outcomes and involvement of the older person and health staff in the three stages (assessment, shared-decision and care-pathways) of the UHCE approach. The results of this logbook, along with the evaluation of other process indicators, were part of the evaluation of process components of the UHCE approach, following the Steckler and Linnan framework. This evaluation has previously been described in more detail.

11 **Description of internal facilitators and barriers potentially influencing the delivery of the intervention as revealed by the process evaluation**

The uptake of care in the Northwest European cities Manchester and Rotterdam was low. In these cities, qualitative analyses of logbooks revealed that many older persons reported that they did not enrol in a care-pathway because they were already involved in other care. Most positive effects of the UHCE approach were found in Rijeka, where all persons in the intervention group enrolled in a care-pathway. Possible explanations for the high uptake of care in Rijeka were a high morale to engage in activities among participants and regular monitoring of the care process by community nurses who had a personal relationship with the participants and acted as care coordinator in this study.

12 **Description of external conditions or factors occurring during the study which might have influenced the delivery of the intervention or mode of action (how it works)**

In all cities except for Pallini, GPs were the first point of contact and had a gatekeeper function towards existing care services. In Pallini, GPs were scarce and specialist care was directly accessible upon appointment.

13 **Description of costs or required resources for the interventions**

No additional monetary incentives were provided to health staff involved in existing care. In the settings where new care was developed, staff was hired on a voluntary bases or compensated. No monetary incentives were provided to participants. For some of the interventions participants could borrow materials needed for the intervention (e.g. tablets).

Supplementary Text S2: Details of measurement of measures

General outcome measures of lifestyle, health and quality of life

Healthy lifestyle was measured with one item on physical activity that assessed whether a person engaged in activities that require low or moderate energy, two items on smoking that assessed whether a persons smoked and the number of cigarettes/cigars or pipes per day, and three items of The Alcohol Use Disorders Identification Test (AUDIT-C)[1]. Healthy lifestyle was defined as engaging in activities that require low or moderate energy more than once per week, not smoking and no high-risk alcohol use. Frailty was measured with the 15-item Tilburg Frailty indicator (TFI)[2], that includes questions on physical, psychological and social components of frailty. Answer options of the items are scored one point each if the frailty component is present. Physical frailty was additionally measured with the SHARE-Frailty instrument which was developed and validated in a European population[3]. The SHARE-frailty instrument consists of 5 items approximating Fried's frailty definition; exhaustion, weight loss, slowness and physical activity and a hand-grip strength measurement. When the hand-grip strength measurement was missing, this item was imputed with a question from the TFI on hand-grip strength. Frailty was calculated via estimation of a discrete *factor model based on the five items[4].* Malnutrition, a component of physical frailty, was measured with the validated Short Nutritional Assessment Questionnaire 65+ (SNAQ-65+)[5]. The SNAQ-65+ instrument consists of 3 items on weight loss, appetite and functioning and a measurement of mid-upper arm circumference. Malnutrition was present when weight loss was present (person lost 6 kg or 13lbs or more during the last six months, or 3kg or 6½lbs or more during the last month) or mid-upper arm circumference was <25 cm. Level of independence was measured with the Groningen activity restriction scale (GARS)[6], which includes 18 items on independence of activities of daily living (ADL) and instrumental activities of daily living (IADL). Four answer options ranged from 'yes I can do this activity fully independently' to ' I can do this activity only with someone's help'. Answer options are scored on a 4-point scale; minimum score is 18 and maximum score is 72, with higher scores representing a lower level of independence. Severely limited function was measured with the one-item Global Activity Limitation Index (GALI)[7]. This item asks about the extent a person is limited in activities people usually. Answer options were not/moderately/severely limited and were categorized into severely limited and not limited/moderately limited. Health-related quality of life was measured with the 12-item short-form (SF-12v2), which consists of physical and mental component summary (PCS/MCS) scores[8]. Number of answer options differed per question. Mental well-being was measured with the full mental well-being scale of the SF-36[9]. Scores of the PCS, MCS and mental-wellbeing instruments range between 0-100; with higher scores representing a higher quality of life.

Specific outcome measures applicable to each care-pathway

Fall risk was measured by two items that assessed whether a person had fallen and the number of falls in the previous year, a single item that assessed whether or not the person was afraid of falling. Fear of falling was also measured by the 7-item Falls Efficacy Scale International (FES-I) short version[10]. This instruments measured whether a person is concerned while performing seven daily activities. Answer options were not at all/somewhat/ fairly/very concerned. Answer options are scored on a 4-point scale; minimum score is 7 and maximum score is 28, with higher scores representing a higher fear of falling. Appropriate medication use was measured with 10 items of the Medication risk questionnaire (MRQ-10)[11]; a validated tool, developed for use by older persons to

identify who is at increased risk of potentially experiencing a medication-related problem. Answer options of the items are scored one point each if the medication risk component is present. Loneliness was measured with the short 6-item version of the Jong Gierveld loneliness scale[12], that assesses the degree of what one wants and what one has in terms of interpersonal affection and intimacy. Answer options were yes/somewhat/no and were scored on a 3-point scale; minimum score is 6 and maximum score is 18; with higher scores representing a higher level of loneliness.

1.Bush, K., Kivlahan, D. R., McDonell, M. B., Fihn, S. D., & Bradley, K. A. (1998). The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking. Ambulatory Care Quality Improvement Project (ACQUIP). Alcohol Use Disorders Identification Test. Arch Intern Med, 158(16), 1789-1795.

2. Gobbens, R. J., van Assen, M. A., Luijkx, K. G., Wijnen-Sponselee, M. T., & Schols, J. M. (2010). The Tilburg Frailty Indicator: psychometric properties. J Am Med Dir Assoc, 11(5), 344-355. doi:10.1016/j.jamda.2009.11.003

3. Romero-Ortuno, R. (2013). The Frailty Instrument for primary care of the Survey of Health, Ageing and Retirement in Europe predicts mortality similarly to a frailty index based on comprehensive geriatric assessment. Geriatr Gerontol Int, 13(2), 497-504. doi:10.1111/j.1447-0594.2012.00948.x

4. Romero-Ortuno, R., Walsh, C. D., Lawlor, B. A., & Kenny, R. A. (2010). A frailty instrument for primary care: findings from the Survey of Health, Ageing and Retirement in Europe (SHARE). BMC Geriatr, 10, 57. doi:1471-2318-10-57 [pii]

5. Wijnhoven, H. A., Schilp, J., van Bokhorst-de van der Schueren, M. A., de Vet, H. C., Kruizenga, H. M., Deeg, D. J., . . . Visser, M. (2012). Development and validation of criteria for determining undernutrition in community-dwelling older men and women: The Short Nutritional Assessment Questionnaire 65+. Clin Nutr, 31(3), 351-358.

6. Suurmeijer, T. P., Doeglas, D. M., Moum, T., Briancon, S., Krol, B., Sanderman, R., . . . van den Heuvel, W. J. (1994). The Groningen Activity Restriction Scale for measuring disability: its utility in international comparisons. Am J Public Health, 84(8), 1270-1273.

7. Berger, N., Van Oyen, H., Cambois, E., Fouweather, T., Jagger, C., Nusselder, W., & Robine, J. M. (2015). Assessing the validity of the Global Activity Limitation Indicator in fourteen European countries. BMC Med Res Methodol, 15, 1. doi:10.1186/1471-2288-15-1

8. Haywood, K. L., Garratt, A. M., & Fitzpatrick, R. (2005). Quality of life in older people: a structured review of generic self-assessed health instruments. Qual Life Res, 14(7), 1651-1668. 10.1186/1471-2318-10-57

9. Ware, J. E., Jr., & Sherbourne, C. D. (1992). The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care, 30(6), 473-483.

10. Yardley, L., Beyer, N., Hauer, K., Kempen, G., Piot-Ziegler, C., & Todd, C. (2005). Development and initial validation of the Falls Efficacy Scale-International (FES-I). Age Ageing, 34(6), 614-619.

11. Barenholtz Levy, H. (2003). Self-administered medication-risk questionnaire in an elderly population. Ann Pharmacother, 37(7-8), 982-987.

12. De Jong Gierveld, J., & Van Tilburg, T. (2010). The De Jong Gierveld short scales for emotional and social loneliness: tested on data from 7 countries in the UN generations and gender surveys. Eur J Ageing, 7(2), 121-130. doi:10.1007/s10433-010-0144-6

Chapter 7

A coordinated preventive care approach for healthy ageing (UHCE) in five European cities: a mixed-methods study of process evaluation components

Carmen B. Franse, Xuxi Zhang, Amy van Grieken, Judith A.C. Rietjens, Tamara Alhambra-Borrás, Estrella Durá, Jorge Garcés-Ferrer, Rob van Staveren, Tasos Rentoumis, Athina Markaki, Lovorka Bilajac, Vanja V. Marchesi, Tomislav Rukavina, Arpana Verma, Greg Williams, Gary Clough, Elin Koppelaar, Rens Martijn, Francesco Mattace Raso, Antonius J.J. Voorham, Hein Raat

[Submitted]

ABSTRACT

Background

There is increasing interest for primary care interventions for older persons that offer coordinated preventive care and integrate health and social care services. However, there is a lack of knowledge on how such interventions are implemented and which older persons are reached in coordinated preventive care. The Urban Health Centres Europe (UHCE) approach was a coordinated preventive care approach that integrated health and social care services aimed at promoting healthy ageing among older persons in European cities.

Objectives

We aimed to examine how the UHCE approach was implemented, which persons were reached and what their experience was with the approach.

Design

Mixed-methods design to evaluate specific process components of the UHCE approach; context, reach, dose delivered and received, and satisfaction.

Settings

Community settings in five cities in the United Kingdom, Greece, Croatia, the Netherlands and Spain.

Participants

Community-dwelling older persons who received the UHCE approach (N=986) and a subset of professionals who were involved in the UHCE approach (N=23).

Methods

Quantitative and qualitative data from logbooks, a questionnaire and focus-groups were collected among older persons who received the UHCE approach. Qualitative data from focus-groups were also collected among care professionals who participated in the UHCE approach.

Results

The place of assessment, type of care-pathways and staff involved in the UHCE approach differed among the five participating cities. Limited function was associated with non-enrolment in two care-pathways ($P<0.01$). The mean rating of the UHCE approach was 8.3 (SD=1.9) out of 10. Feeling supported by a care professional was mentioned as a benefit for older persons. Mistrust towards unfamiliar care providers and lack of confidence to engage in care activities were mentioned as barriers towards engagement in care.

Conclusions

Implementation of coordinated preventive care interventions for older persons is strongly dependent on the context. Care activities that require transport or a higher level of activity might not reach older persons who are limited in their functioning and should be adapted for this group. It is furthermore important for care professionals to build a trusted relationship with their older clients and focus on psychosocial barriers that might affect their care decisions.

BACKGROUND

Europe has the highest proportion of persons over 65 years compared to any other continent[1]. Multi-morbidity; the co-occurrence of two or more diseases, increases with age and has become a large problem in Europe[2 3]. Older persons are the majority users of health and social care services[4-6]. This poses a challenge for healthcare systems. As the number of older persons is increasing, there will be relatively fewer beds available in inpatient care facilities, such as hospitals, nursing homes or care homes. In addition, most older persons prefer to live independently as much as possible, receive care at home and die at home[7 8]. Because of this, it is important to have a well-functioning primary care system that supports older persons in living independently for as long as possible. Primary care interventions for older persons that offer coordinated preventive care and integrate health and social care services could answer both older persons' and societies' needs[9 10]. Coordinated preventive care interventions for older persons often include a multidimensional assessment of health and multidisciplinary coordinated follow-up care[11-14]. Care coordination is typically done by a nurse or practice assistant to alleviate the workload for the general practitioner.

Coordinated preventive care interventions for older persons are considered to be complex to carry out, because they consist of multiple interconnecting parts and involve multiple care professionals[15]. However, studies often do not report how interventions are carried out, such as the specific context in which the intervention is implemented and whether the intervention is implemented as planned[16]. Therefore there is a lack of knowledge on how interventions are implemented and which older persons are reached in coordinated preventive care. Steckler and Linnan have developed a framework to study specific components of process evaluation for public health interventions[17 18]. In this framework, specific components which are evaluated include: the context in which the intervention is implemented, reach of the target population, dose of the intervention actually delivered to and received by participants, and satisfaction of main stakeholders with the intervention[17]. The Stecklar and Linnan framework is recommended for the development and reporting of complex interventions because it provides transparency about the delivery of the intervention[19]. Evaluation of process components may increase the understanding of the implementation of and persons reached by coordinated preventive care for older persons in diverse settings.

Objective

The Urban Health Centres Europe (UHCE) approach was a preventive coordinated care approach aimed at improving the healthy lifestyle, health and quality of life of older European persons[20]. The UHCE approach included a preventive multidimensional assessment of health risks and, if indicated, coordinated follow-up health and social care pathways. Results on the effects of the UHCE approach for older persons in five European cities are currently

in press[21]. The UHCE approach showed promising, but minor positive effects in tackling recurrent falls and frailty and promoting physical health-related quality of life and mental well-being compared to care as usual. In the current study, we aimed to evaluate process components of the UHCE approach by applying the framework developed by Steckler and Linnan. The following research questions will be answered:

1) In what context was the intervention template implemented?
2) Which population did the UHCE approach reach?
3) What dose of the intervention was actually delivered to and received by participants?
4) What was the satisfaction and experience of the main stakeholders involved in the UHCE approach?

METHODS

Intervention template

A general template for the UHCE approach intervention has been previously described[20,21]. The UHCE approach was specifically targeted at fall risk, appropriate medication use, loneliness and frailty. The development of the UHCE approach followed an intervention mapping approach[22]. An integral conceptual model of frailty was applied, which includes physical as well as social and psychological components and is geared towards a multidisciplinary approach[23]. The general template of the UHCE approach consisted of three stages. The first stage of the UHCE approach consisted of a health assessment of fall risk, polypharmacy, loneliness and frailty in order to identify whether he/she had an indication of a need for a follow-up care-pathway. A short standardized assessment form was developed for all cities, which consisted of validated instruments. For assessment of fall risk, a validated protocol developed by the Dutch safety research institute was included[24]. Assessment of polypharmacy followed the common definition of using of five or more different medicines[25], in addition difficulty in taking medications as prescribed was assessed[26]. Assessment of loneliness made use of the social subscale of the Tilburg Frailty Indicator[27] and if loneliness was indicated further assessment with the Jong-Gierveld loneliness scale was recommended[28]. For the assessment of frailty, the Tilburg Frailty indicator was included[27]. In each city, the assessment was piloted in at least five older persons. Misinterpretation of questions were identified and minor changes were made. The second stage of the UHCE approach consisted of shared-decision making. Shared-decision making was included in order to develop a care plan which was adapted to the preferences of the older person, which was thought to promote involvement in care-pathways. It was recommended to discuss results of the assessment between the older person, the person in charge of care coordination and the physician and to encourage the older person to involve an informal caregiver in the shared-

decision making process. The third stage of the UHCE approach consisted of referral to care-pathways. As a result of the shared decision-making process, a decision on an individualized care plan was made and each participant was referred to care-pathways according to their indication. In the UHCE template, evidence-based interventions for each care-pathway were recommended, which were identified in the literature search. The main care-pathways were: 1) fall prevention actions; recommended evidence-based interventions were home-based exercise programmes, group exercise programmes and multifactorial assessment and intervention programmes, 2) actions addressing polypharmacy (adherence and/or appropriate prescribing actions); recommended evidence-based interventions focused on self-monitoring programmes to improve adherence and/or multifaceted pharmaceutical care for appropriate prescribing, 3) actions addressing loneliness; recommended evidence-based interventions were social activities and/or support within a group format, and 4) frailty/medical action; recommended evidence-based interventions included group exercise programmes and multidisciplinary care. Additionally in this care-pathway, other medical care which did not fall under care-pathways 1-3 could be given when the healthcare provider deemed this necessary. The care coordinator was asked to monitor the progress of each individual care plan under the supervision of a physician. Follow-up visits could be scheduled if needed. The general template of the UHCE approach was then adapted to the national standards and context of each of the five participating cities. The study was registered in the ISRCTN registry under number ISRCTN52788952.

Design

For the purpose of the current study, we studied the intervention group. We applied a mix of quantitative and qualitative data collection methods based on the theoretical framework for public health interventions as developed by Steckler and Linnan to evaluate process components of the UHCE approach[17 18]. Specific process components which were evaluated included: the context in which the intervention was implemented, reach of the target population, dose of the intervention actually delivered and received by participants, and satisfaction and experience of main stakeholders with the intervention[17]. The study was conducted between May 2015 and June 2017.

Participants

Older persons

In each city, the initial target population of the UHCE approach consisted of persons living independently, aged 75 years or older, who were, according to their physician, able to participate in the study for at least 6 months. Persons were not eligible to participate if they were not able to comprehend the information provided in the local language or if they were not able to cognitively evaluate the risks and benefits of participation and were not expected to be able to make an informed decision regarding participation in the study, according to their physician. In two cities; Pallini and Valencia, the age of the target population was lowered to 70 years or older due to difficulties encountered during the recruitment period.

Professionals

In each city, health and social care professionals participated in the UHCE approach. Care decisions were made by a physician, together with the care coordinator, older person and sometimes an informal caregiver (e.g. partner or family member). Other professionals involved in the care-pathways were physiotherapists, occupational therapists, physical educators, psychologists, social workers, pharmacists and volunteers; depending on the context of the local setting.

Data collection

Data collection measures consisted of a mix of quantitative and qualitative methods. Table 1 presents an overview of process evaluation components for each study question and the way these were measured in the study.

Table 1: Components of the process evaluation, related research questions and method of measurement

Component	Research question	Measurement			
		Log books	**Focus groups**	**Questionnaire**	**Other***
Context	In what context was the intervention template implemented?				X
Reach	Which population did the UHCE approach reach?				
	- How many persons accepted to participate in the UHCE approach?				X
	- What were characteristics of persons who were lost to follow-up between baseline and follow-up?			X	
Dose delivered and received	What dose of the intervention was actually delivered to and received by participants?				
	- To what extent were three stages of the UHCE approach (assessment, shared-decision making, care-pathways) delivered to older persons?	X			
	- What were factors associated with non-enrollment in care-pathways?			X	
	- What were reasons for non-enrolment in care-pathways?	X			
Satisfaction and experience	What was the satisfaction and experience of the main stakeholders involved in the UHCE approach?				
	- Were older persons satisfied with the UHCE approach?			X	
	- What benefits, barriers and improvements did older persons and health professionals report?		X		

*Context was measured by structured forms; number of persons reached was recorded in project registries. Abbreviations; UHCE=Urban Health Centres Europe

Logbooks

A uniform logbook was developed for all cities. This logbook was kept for each older person that received the UHCE approach (N=986). This logbook included delivery and involvement of the older person in the three different stages of the UHCE approach: 1. Whether or not a health assessment took place and whether the participant had an indication for any care-pathways, 2. Whether or not shared decision making took place, and 3. Whether or not the participant followed any care-pathways and if not, reason for not following any care-pathways. At least after 6 months, the care coordinator recorded (if needed telephone contact with the participant or responsible health care provider was sought) whether these different stages of the UHCE approach were delivered. The paper participant logbooks were entered into an electronic data-entry form by research staff. Electronic data were checked for missing or incorrect data. If needed, responsible staff were contacted for clarification.

Questionnaire

A self-report questionnaire was administered to all older persons at baseline and at follow-up after 12 months (N=986). The questionnaire was developed in English and translated into local languages if no validated translation was already available in the literature. Items were translated into the local languages and backward into English. Backward English translations were discussed among the study team and translation was adapted when needed. In each city, the questionnaire was piloted in at least five older persons. Misinterpretation of questions were identified and minor changes were made. Age (in years), sex, living situation (alone/not alone), education level, function and mental health were assessed in the baseline questionnaire. Education level was measured by asking the highest level of education completed and categorised according to the 2011 International Standard Classification of Education (ISCED) into 'lower' (ISCED 0-2) and 'higher' (ISCED 3-8)[29]. Function was measured with the one-item Global Activity Limitation Index (GALI) and categorised into 'limited' (moderately or severely limited) and 'not limited'[30 31]. Poor mental health was measured with the full 5-item mental well-being scale of the SF-36 (MHI-5)[32]. The MHI-5 measures nervousness, downheartedness and feeling sad, jollity, calmness and happiness using a Likert scale (range 1–6). Mental health was categorized into 'poor mental health' (score≤52) and 'good mental health' (score>52)[33]. Satisfaction with the UHCE approach was measured in the follow-up questionnaire. Four items measured whether persons agreed on being satisfied with each of the three UHCE stages. Answers were categorized into 'agree/strongly agree' and 'neither agree nor disagree/disagree/strongly disagree'. A final question rated person's satisfaction with the full UHCE approach on a scale from 1 to 10.

Focus groups

Focus groups were held around the time of the follow-up assessment (12 months after baseline). Semi-structured focus group guides were developed which included probe questions on experiences with the three different stages of the UHCE approach; the benefits

and barriers encountered and improvements that could be made. In each city we organised one focus group with four to six older persons and informal caregivers; except in Manchester, where we organized two focus groups with four older persons and one informal caregiver each. Older persons and caregivers involved in the focus groups were selected when they were physically and mentally able to participate in the focus group and enrolled (or when the person they cared for enrolled) in at least one care-pathway. In each city we organized one focus group with four to six social and health care professionals (general practitioners, nurses, physical therapists, occupational therapists, pharmacists, social workers) involved in the UHCE approach. In Manchester, an in-depth interview was held with two professionals involved in UHCE. In total: 26 older persons, four informal caregivers and 23 professionals were interviewed in the focus groups and in-depth interview. The focus group discussions and in-depth interview were recorded, transcribed into the local language and translated into English where appropriate.

Data analysis

Quantitative data on dose delivered in three stages of the UHCE approach as reported in the logbooks and satisfaction with the UHCE approach as reported in the follow-up questionnaires were summarised using descriptive statistics (frequencies, means and percentages). We analysed factors associated with non-enrolment among persons who enrolled in a specific care-pathway (falls, polypharmacy, loneliness and frailty/medical) and persons who did not enrol in that care-pathway but had an indication to receive that care-pathway. For this, a multilevel modelling approach was used, taking into account clustering effects at city-level. Four multilevel logistic regression models were built (one for each care-pathway) to analyse the association of factors (age, sex, living situation, education level, function and mental health) with non-enrolment. We corrected the effect estimates of multilevel analyses for all factors.

Thematic analysis of focus-group data and reasons why persons did not enrol in a care-pathway as reported in the logbooks was done using a pre-defined coding framework which was developed through discussion and consensus among the research team[34]. Focus group transcripts and reasons why persons did not enrol in a care-pathway as reported in the logbooks were read multiple times and coded into overarching themes by two independent researchers (CF and XZ). If discrepancy in coding between the two researchers existed, the codes were discussed among the researchers until consensus was reached. We considered a P-value of 0.05 or lower to be statistically significant. All quantitative analyses were performed using SPSS version 23.0 (IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp).

RESULTS

Context

The place of assessment, type of care-pathways, staff involved and context of each of the five participating cities and are described in more detail in Table 2. In all cities, except for Pallini, general practices were involved in the UHCE approach. In Pallini, the UHCE approach was provided by a health team from the municipal health centre newly employed for this study. The health assessment took place at the person's home in all cities except for Pallini, where the assessment took place at a community centre. Care coordination was performed by nurses in three settings and by trained assistants under the supervision of a general practitioner in two settings. In Rotterdam and Manchester, the UHCE approach made use of existing care interventions. In Rijeka and Valencia, some new care provisions were developed and in Pallini all care provisions were newly developed. Falls care-pathways varied among settings, including group-based exercise programs, home adjustments and physiotherapy. In Rijeka and Valencia persons who had a frailty indication were also offered to enrol in the falls care-pathway. In Rijeka and Pallini, the polypharmacy care-pathway included a self-managed medication adherence application. In the other settings, persons entering this care-pathway received a medication review by a pharmacist. The loneliness care-pathway included group-based activities and support groups. No additional monetary incentives were provided to health staff involved in existing care. In the settings where new care was developed, staff was hired on a voluntary bases or compensated. No monetary incentives were provided to participants. For some of the interventions participants could borrow materials needed for the intervention.

Table 2. Context of the cities involved in UHCE

	Manchester, UK	Pallini, GR	Rijeka, HR	Rotterdam, NL	Valencia, ES
Location UHCE approach	General practices in Tameside and Glossop districts.	Municipality/senior centres Pallini	General practices in Western Rijeka.	Primary health center in Ommoord neighbourhood.	Primary health center in Nou Moles neighbourhood
Assessment	At home by trained assistant	At senior/health centre by health professional	At home by community nurse	At home by trained assistant	At home by trained assistant
Care coordinator	Trained assistant supervised by GP	Health professional or social worker	Community nurse	Geriatric nurse practitioner	Trained assistant supervised by GP
Type of care in care-pathways	Multiple per pathway; e.g. home adjustment by OT, walking group by volunteers (falls); medication review by GP (polypharmacy); buddying services by volunteers (loneliness); further care by GP (frailty).	Group based endurance and balance training by PE (falls); self-managed medication adherence App supported by physician (polypharmacy); support groups by psychologist (loneliness); further care by physician (frailty).	Group based balance and strength training by PT (falls and frailty); self-managed medication adherence App (polypharmacy); social group activities (loneliness).	Multiple per pathway; e.g. physiotherapy by PT (falls); medication review by pharmacist (polypharmacy); social activities (loneliness); further care by GP (frailty).	Group based balance and strength training by PT (falls and frailty), medication review according to national protocol by GP (polypharmacy), social support group led by social worker (loneliness).
Care existing or newly developed	All existing; offered by local charity organisation and according to practice GP	All newly developed	Falls, frailty and polypharmacy newly developed. Loneliness existing services	All existing, medical care according to practice GP and social care by local organizations	Falls, frailty and loneliness newly developed. Polypharmacy existing protocol

Abbreviations: ES=Spain; GP=general practitioner; GR=Greece; HR=Croatia; NL=The Netherlands; OT=occupational therapist; PE=physical educator; PT=physical therapist; UK=United Kingdom.

Reach, dose delivered and received

Overall, 2,825 persons were invited to participate in the UHCE approach and 1,215 persons (43.0%) accepted the invitation and completed the baseline health assessment (Table 3). Of these persons, 986 persons (81.2%) completed the follow-up questionnaire at 12-month follow-up. A comparison of persons included at follow-up (N=986) with persons who dropped out of the study after baseline (N=229) did not indicate significant differences in terms of sex (P=0.164), living situation (P=0.519), function (P=0.593) and mental health (P=0.463). However, persons who dropped out of the study after baseline were older (P<0.001) and lower educated (P=0.001).

Of the 986 persons who received the UHCE approach, according to the UHCE template; 502 persons (50.9%) had an indication to follow the falls care-pathway, 495 (50.2%) had an indication to follow the polypharmacy care-pathway, 280 (28.4%) had an indication to follow the loneliness care-pathway and 532 (54.0%) had an indication to follow the frailty care-pathway (Table 3). Indications for care-pathways, as reported in logbooks differed from those proposed in the UHCE template. More persons had an indication for the falls and loneliness care-pathways and less persons for the polypharmacy and frailty care-pathways. Shared-decision making was done with 969 (98.3%) of participants. In total, 520 persons (53.6%) enrolled in any care-pathway during the UHCE study. Enrolment in any care-pathway varied between 99.5% in Rijeka to 14.6% in Rotterdam. Most persons; 278 (28.6%) enrolled in the falls care-pathway, followed by 223 persons (23.0%) enrolled in the loneliness care-pathway, 130 persons (13.7%) enrolled in the polypharmacy care-pathway and 94 persons (9.9%) enrolled in the frailty/medical care-pathway.

Factors associated with non-enrolment in care-pathways among older persons involved in the UHCE approach are presented in Table 4. Limited function was positively associated with non-enrolment in the falls and loneliness care-pathways (p<0.01). Female gender was positively associated with non-enrolment in the polypharmacy care-pathway, but negatively associated with non-enrollment in the loneliness care-pathway (p<0.05).

Table 3. Reach and dose delivered for each stage of the UHCE approach

Stage	Total N (%)	Manchester N (%)	Pallini N (%)	Rijeka N (%)	Rotterdam N (%)	Valencia N (%)
Invited for UHCE approach	2825	1166	500	277	512	370
Completed baseline health assessment	1215(40.3)	274(23.5)	190(38.0)	249(89.9)	243(47.5)	259(70.0)
Completed follow-up questionnaire	986(81.2)	212(77.4)	154(81.1)	221(88.8)	192(79.0)	207(79.9)
Indication for care-pathway in UHCE template[a]						
Falls indication	502(50.9)	114(53.8)	69(44.8)	129(58.4)	85(44.3)	105(50.7)
Polypharmacy indication	495(50.2)	132(62.3)	83(53.9)	100(45.2)	104(54.2)	76(36.7)
Loneliness indication	280(28.6)	26(12.4)	62(40.5)	102(46.6)	46(24.1)	44(21.3)
Frailty/medical indication	532(54.0)	100(47.2)	105(68.2)	140(63.6)	81(42.2)	106(51.2)
Indication for care-pathway reported in logbooks[a]						
Falls indication	549(56.5)	114(53.8)	74(48.1)	168(76.4)	75(42.1)	118(57.0)
Polypharmacy indication	322(33.9)	9(0.04)	49(31.8)	116(52.7)	88(49.4)	60(32.1)
Loneliness indication	464(47.8)	89(42.0)	109(70.8)	153(69.5)	46(25.8)	58(31.0)
Frailty/medical indication	314(33.0)	101(47.6)	71(46.1)	165(74.7)	83(46.6)	67(32.4)
Shared decision making[a]	969(98.3)	212(100)	154(100)	220(99.5)	176(91.7)	207(100)
Enrollment any care-pathway[a]	520(52.7)	47(22.2)	112(72.7)	220(99.5)	28(14.6)	113(54.6)
Enrollment Falls care-pathway	278(28.6)	39(18.4)	24(15.6)	143(65.0)	0[b]	72(34.8)
Enrollment Polypharmacy care-pathway	130(13.7)	2(0.9)	46(29.9)	22(10.0)	5(2.8)[b]	55(29.4)
Enrollment Loneliness care-pathway	223(23.0)	4(1.9)	55(35.7)	133(60.5)	1(0.6)[b]	30(14.5)
Enrollment Frailty/medical care-pathway	94(9.9)	16(7.5)	53(34.4)	NA	25(14.0)	NA

Abbreviations: NA=not applicable; UHCE=Urban Health Centres Europe. Missing items: Indication for care-pathway as in UHCE template; Frailty =1, Loneliness =7; Indication for care-pathway as reported in logbooks; Frailty=35, Falls=15, Polypharmacy=35, Loneliness=15; Enrollment in any care-pathway=4; Frailty=24, Falls=4, Polypharmacy=24, Loneliness=4. a) The percentage reported is of the participants who completed the follow-up questionnaire and with complete information for the item; b) These are persons finishing the care-pathway; respectively 23, 90 and 7 persons followed the falls, polypharmacy and loneliness care-pathways without formally finishing it.

Table 4. Factors associated with non-enrolment among persons enrolled in the care-pathway and persons not enrolled in the care-pathway who had an indication for the care-pathway.

	Falls care-pathway			Polypharmacy care-pathway			Loneliness care-pathway			Frailty/medical care-pathway		
	Enrolled N=278	Not Enrolled N=283	OR (95% CI)*	Enrolled N=130	Not Enrolled N=355	OR (95% CI)*	Enrolled N=223	Not Enrolled N=167	OR (95% CI)*	Enrolled N=94	Not Enrolled N=857	OR (95% CI)*
Age ≥80 years	132 (47.5)	305 (44.0)	1.38 (0.87, 2.19)	51 (39.2)	381 (46.4)	0.59 (0.32, 1.10)	101 (45.3)	336(44.9)	0.97 (0.57, 1.65)	41 (43.6)	391 (45.6)	0.96 (0.52, 1.76)
Female	195 (70.1)	181 (64.0)	0.77 (0.48, 1.23)	66 (50.8)	207 (58.3)	**2.30 (1.25, 4.24)**[b]	159 (71.3)	109 (65.3)	**0.50 (0.28, 0.89)**[a]	59 (62.8)	514 (60.0)	1.00 (0.56, 1.80)
Low education	152 (54.7)	153 (54.3)	0.68 (0.42, 1.10)	89 (68.5)	157 (44.4)	0.64 (0.35, 1.17)	110 (49.3)	98 (58.7)	1.73 (0.98, 3.03)	55 (59.1)	425 (49.7)	0.83 (0.47, 1.44)
Living alone	105 (37.8)	136 (48.1)	0.93 (0.58, 1.49)	38 (29.2)	153 (43.1)	0.71 (0.37, 1.36)	84 (37.7)	87 (52.1)	1.17 (0.68, 2.02)	34 (36.2)	331 (38.6)	1.78 (0.98, 3.23)
Limited function	164 (59.2)	199 (70.3)	**1.92 (1.22, 3.03)**[b]	85 (65.4)	236 (66.9)	0.75 (0.41, 1.37)	124 (55.9)	125 (75.3)	**2.10 (1.23, 3.43)**[b]	68 (73.1)	435 (50.9)	0.84 (0.46, 1.53)
Poor mental health	47 (17.0)	40 (14.2)	1.42 (0.80, 2.53)	24 (18.8)	42 (11.8)	1.56 (0.76, 3.21)	53 (23.9)	38 (22.9)	1.05 (0.60, 1.86)	14 (15.1)	94 (11.0)	0.99 (0.45, 2.18)

Missing items: falls care-pathway; low education=1, limited foundation=1, poor mental health=2; polypharmacy care-pathway; low education=1, limited foundation=2, poor mental health=2; loneliness care-pathway; limited foundation=2, poor mental health=2; frailty/medical care-pathway; low education=3, limited foundation=3, poor mental health=4. *Values are derived from random-intercept multilevel logistic regression models adjusted for clustering by city and adjusted for age, gender, education, living situation, function and mental health. a=P-value<0.05; b=P-value<0.01.

The reasons older persons reported for why they did not enroll in care-pathways are presented in table 5. Of the 466 persons who were non-enrolled, 326 had an indication for a care-pathway according to the logbooks. Of those, 173 persons reported a reason for non-enrolment. Most of these persons (28.3%) reported that they wanted to deal with health problem themselves. Other reported reasons were lack of willingness (27.2%), already being involved in other care or exercise (22.0%) and health problems preventing participation (11.6%).

Table 5. Reasons participants reported why they did not enroll in care-pathways (N=173)

Reason reported*	N (%)
Wants to deal with it themselves	49 (28.3)
Does not want	47 (27.2)
Involved other care or exercise	38 (22.0)
Health problems prevent participation	20 (11.6)
Interested but not yet applied	15 (8.7)
Feels too healthy	9 (5.2)
Too far/transportation difficulties	9 (5.2)
Too busy to participate	6 (3.5)
Moved	2 (1.2)
Care for someone, too busy	2 (1.2)

*Multiple reasons could be reported per person

Satisfaction and experience UHCE approach

Satisfaction with the UHCE approach among older persons is reported in Table S1. Persons were generally satisfied with the UHCE approach. Overall, 82.1% of persons in all cities felt they had benefitted from the health assessment and 85.4% of persons felt it was worth the time and effort. The mean rating of the UHCE approach was 8.3 (SD=1.9) out of 10, ranging from 6.5 (SD=2.4) in Pallini to 9.3 (SD=1.2) in Manchester.

In the focus groups, several benefits of the UHCE approach for older persons were mentioned by both older persons and professionals. They mentioned that older persons valued the feeling that someone looked out for them; either the care coordinator or care professionals in the care-pathways. Another benefit which was mentioned by both older persons and professionals was that the group-based care-pathways of UHCE had given older persons involved in these activities the opportunity to meet other people. An older woman in Valencia mentioned that the social support group had helped her to open up to people. Older persons and professionals from several cities also mentioned that results from the assessment and contact with care professionals had motivated older persons to take action

regarding their health. Some benefits for care professionals were also mentioned in focus groups with care professionals. Using a structured approach in preventively recording older person's health was valued. Care professionals in Rotterdam mentioned that this aided them in future care decisions, because they were able to look back in the records.

Some barriers and recommendations were mentioned in focus groups by both older persons and care professionals. One of the main barriers towards engagement in care that was mentioned in all cities was mistrust among older persons towards unfamiliar care professionals and activities. Several care professionals stressed the importance of building a trusted relationship with their clients. A geriatric nurse in Rotterdam mentioned the importance of long-term investing in the relationship and repeating of health promotion messages. Feeling embarrassed or lacking confidence about engaging in activities was also mentioned as a barrier to engage in care by several older persons. An older woman in Manchester mentioned that after she fell down, she lacked the confidence to go out alone. An older man in Pallini mentioned he felt uncomfortable about sharing his feelings in a group. Another barrier towards participation in activities mentioned in several cities were health constraints. A recommendation that was made by care professionals in Rijeka, was to further adapt preventive care activities to needs of specific groups of older persons such as persons with chronic illnesses. In cities where activities were not embedded in existing care, both older persons and care professionals expressed the desire to continue activities beyond the project. In Rijeka and Rotterdam, care professionals reported unfamiliarity in collaborating with social care professionals. Care professionals in Rijeka suggested that meetings with health and social care professionals could be organized in order to improve collaboration. Time constraints were also mentioned as a barrier by care professionals in several cities.

DISCUSSION

In this study, we examined how a coordinated preventive social and health care approach aimed at healthy ageing was implemented, which persons were reached and their experience with the approach. We found that the context of implementation varied between the European settings. Limited function was associated with non-enrolment for falls and loneliness pathways. Feeling supported by a care professional was mentioned as a benefit for older persons. Mistrust towards unfamiliar care providers and lack of confidence to engage in certain care activities were mentioned as barriers.

The implementation of the UHCE template was strongly dependent on availability of staff and services in the local communities of the five European cities. Although most cities worked with GP practices, this was not possible in Pallini because GP services were limited.

Greece has one of the lowest numbers of GPs with 1 per 2500 inhabitants compared to The Netherlands with 1 per 650 inhabitants[35]. The extent of integration of the UHCE approach within the existing care system also differed among cities. In some cities, the availability of existing care was limited or the referral to existing care proved to be difficult. This could have impacted on the sustainability of the UHCE approach, in fact, participants mentioned they wished activities would continue beyond the project. Typical models for coordinated preventive care for older persons [36-39], which work with GPs and include various social and health services might be difficult to implement in certain European settings. Differences in the implementation of the UHCE approach was also reflected by differences in health assessment indications between the original template and used by some cities. These cities reported sometimes using additional instruments or basing decisions on further clinical judgement. Further cross-cultural adaptation and validation of health assessment instruments could improve medical decision-making, such as has been done for the Tilburg Frailty Indicator in some countries[40 41].

In a previous study we found minor effects of the UHCE approach on the lifestyle, health and quality of life of older persons and hypothesized that this was due to only around half of the persons in the intervention group enrolling in care-pathways[21]. Results from the current study imply that persons in poor health might have enrolled less often. Interventions in the falls and loneliness care-pathways required persons to move to the training location and included active activities such as balance and strength training or social group activities. Persons who were limited in function might have not been able to participate in these activities. In most cities, care in the frailty and polypharmacy care-pathways consisted of further assessment or referral to other care services. So these pathways required a less active involvement of older persons. Future interventions should develop strategies to reach older persons with limited functioning. Further adapting interventions to needs of groups with specific health problems were recommended by care professionals in this study. This is supported by findings from a large meta-analysis of complex care interventions which found no benefits of any specific type of intervention and recommended tailoring of interventions to client needs[42].

Older persons were generally satisfied with the UHCE approach. A benefit for older persons was feeling that a care professional looked out for them. Feeling supported by and experiencing a better relationship with the care provider has also been reported in other coordinated care interventions [43-45]. Trust appears to be the foundation of the relationship between care provider and older person and impacts on the acceptance of offered care[46-48]. Also in our study, mistrust among older persons towards unfamiliar services and care providers was the main barrier towards participation in care. Psychosocial reasons were also a barrier towards care uptake in our study. Some older persons did not want to engage in activities that could put them in awkward social situations. Others did not feel confident

enough to travel to activity locations because they were afraid of falling. It is therefore important for care professionals to focus on these psychosocial factors that influence care decisions. Even more so, because older persons themselves appear to prefer that care professionals focus on their psychosocial context[48].

Strengths and limitations

The main strength of our study is that we did an extensive evaluation of process components based on a theoretical framework proposed by Stecklar and Linnan[17]. By combining quantitative and qualitative methods we were able to triangulate some important study findings. This study also has some limitations. First, logbooks were completed by staff involved in the UHCE approach. This might have caused a bias and positive reporting of the execution of logbook components. For example, cities reported that shared-decision making was done in almost 100% of cases. However, it was unclear how and to what extent the older person was involved in this process. Perhaps the definition of shared-decision making has been interpreted differently by cities. Secondly, older persons included in the focus groups might have been those that were most positive about the UHCE approach as these persons were selected by care professionals involved in the study. Third, there were many missings for the questions on satisfaction of the UHCE approach. Persons who did not reply to some of these questions could have thought these questions were not applicable to them or were the persons who were less involved in the UHCE approach. The responses could have therefore been biased towards the more active participants who might have been more positive about the UHCE approach. Last, we did not include a representative number of informal care-givers in the focus groups. Having the perspective of this group of stakeholders would have strengthened our findings.

Conclusions

Implementation of coordinated preventive care interventions for older persons is strongly dependent on the context. Care activities that require transport or a higher level of activity might not reach older persons who are limited in their functioning and should be adapted for this group of older persons. Mistrust towards unfamiliar care providers and lack of confidence to engage in certain care activities are main barriers towards engagement in care among older persons. It is therefore important for care professionals to build a trusted relationship with their older clients and focus on psychosocial barriers that might affect their care decisions.

REFERENCES

1. United Nations Department of Economic and Social affairs. World Population Prospects: United Nations; 2017 [Available from: https://esa.un.org/unpd/wpp/dataquery/.
2. Onder G, Liperoti R, Soldato M, et al. Case management and risk of nursing home admission for older adults in home care: results of the AgeD in HOme Care Study. *J Am Geriatr Soc* 2007;55(3):439-44. doi: JGS1079 [pii]10.1111/j.1532-5415.2007.01079.x [published Online First: 2007/03/08]
3. Navickas R, Petric VK, Feigl AB, et al. Multimorbidity: What do we know? What should we do? *J Comorb* 2016;6(1):4-11. doi: 10.15256/joc.2016.6.72
4. Andrew MK, Mitnitski A, Kirkland SA, et al. The impact of social vulnerability on the survival of the fittest older adults. *Age Ageing* 2012;41(2):161-65.
5. Fratiglioni L, Wang HX, Ericsson K, et al. Influence of social network on occurrence of dementia: a community-based longitudinal study. *Lancet* 2000;355(9212):1315-9. doi: 10.1016/S0140-6736(00)02113-9
6. Mendes de Leon CF, Glass TA, Berkman LF. Social engagement and disability in a community population of older adults: the New Haven EPESE. *Am J Epidemiol* 2003;157(7):633-42.
7. Gomes B, Calanzani N, Gysels M, et al. Heterogeneity and changes in preferences for dying at home: a systematic review. *BMC Palliat Care* 2013;12:7. doi: 10.1186/1472-684X-12-7
8. Gomes B, Higginson IJ, Calanzani N, et al. Preferences for place of death if faced with advanced cancer: a population survey in England, Flanders, Germany, Italy, the Netherlands, Portugal and Spain. *Ann Oncol* 2012;23(8):2006-15. doi: 10.1093/annonc/mdr602
9. Nolte E, Knai C, McKee M, et al. Managing chronic conditions : experience in eight countries. Copenhagen: World Health Organization on behalf of the European Observatory on Health Systems and Policies 2009.
10. Kringos DS, Boerma WGW, Hutchinson A, et al. Building primary care in a changing Europe2015.
11. Frich LM. Nursing interventions for patients with chronic conditions. *J Adv Nurs* 2003;44(2):137-53. doi: 2779 [pii] [published Online First: 2003/10/03]
12. Markle-Reid M, Browne G, Weir R, et al. The effectiveness and efficiency of home-based nursing health promotion for older people: a review of the literature. *Med Care Res Rev* 2006;63(5):531-69. doi: 63/5/531 [pii]10.1177/1077558706290941 [published Online First: 2006/09/07]
13. Markle-Reid M, Browne G, Gafni A. Nurse-led health promotion interventions improve quality of life in frail older home care clients: Lessons learned from three randomized trials in Ontario, Canada. *J Eval Clin Pract* 2013;19(1):118-31.
14. Liebel DV, Friedman B, Watson NM, et al. Review of nurse home visiting interventions for community-dwelling older persons with existing disability. *Med Care Res Rev* 2009;66(2):119-46. doi: 1077558708328815 [pii]10.1177/1077558708328815 [published Online First: 2008/12/31]
15. Campbell M, Fitzpatrick R, Haines A, et al. Framework for design and evaluation of complex interventions to improve health. *BMJ* 2000;321(7262):694-6. [published Online First: 2000/09/15]

16. Smit LC, Schuurmans MJ, Blom JW, et al. Unravelling complex primary-care programs to maintain independent living in older people: a systematic overview. *J Clin Epidemiol* 2017 doi: 10.1016/j.jclinepi.2017.12.013 [published Online First: 2018/01/01]
17. Steckler A., Linnan L. Process evaluation for public health interventions and research. San Francisco, Calif.: Jossey-Bass 2002.
18. Saunders RP, Evans MH, Joshi P. Developing a process-evaluation plan for assessing health promotion program implementation: a how-to guide. *Health Promot Pract* 2005;6(2):134-47. doi: 6/2/134 [pii]10.1177/1524839904273387 [published Online First: 2005/04/28]
19. Mohler R, Kopke S, Meyer G. Criteria for Reporting the Development and Evaluation of Complex Interventions in healthcare: revised guideline (CReDECI 2). *Trials* 2015;16:204. doi: 10.1186/s13063-015-0709-y
20. Franse CB, Voorham AJJ, van Staveren R, et al. Evaluation design of Urban Health Centres Europe (UHCE): preventive integrated health and social care for community-dwelling older persons in five European cities. *BMC Geriatr* 2017;17(1):209. doi: 10.1186/s12877-017-0606-1
21. Franse CB, Van Grieken A, Alhambra-Borras T, et al. The effectiveness of a coordinated preventive care approach for healthy ageing (UHCE) among older persons in five European cities: a pre-post controlled trial. *Int J Nurs Stud* 2018;In press, Accepted Manuscript doi: https://doi.org/10.1016/j.ijnurstu.2018.09.006
22. Bartholomew LK, Parcel GS, Kok G. Intervention mapping: a process for developing theory- and evidence-based health education programs. *Health Educ Behav* 1998;25(5):545-63. [published Online First: 1998/10/13]
23. Gobbens RJ, Luijkx KG, Wijnen-Sponselee MT, et al. Towards an integral conceptual model of frailty. *J Nutr Health Aging* 2010;14(3):175-81.
24. Veiligheid.nl. Fall risk test Veiligheid.nl; [Available from: http://www.veiligheid.nl/voorlichtingsmateriaal/valanalyse-inventarisatie-valrisico-65-door-de-eerstelijnszorg accessed 7 july 2014.
25. Maher RL, Hanlon J, Hajjar ER. Clinical consequences of polypharmacy in elderly. *Expert Opin Drug Saf* 2014;13(1):57-65. doi: 10.1517/14740338.2013.827660
26. Barenholtz Levy H. Self-administered medication-risk questionnaire in an elderly population. *Annals of Pharmacotherapy* 2003;37(7-8):982-7.
27. Gobbens RJ, van Assen MA, Luijkx KG, et al. The Tilburg Frailty Indicator: psychometric properties. *J Am Med Dir Assoc* 2010;11(5):344-55. doi: 10.1016/j.jamda.2009.11.003
28. De Jong Gierveld J, Van Tilburg T. The De Jong Gierveld short scales for emotional and social loneliness: tested on data from 7 countries in the UN generations and gender surveys. *Eur J Ageing* 2010;7(2):121-30. doi: 10.1007/s10433-010-0144-6
29. Organisation for Economic Co-operation and Development. Classifying educational programmes : manual for ISCED-97 implementation in OECD countries. Paris: Organisation for Economic Co-operation and Development 1999.
30. van Oyen H, Van der Heyden J, Perenboom R, et al. Monitoring population disability: evaluation of a new Global Activity Limitation Indicator (GALI). *Soz Praventivmed* 2006;51(3):153-61.

31. Berger N, Van Oyen H, Cambois E, et al. Assessing the validity of the Global Activity Limitation Indicator in fourteen European countries. *BMC Med Res Methodol* 2015;15:1. doi: 10.1186/1471-2288-15-1
32. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;30(6):473-83.
33. Berwick DM, Murphy JM, Goldman PA, et al. Performance of a five-item mental health screening test. *Med Care* 1991;29(2):169-76.
34. Boyatzis RE. Transforming qualitative information : thematic analysis and code development. Thousand Oaks [u.a.]: Sage 2009.
35. Eurostat. Healthcare personnel statistics - physicians: European Commission; 2017 [Available from: http://ec.europa.eu/eurostat/statistics-explained/index.php/Healthcare_personnel_statistics_-_physicians#Further_Eurostat_information accessed 17/11/2017 2017.
36. Veras RP, Caldas CP, Motta LB, et al. Integration and continuity of Care in health care network models for frail older adults. *Rev Saude Publica* 2014;48(2):357-65.
37. Waterson P, Eason K, Tutt D, et al. Using HIT to deliver integrated care for the frail elderly in the UK: current barriers and future challenges. *Work* 2012;41 Suppl 1:4490-3. doi: 10.3233/WOR-2012-0750-4490
38. Fabbricotti IN, Janse B, Looman WM, et al. Integrated care for frail elderly compared to usual care: a study protocol of a quasi-experiment on the effects on the frail elderly, their caregivers, health professionals and health care costs. *BMC Geriatr* 2013;13:31. doi: 1471-2318-13-31 [pii]10.1186/1471-2318-13-31 [published Online First: 2013/04/17]
39. Ruikes FG, Meys AR, van de Wetering G, et al. The CareWell-primary care program: design of a cluster controlled trial and process evaluation of a complex intervention targeting community-dwelling frail elderly. *BMC Fam Pract* 2012;13:115. doi: 1471-2296-13-115 [pii] 10.1186/1471-2296-13-115 [published Online First: 2012/12/12]
40. Coelho T, Santos R, Paul C, et al. Portuguese version of the Tilburg Frailty Indicator: Transcultural adaptation and psychometric validation. *Geriatr Gerontol Int* 2015;15(8):951-60. doi: 10.1111/ggi.12373
41. Uchmanowicz I, Jankowska-Polanska B, Loboz-Rudnicka M, et al. Cross-cultural adaptation and reliability testing of the Tilburg Frailty Indicator for optimizing care of Polish patients with frailty syndrome. *Clin Interv Aging* 2014;9:997-1001. doi: 10.2147/CIA.S64853cia-9-997 [pii] [published Online First: 2014/07/17]
42. Beswick AD, Rees K, Dieppe P, et al. Complex interventions to improve physical function and maintain independent living in elderly people: a systematic review and meta-analysis. *Lancet* 2008;371(9614):725-35. doi: S0140-6736(08)60342-6 [pii]10.1016/S0140-6736(08)60342-6 [published Online First: 2008/03/04]
43. Poot AJ, Caljouw MA, Waard CS, et al. Satisfaction in Older Persons and General Practitioners during the Implementation of Integrated Care. *PLoS One* 2016;11(10):e0164536. doi: 10.1371/journal.pone.0164536

44. Baxter P, Markle-Reid M. An interprofessional team approach to fall prevention for older home care clients 'at risk' of falling: health care providers share their experiences. *Int J Integr Care* 2009;9:e15.
45. Metzelthin SF, Daniels R, van Rossum E, et al. A nurse-led interdisciplinary primary care approach to prevent disability among community-dwelling frail older people: a large-scale process evaluation. *Int J Nurs Stud* 2013;50(9):1184-96. doi: S0020-7489(12)00458-0 [pii]10.1016/j.ijnurstu.2012.12.016 [published Online First: 2013/02/07]
46. Muntinga ME, van Leeuwen KM, Jansen APD, et al. The Importance of Trust in Successful Home Visit Programs for Older People. *Glob Qual Nurs Res* 2016;3:2333393616681935. doi: 10.1177/2333393616681935
47. Bindels J, Cox K, Widdershoven G, et al. Care for community-dwelling frail older people: a practice nurse perspective. *J Clin Nurs* 2014;23(15-16):2313-22. doi: 10.1111/jocn.12513
48. van Kempen JA, Robben SH, Zuidema SU, et al. Home visits for frail older people: a qualitative study on the needs and preferences of frail older people and their informal caregivers. *Br J Gen Pract* 2012;62(601):e554-60. doi: 10.3399/bjgp12X653606

SUPPLEMENTAL MATERIAL

Table S1. Satisfaction among older persons with the UHCE approach

Satisfaction statements	Total	Manchester	Pallini	Rijeka	Rotterdam	Valencia
Agree or strongly agree; n/N (%)						
I can benefit from the health assessment	630/767 (82.1)	167/212 (78.8)	76/104 (73.1)	194/221 (87.8)	13/23 (56.5)	180/207 (87.0)
The health assessment was worth the time and effort	650/761 (85.4)	189/211 (89.6)	74/99 (74.7)	192/221 (86.9)	15/23 (65.2)	180/207 (87.0)
I had a say in decisions about my health	372/474 (78.5)	2/3 (66.7)	65/97 (67.0)	199/221 (90.0)	16/23 (69.6)	90/130 (69.2)
I am satisfied with the care I received	433/532 (81.4)	5/5 (100)	75/111 (67.6)	191/221 (86.4)	15/23 (65.2)	146/171 (85.4)
Scale 1-10; mean±SD						
I am satisfied with the UHCE approach (scale 1-10)	8.3±1.9	9.3±1.2	6.5±2.4	8.3±1.8	7.9±0.9	8.8±1.5

* Missing/not applicable: Benefit from health assessment=219; Worth time and effort=225; Results discussed with me=622; Had a say in decisions=512; Satisfied with care=454; Satisfied UHCE approach=188.

Chapter 8

General discussion

The aims of this thesis were twofold. Firstly, this thesis aimed to study the variation in indicators of healthy ageing among populations in Europe. More specifically, variation in frailty according to socioeconomic status and ethnic background and between-country variation in falling and fall risk were studied. The second aim was to evaluate the effects and process components of a coordinated preventive care approach aimed at promoting healthy ageing among older persons in Europe.

In this chapter the main findings of the studies reported in this thesis will be discussed. The methodological issues that could have affected these findings will then be addressed. Finally, recommendations for future research and implications for policy and practice will be specified.

8.1 Main findings and interpretation

What is the association of socioeconomic status and ethnic background with frailty among older persons in the Netherlands?

Data of The Older Persons and Informal Caregivers Survey Minimum DataSet (TOPICS-MDS) in the Netherlands were analysed to study the association of socioeconomic status and ethnic background with frailty and frailty components. Frailty was measured with a validated Frailty Index, which consisted of six components: morbidities, activities of daily living, instrumental activities of daily living, health-related quality of life, psychosocial health and self-rated health. In **Chapter 2**, the associations of socioeconomic status (education level and neighbourhood socioeconomic status) with frailty and frailty components among community-dwelling older persons in the Netherlands were studied. The results showed that older persons who had primary or secondary education were frailer compared with older persons who had tertiary education. Persons living in neighbourhoods with the lowest socioeconomic status (lowest quartile) were frailer compared with persons living in neighbourhoods with the highest socioeconomic status (highest quartile). In **Chapter 3**, the association of ethnic background (Dutch, Indonesian, Surinamese, Moroccan or Turkish) with frailty and frailty components among community-dwelling older persons in the Netherlands was studied. Persons with a Turkish, Moroccan or Surinamese background, were frailer compared with persons with a Dutch background. There were no significant differences in frailty between persons with an Indonesian background compared with persons with a Dutch background.

Our study, as well as other studies confirm that socioeconomic disadvantage is an important factor associated with a higher level of frailty among older persons [1-4]. These inequalities in frailty could arise because of an accumulation of health risks; such as mental and physical health problems, over the life course. Chronic diseases and multimorbidity are more

prevalent among middle aged persons with a low socioeconomic status and persons from ethnic minority groups[5 6]. In our study we found that the number of morbidities moderately to strongly contributed to educational inequalities in frailty. A Scottish study found a high level of mixed mental and physical conditions among the most deprived particularly at earlier age[6]. A Dutch study showed that psychiatric diseases are more common among Turkish and Moroccan immigrants and diabetes is more common among Surinamese immigrants compared with persons with a Dutch background[5 7 8]. These factors along with other factors we did not study, such as smoking, low exercise level and low social participation are likely associated with a high level of frailty among socioeconomically disadvantaged groups[6 9 10]. Among immigrant groups, other factors such as poor healthcare experience and discrimination have been reported and could also play a role in the development of health problems and frailty[11-13]. Communication with health care providers can be challenging and care is often not adapted to specific needs of immigrant groups[14].

We found inequalities in frailty and frailty components according to education level and neighbourhood socioeconomic status even among the youngest old, aged 55-69 years. Persons with only primary education level or living in the most deprived neighbourhoods appear to become frail at a relatively early age[15]. The sample of persons with a Surinamese, Moroccan or Turkish background was relatively young compared with persons with a Dutch background and had a high level of frailty. This was also found in another Dutch study[7]. It is unclear whether these inequalities in frailty become increasingly larger at older age. Longitudinal research shows contradicting findings, depending on the indicator by which socioeconomic status and health is measured[16 17]. We found smaller socioeconomic inequalities among older-old, which is more often found in cross-sectional research and could be due to a healthy survivor effect[18-21].

What is the rate of falling and intrinsic fall risk among older persons in Europe and can between-country variation in falling be explained by intrinsic fall risk?

To study the variation in falling and fall risk across European countries data of the Survey of Health, Ageing and Retirement in Europe (SHARE) were used. This study was described in **Chapter 4**. The results of this study showed that there is a considerable variation in the rate of falling between European countries. Persons in Switzerland, Denmark, Sweden and Austria reported relatively few falls compared with the other countries and persons in Estonia, France, Spain and the Czech Republic reported the most falls. We found that the between-country variation in falling could indeed largely be explained by the between-country variation in the prevalence of intrinsic fall risk factors.

To our knowledge our research was the first to study between-country differences in falling and fall risk. Literature has focused on geographical differences in limb fractures and has found that hip fracture rates are highest in Scandinavian countries[22-24], which appears to

contradict our findings. However, a hip fracture arises predominantly from the combination of a fall and low bone density, but the literature is inconclusive about the contribution of either one to the hip fractures [25-27]. It could be that a low bone density due to a Vitamin D deficiency is a strong contributor to a bone fracture in Scandinavian countries[24]. Furthermore, data from studies on geographical differences in limb fractures have come from hospital registers, which include institutionalised elderly as opposed to our study which includes community-dwelling older persons[22 23].

Socioeconomic factors likely explain the found differences in falling and fall risk between countries in our study. Important socioeconomic indicators such as the wealth and expenditure on elderly care differ between the countries in our study[28]. Older citizens in the original EU-15 countries are in better health compared with those in eastern European countries and within the EU-15 countries a north-south gradient for several health indicators at older age has been shown[15 28-30]. Our findings highlight the countries which could prioritise fall prevention strategies in particular. Fall prevention strategies such as exercise programs, multifactorial fall prevention strategies and home safety interventions have shown to be effective in reducing falls[31-33]. Former research has furthermore shown that home safety and improvement interventions are especially effective in populations with a high intrinsic fall risk[32].

What are the effects of a coordinated preventive care approach on the lifestyle, health and quality of life among older persons in Europe and how does this approach perform in terms of process components?

To promote healthy ageing among older persons, a coordinated preventive health and social care approach, Urban Health Centres Europe (UHCE), was developed and implemented in five European cities (Greater Manchester, United Kingdom; Pallini, Greece; Rijeka, Croatia; Rotterdam, the Netherlands; and Valencia, Spain). A pre-post controlled trial was conducted to evaluate the effects of the UHCE approach on the lifestyle, health and quality of life of older persons in these cities. Process components were evaluated alongside the effects of the UHCE approach. Participants in the intervention group received care according to the UHCE approach and participants in the control group received care as usual. The UHCE approach consisted of a multidimensional health assessment and, if a person was at-risk, coordinated care-pathways targeted at fall risk, appropriate medication use, loneliness and frailty. The design and evaluation of this approach were described in **Chapter 5, 6 and 7**. The UHCE approach showed minor positive effects in tackling recurrent falls and frailty and promoting physical health-related quality of life and mental well-being compared with care as usual. The context of implementation varied strongly between the European settings. Although satisfaction was high, several barriers towards engagement in care were identified.

Several systematic reviews have been done on the effects of coordinated preventive care interventions for older persons[34-38]. Some systematic reviews report favourable effects on falls, functional decline, nursing home admissions and mortality[34-36], but others do not[37 38]. The evidence regarding the effects on quality of life has been reported to be of relatively low quality[37]. Coordinated preventive care approaches have been criticised to be a black box, because the specific contents of the intervention are largely unknown or underreported[39]. An analysis of nine complex care interventions showed that the evaluation of certain aspects was rarely done: context, intervention fidelity and adaptation to the implementation context, and training for those delivering the intervention[39]. A main reason for the minor and mixed effects found for the health of older persons in our and other studies could be a low enrolment and engagement in care among older persons involved. In our study, around half of the persons who received the UHCE approach enrolled in a care-pathway. We found that persons in poor health enrolled less often. For older persons, poor health and mobility problems can be barriers to engagement in care interventions[40 41]. Mistrust among older persons towards unfamiliar services and care providers was another main barrier towards participation in care in our study. Trust appears to be the foundation of the relationship between care provider and older person and impacts on the acceptance of offered care[42-44].

Coordinated preventive care interventions in primary care such as the UHCE approach usually include a multidimensional frailty assessment. Although the benefits of frailty assessments are recognised, there is still debate on which instrument is most appropriate[45]. The ability of frailty instruments to predict mortality is moderate[46]. Therefore, using frailty instruments as a strict diagnostic test for frailty and adverse outcomes has limitations. However, clinical judgement alone is also found to be inappropriate to identify frail older persons[47]. General practitioners are used to focus on specific diseases and not on frailty as a multicomponent condition. General practitioners have mentioned that the use of a frailty instrument directs their attention towards health problems in multiple domains which may otherwise go unnoticed[48]. It can as such provide a starting point for further investigation. A structured two-step procedure performed by the general practitioner has been found to perform nearly as well as a comprehensive geriatric assessment performed by a geriatrician[49].

8.2 Methodological considerations

The results of this thesis should be viewed in the light of some methodological considerations. Here, the main methodological considerations of the studies in this thesis are discussed. These methodological considerations relate to: study design, participants, measurements, confounding, mediation, moderation and treatment fidelity.

Study design

In chapter 2 and 3, cross-sectional studies of pooled data from multiple studies were done to study the association of ethnic background with frailty and of socioeconomic status with frailty. Data on both the determinants and outcomes were collected at one point in time. Reverse causation can therefore not be excluded. However, we selected study determinants that logically are expected to precede the outcomes in time: socioeconomic status, morbidities and ethnic background. However, in the case of socioeconomic status, health could also impact a person's socioeconomic status, which is defined as health selection. The effect of health selection is however considered to be relatively small[50].

The pooled data used in chapter 2 and 3 consisted of studies included in The Older Persons and Informal Caregivers Survey Minimum DataSet (TOPICS-MDS). There was considerable variation between the included studies regarding sampling frame, inclusion criteria, study design, sample size, and data collection method. Therefore, the results of chapter 2 and 3 should be interpreted with caution. However, generally, these pooled data may provide more information regarding the associations studied than data from a single study.

In chapter 4, a longitudinal design was used to study the association of intrinsic fall risk factors with falling. Intrinsic fall risk factors were measured in wave 4 of the SHARE study and falling was measured in wave 5, two years later. This longitudinal design ensured that the intrinsic fall risk factors preceded fall outcomes. However, a longitudinal design is still an observational design and therefore causality cannot be inferred. In contrast to randomised trials, the determinant of interest is not randomly distributed among all persons. Participants with and without the determinant may differ with respect to unmeasured characteristics. If these unmeasured characteristics are also associated with the outcome of interest, residual confounding cannot be excluded[51].

In chapter 6 we applied a non-randomised design to evaluate the effect of the UHCE approach on the lifestyle, health and quality of life of older persons in these cities in all cities except for Pallini. A non-randomised design makes results subject to confounding variables. Randomization within general practices was not desirable for cities that worked with general practitioners as it is not feasible for general practitioners to provide both 'usual care' and the UHCE approach at the same time. A cluster randomised trial was not feasible as the cities in this study worked with too few general practices to have enough clusters for randomization. For example in the case of Rotterdam, general practices were embedded in three primary care centres. In our analyses we included the most important confounding variables; however it remains possible that we missed other relevant variables.

In chapter 7 we followed a theoretical framework developed by Stecklar and Linnan to evaluate process components of the UHCE approach implementation. One of the reasons

why process evaluations were developed, was to explain why certain effects were found in effect evaluations and pinpoint to components of interventions that were effective[52]. It is however difficult to identify specific components of the intervention that were effective or ineffective and explain results. Especially in complex interventions, the interplay of multiple components could play a role in the found intervention effects.

Participants

All studies in this thesis, with the exception of chapter 4, use opportunity samples of older persons. This might limit the generalizability of the results of these studies, because the sample populations might not be representative of the target population. Another important indicator of the introduction of possible selection bias in our studies is the participation rate, as it is likely that only a specific subsample of persons with certain characteristics participate. Usually, persons who agree to participate in a study are healthier compared with persons who do not participate; known as healthy participant bias[53 54]. We observed that there was considerable variation in the participation rate between the projects in the studies in Chapter 2 and 3 and between the countries included in the studies in Chapter 4 and 6. It is therefore likely that the participants of these studies are healthier compared with the general population of community-dwelling older persons. However, we could not compare persons participating in the studies with persons who did not want to participate as we did not have characteristics of those not participating. In chapter 7, we used qualitative data from focus groups with older persons and professionals. Older persons included in the focus groups might have been those that were most positive about the UHCE approach as these persons were selected by care professionals involved in the study.

Bias can also arise when some data are not missing at random, because persons with certain characteristics do not answer a study question or drop-out of the study[51]. In Chapter 2 and 3 there was some missing data in the outcome and relatively few missing data in the covariates. We used multiple imputation to account for missing data in the covariates[55]. In Chapter 4 and 6, persons who dropped out of the studies were older and in worse health. In longitudinal and experimental studies, especially in an older population, attrition is common. In chapter 4 we accounted for this attrition by using standardised sampling weights. In chapter 6 we could not account for attrition. Around 20% of persons were lost to follow-up between baseline and follow-up measurements, which was as expected in this older population[56]. In chapter 7, there were many missing data for the questions on satisfaction of the UHCE approach. Persons who did not reply to some of these questions could have thought these questions were not applicable to them or were the persons who were less involved in the UHCE approach. The responses could have therefore been biased towards the more active participants who might have been more positive about the UHCE approach.

Measurements

Most data collected in the studies were based on self-reported data. This could have led to certain types of response bias. Data was mostly collected by interviewers, which could increase the chance for older persons to give socially desirable answers. Furthermore, older persons might have not reported health problems such as falls in the past year because they could not remember. This problem, known as recall bias, is common in studies with older persons. Therefore, health problems might have been underreported in our studies. In all studies of this thesis, with the exception of chapter 2, persons from different countries or with a different ethnic background were included. It is possible that cultural differences in the interpretation of a survey question might have caused variation between these subgroups. This is known as differential item functioning and affects all cross-national research. Questionnaires were however translated using rigorous methodology and wherever possible, we used measures that had been validated in different populations. The TOPICS-MDS questionnaire was translated and cross-culturally validated for use in the main immigrant groups in the Netherlands.

Confounding, mediation and moderation

Unmeasured confounders could have affected the results in this thesis. A confounder is a variables that is both associated with the determinant and the outcome studied and which is not on the causal pathway. Ignoring confounding could lead to under or over estimation of the association between determinant and outcome, it could even lead to a change in the direction of the effect. The studies presented in these thesis were adjusted for confounders carefully chosen based on previous literature, availability in the data and exploratory analyses. However, the possibility of residual confounding by unmeasured confounders cannot be ruled out.

To analyse mediation, we used the Baron and Kenny method in chapter 3. Mediators are variables that are associated with the determinant and outcome and are on the causal pathway between determinant and outcome. Limitations of the Baron and Kenny method have been mentioned which include that it requires a significant overall relation between the exposure and outcome and allows no exposure-mediator interaction[57]. In our study, the association between exposure and outcome was not always significant, therefore we might have missed mediation in non-significant associations. Furthermore, since causality cannot be established in observational research, it is possible that some associations were not causal.

In our studies, we tested moderation by means of formal interaction tests and stratified data when there was significant interaction. Moderation happens when the association between the determinant and outcomes varies according to a third variable[51]. This third variable is known as a moderator, or effect modifier. Stratification according to the different values

of the moderator will give different associations of the determinant with the outcome. Interaction tests are highly dependent on population size. Because we applied many interaction tests, we applied the Bonferroni corrections for interaction testing[58]. This might have increased the chance of false negatives, that is, not finding significant moderation when in reality there was moderation.

Treatment fidelity

As discussed earlier, coordinated preventive care studies are often affected by a low intervention fidelity due to them being time-consuming and complex[41 59]. With this in mind the UHCE intervention was designed as a two-step approach. First assessing health problems by using simple validated tools for use in primary care and then if needed, further assessment and follow-up care by means of evidence-based interventions. We also decided to limit the intervention to four main health problems reported by older persons in our focus groups and in the literature; frailty, falls, polypharmacy and loneliness. We found that the UHCE approach was implemented differently in the five settings. Parts of the intervention were inappropriate to carry out by healthcare providers in certain settings. Furthermore, although we had information on whether or not persons enrolled in a care-pathway, we did not have information on whether they dropped-out before termination of the care-pathway or the extent to which they adhered to the care-pathway. We also do not know what kind of care was provided by the health care providers in the control group. A preventive, case-finding approach and follow-up care of frail older persons is recommended by the Dutch National General Practitioner's association and the National Health Service in the UK[60 61]. General practitioners in the control group might therefore have integrated some form of this approach in their daily practice. The difference in care and positive effects for the health of older persons between the control group and the intervention group might have therefore been too small to detect in these settings.

8.3 Recommendations for future research

Studying variation in healthy ageing

How socioeconomic status impacts on age-related conditions such as frailty during the life-course is still largely unknown. Longitudinal life-course studies are needed to assess the effect of socioeconomic status on frailty. It is important to evaluate several indicators of socioeconomic status such as education level, income and wealth as results may vary depending on the indicator. More longitudinal research is also needed to study the factors that contribute to these socioeconomic inequalities in frailty. Besides chronic diseases, other factors such as lifestyle behaviours, social participation and social support could also be important mediators. Lastly, it is also important to study the role of physical and mental diseases in the progression of frailty.

Older immigrants are a growing group in Europe and it is therefore important to study the health and health-conditions related to ageing in this group. Just as with socio-economic inequalities in frailty, ethnic inequalities in frailty could potentially be explained by certain morbidities as the disease burden among immigrant groups is higher compared with native-born persons. There is however a lack of research on ethnic variation in health. Cohort studies often lack a substantial number of respondents from ethnic minority groups, which makes exploration of ethnic differences in health difficult. Our study on ethnic inequalities in frailty found important differences between specific immigrant groups and it is therefore recommended to study specific immigrant groups separately.

It is furthermore important to conduct more research on the translation and cross-cultural validation of frailty instruments. Cross-cultural validation studies of instruments are lacking and when conducted, often inadequately done[62]. Especially frailty instruments that rely on self-report should be cross-culturally validated as interpretation of survey questions differs culturally.

As our study was the first to study international variation in falling and fall risk in older persons, replication studies are needed. To increase the validity of measurement of falls, the number of falls should be measured prospectively on a weekly basis. Further research could also study international variation in extrinsic fall risk factors and behavioural fall risk factors, besides intrinsic factors. Extrinsic fall risk factors such as medication use and home hazards have been found to be associated with falls, although associations were less strong compared with most intrinsic risk factors such as balance and mobility[63-65]. However, this could vary between countries as most studies have been done in Western settings. It is important to study fall risk factors in populations of non-Western settings to be able to adapt fall prevention strategies to these specific contexts.

Intervention studies aimed at the promotion of healthy ageing

One of the difficulties in coordinated preventive care studies is the use of appropriate outcomes to measure beneficial health effects. The persons included in the intervention are often a heterogeneous group. The actual care interventions persons receive are also heterogeneous. It is therefore difficult to capture effects in a single outcome measure. Broad outcomes such as health-related quality of life and disability have often been used to capture health effects across different domains[59]. However, these outcomes might not adequately capture health improvements in specific outcomes. A study by Rockwood et al. has found that among frail older persons, measuring multiple individualised goals detects more clinically relevant changes than measuring broad health outcomes such as disability and quality of life[66]. Individualised goals could also be appropriate for a heterogeneous population with healthier and unhealthier older persons as goals are specific for each individual. Other outcomes such as institutionalization and mortality are more objective

measures of health benefits. However, most intervention studies that have been done had a follow-up time of 12 to 24 months[34 59 67]. This might not be long enough to measure an effect on these outcomes. Structured and preventive monitoring of health as done in coordinated preventive care interventions, could also result in other health benefits within a longer time span, but research is lacking. Future studies should investigate the long-term effects of a coordinated preventive care approach for older persons.

Most research has focused on frailty as a risk factor for functional decline and loss of independence and used frailty instruments to identify persons who are frail and at-risk for functional decline. However, studies have found that frailty is indeed a reversible state[15]. Thus, focusing interventions on the prevention or treatment of frailty could be a next step. These interventions could target persons at an earlier age and focus on the promotion of healthy ageing rather than prevention of functional decline. Including older persons with a low socioeconomic status and from ethnic minority groups in these interventions and adapting interventions to their situation could be key, as intervention studies among these groups are currently scarce.

Future research could also have a stronger focus on intervention processes and qualitative measures besides quantitative measures. Especially the context, modelling of processes and outcomes, fidelity, and training of persons involved in the intervention may be described. The Criteria for Reporting the Development and Evaluation of Complex Interventions in healthcare (CREDICI) criteria have been developed as a reporting guideline for complex interventions[68]. The template for intervention description and replication (TIDieR) checklist developed in 2014 may provide a useful tool for the reporting of details of intervention elements[69]. It is recommended to encourage researchers to use these guidelines in the designing and reporting of interventions. These guidelines could be used in templates for ethical applications, trial registration and scientific papers.

8.4 Implications for practice and policy

Addressing socioeconomic and ethnic inequalities in healthy ageing

It is important that health interventions target persons who are frail or at risk of becoming frail. Persons with a low socioeconomic status appear to be an important group of persons with a high risk of frailty. Older immigrants appear to be another group with a high frailty level. Interventions could target modifiable mediating factors that contribute to socioeconomic and ethnic inequalities in frailty. Although it is important to have a better understanding which mediating factors explain these differences in frailty, there is growing evidence that morbidities contribute to these differences. Obesity, depression, cognitive impairment, musco-skeletal disease and multimorbidity have been linked to

socioeconomic inequalities in frailty and could be target points for early intervention[70-72]. Psychiatric diseases appear more common among Turkish and Moroccan immigrants and diabetes appears more common among Surinamese immigrants compared with persons with a Dutch background and could be targeted[5 7 8]. It is furthermore important to manage the progression of these chronic diseases. The presence of frailty in persons with chronic diseases such as diabetes and COPD has been associated with increased mortality[73 74]. We recommend to evaluate whether targeted assessment of frailty among older persons with (multiple) chronic diseases is feasible and effective.

As frailty appears to arise at a relatively younger age among persons with a low socioeconomic status and among persons with a Turkish, Moroccan or Surinamese background, interventions could be targeted at a younger age in these persons to prevent an increase in frailty level. Physical exercise interventions could be a promising strategy because they promote an active lifestyle and have been found to be effective in reducing frailty, falls, disability and depression in older persons[75-78]. However, participation in physical exercise programs is often low and strategies are needed to improve participation[79].

Interventions could also be developed that directly target social disadvantage among older persons. Although this is considered difficult to change, there are examples of interventions that target social disadvantage for older age groups in Europe such as public pension funds, free public transport or cultural activities schemes.

Coordinated preventive care interventions and European policy

A general template for coordinated preventive care could be a promising strategy for the promotion of healthy ageing in various European settings. We recommend developing and evaluating strategies to increase the participation in care among older persons. Such strategies may focus on increasing the engagement in health promotion activities by tailoring such activities to the needs of older persons. Both environmental barriers as well as personal barriers appear to affect care decisions among older persons. An environmental strategy could be the provision of transport for functionally impaired persons. Personal strategies could be the building of a trusting relationship between care provider and client. Within a trusting relationship, psychosocial factors that influence care decisions among older persons could be identified and addressed.

The between-country differences of falls and fall risk factors we found could help (inter) national policy makers to prioritise the right fall prevention strategies or continue successful efforts. Several fall prevention strategies have shown to be effective in reducing falls[31-33]. Home safety interventions have been found to be especially effective in persons with a higher intrinsic fall risk and might be appropriate in countries with a high intrinsic fall risk[32]. Although we did not study variation in other health outcomes at older age among European countries,

other studies also find a higher frailty level and disability in persons of countries in Southern Europe and Eastern Europe compared to North-Western Europe[15 28-30], which they attribute to socioeconomic differences between the countries. Policies that target social disadvantage in Europe could improve underlying health problems and health-related quality.

Promotion of healthy ageing

Thirty years after Rowe and Kayn introduced their concept of successful ageing[80], we still mostly look at promotion of healthy ageing from a medical point of view; focusing on identifying and treating age-related health problems. This is understandable because research in this field has been done within the medical discipline. The studies in this thesis also focused on identifying and preventing age-related health problems. Frailty instruments assess the presence of health problems such as poor mobility or low muscle strength[81 82]. By merely focusing on treating health problems and disability we could overlook potential protective factors that might be present. For example, social support and participation, are suggested to be protective factors for developing and worsening of frailty[9 10]. When we identify potential protective factors of ageing, we could aim to create an environment to nourish and promote them. In 2011, Huber introduced a new definition of health as "the ability to adapt and to self-manage"[83]. This definition is particularly useful in the context of ageing, as older persons are rarely free from diseases or conditions. Advancements in the field of smart design and technology could potentially support self-management of health. Examples of such advancements could be the attractive design of aids for older persons and supportive technology to promote an active and social lifestyle.

8.5 General conclusions

Some general conclusions can be drawn from the studies in this thesis. First, we established the presence of socioeconomic and ethnic inequalities in frailty among older persons in our studies. Second, falling and fall risk was found to vary considerably between European countries. Last, a coordinated preventive health- and social care approach for the promotion of healthy ageing among older persons in varied European settings was received positively and showed promising results. However, the effects of such a coordinated preventive care approach on the health and quality of life of older persons could be greater when older person's engagement in the approach is promoted.

Future research is recommended, that focusses on the role that morbidities and other factors play in the onset and progression of frailty among socially disadvantaged groups. Additionally, it is suggested to evaluate coordinated preventive care interventions with longer follow-up periods that include a thorough process evaluation. In conclusion, coordinated

preventive approaches that integrate health- and social care should be developed further, and might be a promising strategy in European policies regarding active and healthy ageing.

REFERENCES

1. Chamberlain AM, St Sauver JL, Jacobson DJ, et al. Social and behavioural factors associated with frailty trajectories in a population-based cohort of older adults. *BMJ Open* 2016;6(5):e011410. doi: 10.1136/bmjopen-2016-011410
2. Harttgen K, Kowal P, Strulik H, et al. Patterns of frailty in older adults: comparing results from higher and lower income countries using the Survey of Health, Ageing and Retirement in Europe (SHARE) and the Study on Global AGEing and Adult Health (SAGE). *PLoS One* 2013;8(10):e75847. doi: 10.1371/journal.pone.0075847
3. Romero-Ortuno R. Frailty Index in Europeans: association with determinants of health. *Geriatr Gerontol Int* 2014;14(2):420-9. doi: 10.1111/ggi.12122
4. Hajizadeh M, Mitnitski A, Rockwood K. Socioeconomic gradient in health in Canada: Is the gap widening or narrowing? *Health Policy* 2016;120(9):1040-50. doi: 10.1016/j.healthpol.2016.07.019
5. Ikram UZ, Kunst AE, Lamkaddem M, et al. The disease burden across different ethnic groups in Amsterdam, the Netherlands, 2011-2030. *Eur J Public Health* 2014;24(4):600-5. doi: 10.1093/eurpub/ckt136
6. McLean G, Gunn J, Wyke S, et al. The influence of socioeconomic deprivation on multimorbidity at different ages: a cross-sectional study. *Br J Gen Pract* 2014;64(624):e440-7. doi: 10.3399/bjgp14X680545
7. van Assen MA, Pallast E, Fakiri FE, et al. Measuring frailty in Dutch community-dwelling older people: Reference values of the Tilburg Frailty Indicator (TFI). *Arch Gerontol Geriatr* 2016;67:120-9. doi: 10.1016/j.archger.2016.07.005
8. de Wit MA, Tuinebreijer WC, Dekker J, et al. Depressive and anxiety disorders in different ethnic groups: a population based study among native Dutch, and Turkish, Moroccan and Surinamese migrants in Amsterdam. *Soc Psychiatry Psychiatr Epidemiol* 2008;43(11):905-12. doi: 10.1007/s00127-008-0382-5
9. Etman A, Kamphuis CB, van der Cammen TJ, et al. Do lifestyle, health and social participation mediate educational inequalities in frailty worsening? *Eur J Public Health* 2014 doi: cku093 [pii]10.1093/eurpub/cku093 [published Online First: 2014/07/26]
10. Feng Z, Lugtenberg M, Franse C, et al. Risk factors and protective factors associated with incident or increase of frailty among community-dwelling older adults: A systematic review of longitudinal studies. *PLoS One* 2017;12(6):e0178383. doi: 10.1371/journal.pone.0178383
11. Evandrou M, Falkingham J, Feng Z, et al. Ethnic inequalities in limiting health and self-reported health in later life revisited. *J Epidemiol Community Health* 2016;70(7):653-62. doi: 10.1136/jech-2015-206074
12. Nazroo JY. The structuring of ethnic inequalities in health: economic position, racial discrimination, and racism. *Am J Public Health* 2003;93(2):277-84.
13. Hudson DL, Puterman E, Bibbins-Domingo K, et al. Race, life course socioeconomic position, racial discrimination, depressive symptoms and self-rated health. *Soc Sci Med* 2013;97:7-14. doi: 10.1016/j.socscimed.2013.07.031

14. Rechel B, Mladovsky P, Ingleby D, et al. Migration and health in an increasingly diverse Europe. *Lancet* 2013;381(9873):1235-45. doi: 10.1016/S0140-6736(12)62086-8
15. Etman A, Burdorf A, Van der Cammen TJ, et al. Socio-demographic determinants of worsening in frailty among community-dwelling older people in 11 European countries. *J Epidemiol Community Health* 2012;66(12):1116-21. doi: jech-2011-200027 [pii]10.1136/jech-2011-200027 [published Online First: 2012/05/01]
16. Stolz E, Mayerl H, Waxenegger A, et al. Impact of socioeconomic position on frailty trajectories in 10 European countries: evidence from the Survey of Health, Ageing and Retirement in Europe (2004-2013). *J Epidemiol Community Health* 2016 doi: 10.1136/jech-2016-207712
17. Benzeval M, Green MJ, Leyland AH. Do social inequalities in health widen or converge with age? Longitudinal evidence from three cohorts in the West of Scotland. *BMC Public Health* 2011;11:947. doi: 10.1186/1471-2458-11-947
18. Huisman M, Kunst AE, Mackenbach JP. Socioeconomic inequalities in morbidity among the elderly; a European overview. *Soc Sci Med* 2003;57(5):861-73.
19. Enroth L, Raitanen J, Hervonen A, et al. Is socioeconomic status a predictor of mortality in nonagenarians? The vitality 90+ study. *Age Ageing* 2015;44(1):123-9. doi: 10.1093/ageing/afu092
20. Gobbens RJ, van Assen MA, Schalk MJ. The prediction of disability by self-reported physical frailty components of the Tilburg Frailty Indicator (TFI). *Arch Gerontol Geriatr* 2014 doi: S0167-4943(14)00101-0 [pii]10.1016/j.archger.2014.06.008 [published Online First: 2014/07/22]
21. Bell CL, Chen R, Masaki K, et al. Late-life factors associated with healthy aging in older men. *J Am Geriatr Soc* 2014;62(5):880-8. doi: 10.1111/jgs.12796
22. Dhanwal DK, Cooper C, Dennison EM. Geographic variation in osteoporotic hip fracture incidence: the growing importance of asian influences in coming decades. *J Osteoporos* 2010;2010:757102. doi: 10.4061/2010/757102
23. Dhanwal DK, Dennison EM, Harvey NC, et al. Epidemiology of hip fracture: Worldwide geographic variation. *Indian J Orthop* 2011;45(1):15-22. doi: 10.4103/0019-5413.73656
24. Litwic A, Edwards M, Cooper C, et al. Geographic differences in fractures among women. *Womens Health (Lond)* 2012;8(6):673-84. doi: 10.2217/whe.12.54
25. Roy DK, Pye SR, Lunt M, et al. Falls explain between-center differences in the incidence of limb fracture across Europe. *Bone* 2002;31(6):712-7. doi: S8756328202009092 [pii] [published Online First: 2003/01/18]
26. Leslie WD, Brennan-Olsen SL, Morin SN, et al. Fracture prediction from repeat BMD measurements in clinical practice. *Osteoporos Int* 2016;27(1):203-10. doi: 10.1007/s00198-015-3259-y
27. Kaptoge S, Benevolenskaya LI, Bhalla AK, et al. Low BMD is less predictive than reported falls for future limb fractures in women across Europe: results from the European Prospective Osteoporosis Study. *Bone* 2005;36(3):387-98. doi: 10.1016/j.bone.2004.11.012
28. Jagger C, Gillies C, Moscone F, et al. Inequalities in healthy life years in the 25 countries of the European Union in 2005: a cross-national meta-regression analysis. *Lancet* 2008;372(9656):2124-31. doi: 10.1016/S0140-6736(08)61594-9

29. Castro-Costa E, Dewey M, Stewart R, et al. Prevalence of depressive symptoms and syndromes in later life in ten European countries: the SHARE study. *Br J Psychiatry* 2007;191:393-401. doi: 191/5/393 [pii]10.1192/bjp.bp.107.036772 [published Online First: 2007/11/06]
30. Santos-Eggimann B, Cuenoud P, Spagnoli J, et al. Prevalence of frailty in middle-aged and older community-dwelling Europeans living in 10 countries. *J Gerontol A Biol Sci Med Sci* 2009;64(6):675-81. doi: glp012 [pii]10.1093/gerona/glp012 [published Online First: 2009/03/12]
31. Gillespie LD, Robertson MC, Gillespie WJ, et al. Interventions for preventing falls in older people living in the community. *Cochrane Database Syst Rev* 2009(2):CD007146. doi: 10.1002/14651858.CD007146.pub2 [published Online First: 2009/04/17]
32. Gillespie LD, Robertson MC, Gillespie WJ, et al. Interventions for preventing falls in older people living in the community. *Cochrane Database Syst Rev* 2012;9:CD007146. doi: 10.1002/14651858.CD007146.pub3
33. Costello E, Edelstein JE. Update on falls prevention for community-dwelling older adults: review of single and multifactorial intervention programs. *J Rehabil Res Dev* 2008;45(8):1135-52. [published Online First: 2009/02/24]
34. Beswick AD, Rees K, Dieppe P, et al. Complex interventions to improve physical function and maintain independent living in elderly people: a systematic review and meta-analysis. *Lancet* 2008;371(9614):725-35. doi: S0140-6736(08)60342-6 [pii]10.1016/S0140-6736(08)60342-6 [published Online First: 2008/03/04]
35. Stuck AE, Egger M, Hammer A, et al. Home visits to prevent nursing home admission and functional decline in elderly people: systematic review and meta-regression analysis. *JAMA* 2002;287(8):1022-8. doi: jma10044 [pii] [published Online First: 2002/02/28]
36. Huss A, Stuck AE, Rubenstein LZ, et al. Multidimensional preventive home visit programs for community-dwelling older adults: a systematic review and meta-analysis of randomized controlled trials. *J Gerontol A Biol Sci Med Sci* 2008;63(3):298-307. doi: 63/3/298 [pii] [published Online First: 2008/04/01]
37. Mayo-Wilson E, Grant S, Burton J, et al. Preventive home visits for mortality, morbidity, and institutionalization in older adults: a systematic review and meta-analysis. *PLoS One* 2014;9(3):e89257. doi: 10.1371/journal.pone.0089257PONE-D-13-47215 [pii] [published Online First: 2014/03/14]
38. Bouman A, van Rossum E, Nelemans P, et al. Effects of intensive home visiting programs for older people with poor health status: a systematic review. *BMC Health Serv Res* 2008;8:74. doi: 1472-6963-8-74 [pii] 10.1186/1472-6963-8-74 [published Online First: 2008/04/05]
39. Smit LC, Schuurmans MJ, Blom JW, et al. Unravelling complex primary-care programs to maintain independent living in older people: a systematic overview. *J Clin Epidemiol* 2017 doi: 10.1016/j.jclinepi.2017.12.013 [published Online First: 2018/01/01]
40. Provencher V, Mortenson WB, Tanguay-Garneau L, et al. Challenges and strategies pertaining to recruitment and retention of frail elderly in research studies: a systematic review. *Arch Gerontol Geriatr* 2014;59(1):18-24. doi: 10.1016/j.archger.2014.03.006

41. Metzelthin SF, Daniels R, van Rossum E, et al. A nurse-led interdisciplinary primary care approach to prevent disability among community-dwelling frail older people: a large-scale process evaluation. *Int J Nurs Stud* 2013;50(9):1184-96. doi: S0020-7489(12)00458-0 [pii]10.1016/j.ijnurstu.2012.12.016 [published Online First: 2013/02/07]
42. Muntinga ME, van Leeuwen KM, Jansen APD, et al. The Importance of Trust in Successful Home Visit Programs for Older People. *Glob Qual Nurs Res* 2016;3:2333393616681935. doi: 10.1177/2333393616681935
43. Bindels J, Cox K, Widdershoven G, et al. Care for community-dwelling frail older people: a practice nurse perspective. *J Clin Nurs* 2014;23(15-16):2313-22. doi: 10.1111/jocn.12513
44. van Kempen JA, Robben SH, Zuidema SU, et al. Home visits for frail older people: a qualitative study on the needs and preferences of frail older people and their informal caregivers. *Br J Gen Pract* 2012;62(601):e554-60. doi: 10.3399/bjgp12X653606
45. Pialoux T, Goyard J, Lesourd B. Screening tools for frailty in primary health care: a systematic review. *Geriatr Gerontol Int* 2012;12(2):189-97. doi: 10.1111/j.1447-0594.2011.00797.x [published Online First: 2012/01/12]
46. Theou O, Brothers TD, Mitnitski A, et al. Operationalization of frailty using eight commonly used scales and comparison of their ability to predict all-cause mortality. *J Am Geriatr Soc* 2013;61(9):1537-51. doi: 10.1111/jgs.12420 [published Online First: 2013/09/14]
47. De Lepeleire J, Iliffe S, Mann E, et al. Frailty: an emerging concept for general practice. *Br J Gen Pract* 2009;59(562):e177-82. doi: 10.3399/bjgp09X420653
48. Keiren SM, van Kempen JA, Schers HJ, et al. Feasibility evaluation of a stepped procedure to identify community-dwelling frail older people in general practice. A mixed methods study. *Eur J Gen Pract* 2014;20(2):107-13. doi: 10.3109/13814788.2013.827167
49. van Kempen JA, Schers HJ, Philp I, et al. Predictive validity of a two-step tool to map frailty in primary care. *BMC Med* 2015;13:287. doi: 10.1186/s12916-015-0519-9
50. Kroger H, Pakpahan E, Hoffmann R. What causes health inequality? A systematic review on the relative importance of social causation and health selection. *Eur J Public Health* 2015;25(6):951-60. doi: 10.1093/eurpub/ckv111
51. Rothman KJ, Greenland S, Lash TL. Modern Epidemiology. Philadelphia: Wolters Kluwer Health 2015.
52. Steckler ABLL. Process evaluation for public health interventions and research. San Francisco, Calif.: Jossey-Bass 2002.
53. Froom P, Melamed S, Kristal-Boneh E, et al. Healthy volunteer effect in industrial workers. *J Clin Epidemiol* 1999;52(8):731-5.
54. Gaertner B, Seitz I, Fuchs J, et al. Baseline participation in a health examination survey of the population 65 years and older: who is missed and why? BMC Geriatr 2016;16:21. doi: 10.1186/s12877-016-0185-6
55. Greenland S, Finkle WD. A critical look at methods for handling missing covariates in epidemiologic regression analyses. *Am J Epidemiol* 1995;142(12):1255-64.

56. Franse CB, Voorham AJJ, van Staveren R, et al. Evaluation design of Urban Health Centres Europe (UHCE): preventive integrated health and social care for community-dwelling older persons in five European cities. *BMC Geriatr* 2017;17(1):209. doi: 10.1186/s12877-017-0606-1
57. VanderWeele TJ. Mediation Analysis: A Practitioner's Guide. *Annu Rev Public Health* 2016;37:17-32. doi: 10.1146/annurev-publhealth-032315-021402
58. McDonald JH, University of D. Handbook of biological statistics. Baltimore, Maryland: Sparky House Publishing 2009.
59. Metzelthin SF, van Rossum E, de Witte LP, et al. Effectiveness of interdisciplinary primary care approach to reduce disability in community dwelling frail older people: cluster randomised controlled trial. *BMJ* 2013;347:f5264. [published Online First: 2013/09/12]
60. Landelijke Huisartsen Vereniging (LHV). Complexe ouderenzorg in verzorgingshuis en thuis: LHV, Utrecht.; 2009 [Available from: http://www.verenso.nl/assets/Uploads/Downloads/Handreikingen/Complouderenzorguiteenstuk.pdf.
61. NHS England, Care Quality Commission, Health Education England, Monitor, Public Health England, Trust Development Authority. NHS five year forward view. NHS England, London. 2014 [Available from: www.england.nhs.uk/ourwork/futurenhs/.
62. Uysal-Bozkir O, Parlevliet JL, de Rooij SE. Insufficient cross-cultural adaptations and psychometric properties for many translated health assessment scales: a systematic review. *J Clin Epidemiol* 2013;66(6):608-18. doi: 10.1016/j.jclinepi.2012.12.004
63. Ganz DA, Bao Y, Shekelle PG, et al. Will my patient fall? *JAMA* 2007;297(1):77-86. doi: 297/1/77 [pii] 10.1001/jama.297.1.77 [published Online First: 2007/01/04]
64. Hartikainen S, Lonnroos E, Louhivuori K. Medication as a risk factor for falls: critical systematic review. *J Gerontol A Biol Sci Med Sci* 2007;62(10):1172-81. doi: 62/10/1172 [pii] [published Online First: 2007/10/09]
65. National Institute for Clinical E. Clinical practice guideline for the assessment and prevention of falls in older people : guidelines commissioned by the National Institute for Clinical Excellence (NICE). London: Royal College of Nursing 2004.
66. Rockwood K, Howlett S, Stadnyk K, et al. Responsiveness of goal attainment scaling in a randomized controlled trial of comprehensive geriatric assessment. *J Clin Epidemiol* 2003;56(8):736-43.
67. Bleijenberg N, Drubbel I, Schuurmans MJ, et al. Effectiveness of a Proactive Primary Care Program on Preserving Daily Functioning of Older People: A Cluster Randomized Controlled Trial. *J Am Geriatr Soc* 2016;64(9):1779-88. doi: 10.1111/jgs.14325
68. Mohler R, Kopke S, Meyer G. Criteria for Reporting the Development and Evaluation of Complex Interventions in healthcare: revised guideline (CReDECI 2). *Trials* 2015;16:204. doi: 10.1186/s13063-015-0709-y
69. Hoffmann TC, Glasziou PP, Boutron I, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ* 2014;348:g1687. doi: 10.1136/bmj.g1687

70. Hoogendijk EO, van Hout HP, Heymans MW, et al. Explaining the association between educational level and frailty in older adults: results from a 13-year longitudinal study in the Netherlands. *Ann Epidemiol* 2014;24(7):538-44 e2. doi: 10.1016/j.annepidem.2014.05.002
71. Soler-Vila H, Garcia-Esquinas E, Leon-Munoz LM, et al. Contribution of health behaviours and clinical factors to socioeconomic differences in frailty among older adults. *J Epidemiol Community Health* 2016;70(4):354-60. doi: 10.1136/jech-2015-206406
72. Gobbens RJ, van Assen MA, Luijkx KG, et al. Determinants of frailty. *J Am Med Dir Assoc* 2010;11(5):356-64. doi: 10.1016/j.jamda.2009.11.008
73. Cacciatore F, Testa G, Galizia G, et al. Clinical frailty and long-term mortality in elderly subjects with diabetes. *Acta Diabetol* 2013;50(2):251-60. doi: 10.1007/s00592-012-0413-2
74. Galizia G, Cacciatore F, Testa G, et al. Role of clinical frailty on long-term mortality of elderly subjects with and without chronic obstructive pulmonary disease. *Aging Clin Exp Res* 2011;23(2):118-25.
75. El-Khoury F, Cassou B, Charles MA, et al. The effect of fall prevention exercise programmes on fall induced injuries in community dwelling older adults: systematic review and meta-analysis of randomised controlled trials. *BMJ* 2013;347:f6234. [published Online First: 2013/10/31]
76. Gine-Garriga M, Roque-Figuls M, Coll-Planas L, et al. Physical exercise interventions for improving performance-based measures of physical function in community-dwelling, frail older adults: A systematic review and meta-analysis. *Arch Phys Med Rehabil* 2014;95(4):753-69.e3.
77. Theou O, Stathokostas L, Roland KP, et al. The effectiveness of exercise interventions for the management of frailty: a systematic review. *J Aging Res* 2011;2011:569194. doi: 10.4061/2011/569194 [published Online First: 2011/05/18]
78. Cooney GM, Dwan K, Greig CA, et al. Exercise for depression *Cochrane Database Syst Rev* 2013;12(9):CD004366. doi.
79. van der Deijl M, Etman A, Kamphuis CB, et al. Participation levels of physical activity programs for community-dwelling older adults: a systematic review. *BMC Public Health* 2014;14:1301. doi: 10.1186/1471-2458-14-1301
80. Rowe JW, Kahn RL. Human aging: usual and successful. *Science* 1987;237(4811):143-9.
81. Rockwood K, Song X, MacKnight C, et al. A global clinical measure of fitness and frailty in elderly people. *CMAJ* 2005;173(5):489-95. doi: 173/5/489 [pii]10.1503/cmaj.050051 [published Online First: 2005/09/01]
82. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001;56(3):M146-56. [published Online First: 2001/03/17]
83. Huber M, Knottnerus JA, Green L, et al. How should we define health? *BMJ* 2011;343:d4163. doi: 10.1136/bmj.d4163

Appendices

Summary

Europe has the highest proportion of persons over 65 years compared with any other continent. In 2015, Europeans over 65 years accounted for 19% of the population and by 2040 this will be 27%. While some persons remain relatively healthy with aging, others become frail and vulnerable to internal and external stressors. Frail older persons are two to four times as likely to develop or worsen disabilities in self-care tasks and household management tasks compared with non-frail older persons. Frailty is manageable and early intervention slows functional decline and reduces hospital admissions and mortality. It is therefore important to identify populations who are frail or at a higher risk of developing frailty in order to target prevention strategies. The care system is currently often characterised by a monodisciplinary approach focussed on one disease or condition. However, older persons often may have multiple physical- and social health problems. This could pose a challenge for health- and social care services. Because of this, the demand for cost-effective models of integrated and coordinated provision of different health and social care services has grown. In addition, because of the pressure on the health care system due to population ageing, the importance of preventive interventions that increase healthy life years among older Europeans has grown.

This thesis therefore aimed to study, 1) the variation in indicators of healthy ageing among older persons in Europe, and, 2) the effects and process components of a coordinated preventive health and social care approach aimed at promoting healthy ageing in Europe. The following research questions were answered:

- What is the association of socioeconomic status and ethnic background with frailty among older persons in the Netherlands?
- What is the rate of falling and intrinsic fall risk among older persons in Europe and can between-country variation in falling be explained by intrinsic fall risk?
- What are the effects of a coordinated preventive care approach on the lifestyle, health and quality of life among older persons in Europe and how does this approach perform in terms of process components?

Data of The Older Persons and Informal Caregivers Survey Minimum DataSet (TOPICS-MDS) in the Netherlands were analysed to study the association of socioeconomic status and ethnic background with frailty and frailty components. Frailty was measured with a validated Frailty Index, which consisted of six components: morbidities, activities of daily living, instrumental activities of daily living, health-related quality of life, psychosocial health and self-rated health. In **Chapter 2,** the associations of socioeconomic status (education level and neighbourhood socioeconomic status) with frailty and frailty components among community-dwelling older persons in the Netherlands were studied. The results showed

that older persons who had primary or secondary education were frailer compared with older persons who had tertiary education. Across all age groups, persons with a lower education level consistently had higher overall frailty levels, more morbidities and worse self-rated health compared with older persons with a high education level. The number of morbidities these persons had, also moderately to strongly contributed to the educational inequalities in frailty. Persons living in neighbourhoods with the lowest socioeconomic status (lowest quartile) were frailer compared with persons living in neighbourhoods with the highest socioeconomic status (highest quartile). However there were fewer neighbourhood inequalities compared with educational inequalities.

In **Chapter 3**, the association of ethnic background (Dutch, Indonesian, Surinamese, Moroccan or Turkish) with frailty and frailty components among community-dwelling older persons in the Netherlands was studied. Persons with a Turkish, Moroccan or Surinamese background, were frailer compared with persons with a Dutch background. There were no differences in frailty between persons with an Indonesian background compared with persons with a Dutch background. Of the frailty components; instrumental activities of daily living, necessary for independent living in the community, were more impaired among all persons with a non-Dutch background compared with persons with a Dutch background.

To study the variation in falling and fall risk across European countries data of the Survey of Health, Ageing and Retirement in Europe (SHARE) were used. This study is described in **Chapter 4**. The results of this study showed that there is a considerable variation in the rate of falling between European countries. Persons in Switzerland, Denmark, Sweden and Austria reported relatively few falls compared with the other countries and persons in Estonia, France, Spain and the Czech Republic reported the most falls. There was also a strong variation in intrinsic fall risk factors such as mobility limitations, self-rated health and impaired vision. The between-country variation in falling could indeed largely be explained by the between-country variation in the prevalence of intrinsic fall risk factors and not by the between-country variation in the studied sociodemographic factors; age, sex, education level and living situation. The associations of five intrinsic fall risk factors; less than good self-rated health, mobility limitations, activities of daily living limitations, dizziness, and depression with falling and older age with falling, were smaller in countries with a high rate of falling compared with countries with a low rate of falling.

To promote healthy ageing among older persons, a coordinated preventive health and social care approach, Urban Health Centres Europe (UHCE), was developed and implemented in five European cities (Greater Manchester, United Kingdom; Pallini, Greece; Rijeka, Croatia; Rotterdam, the Netherlands; and Valencia, Spain). A pre-post controlled trial was conducted to evaluate the effects of the UHCE approach on the lifestyle, health and quality of life of older persons in these cities. Process components were evaluated alongside the effects

of the UHCE approach. Participants in the intervention group received care according to the UHCE approach and participants in the control group received care as usual. The UHCE approach consisted of a multidimensional health assessment and, if a person was at-risk, coordinated care-pathways targeted at fall risk, appropriate medication use, loneliness and frailty. The design and evaluation of this approach are described in **Chapter 5, 6 and 7**. The UHCE approach showed minor positive effects in tackling recurrent falls and frailty and promoting physical health-related quality of life and mental well-being compared with care as usual. These effects appeared stronger in the subgroup of persons who enrolled in care-pathways. The context of implementation varied between the European settings. Non-enrolment was higher among persons with limited function in the falls and loneliness pathways compared with persons with better function. Feeling supported by a care professional was mentioned as a benefit of the UHCE approach for older persons. Mistrust towards unfamiliar care providers and lack of confidence to engage in certain care activities were mentioned as barriers.

In **Chapter 8**, the main findings of the studies reported in this thesis are discussed in the context of existing literature. Subsequently, the methodological issues that could have affected these findings are addressed. Finally, recommendations for future research and implications for policy and practice are specified and conclusions from this research are drawn. Future research is recommended, that focusses on the role that morbidities and other factors play in the onset and progression of frailty among socially disadvantaged groups. Additionally, it is suggested to evaluate coordinated preventive care interventions with longer follow-up periods that include a thorough process evaluation. In conclusion, coordinated preventive approaches that integrate health- and social care should be developed further, and might be a promising strategy in European policies regarding active and healthy ageing.

Samenvatting

Europa heeft de grootste proportie mensen boven de 65 jaar vergeleken met elk ander continent. In 2015 was 19% van de Europeanen boven de 65 jaar en in 2040 zal dit oplopen tot 27%. Terwijl sommige mensen wanneer ze ouder worden relatief gezond blijven, worden anderen kwetsbaar en ontvankelijk voor interne en externe stressoren. Het is voor kwetsbare ouderen twee tot vier keer zo waarschijnlijk dat ze hun zelfredzaamheid verliezen in het uitvoeren van zelfzorgactiviteiten en huishoudelijke activiteiten vergeleken met niet-kwetsbare ouderen. Kwetsbaarheid is omkeerbaar en vroege interventie vertraagt functionele achteruitgang en vermindert ziekenhuisopname en mortaliteit. Het is daarom belangrijk om populaties te identificeren die kwetsbaar zijn of een verhoogd risico hebben om kwetsbaar te worden, zodat preventieve strategieën gericht kunnen worden ingezet. In de zorg is er op dit moment relatief vaak een monodisciplinaire aanpak die aandacht besteedt aan één aandoening of ziekte. Ouderen kunnen echter meerdere fysieke-, mentale- en sociale gezondheidsproblemen tegelijk hebben. Dit is een uitdaging voor gezondheids- en sociale zorg. Om deze reden is de vraag toegenomen naar kosteneffectieve modellen van geïntegreerd en gecoördineerd aanbieden van verschillende gezondheids- en sociale diensten. Daar komt bij dat door de druk op het zorgsysteem door de vergrijzing het belang is toegenomen van preventieve interventies die het aantal gezonde levensjaren van oudere Europeanen verhogen.

Het doel van deze thesis was daarom om 1) de variatie in indicatoren van gezond ouder worden onder ouderen in Europa te onderzoeken, en om 2) de effecten en procescomponenten van een gecoördineerde preventieve gezondheids- en sociale zorgaanpak gericht op de bevordering van gezond ouder worden te evalueren in verschillende Europese steden. De volgende onderzoeksvragen werden beantwoord:

- Wat is het verband tussen sociaaleconomische status, etnische achtergrond en kwetsbaarheid onder ouderen in Nederland?
- Wat is de mate van vallen en intrinsiek valrisico onder ouderen in Europa en kan variatie tussen landen in vallen verklaard worden door variatie tussen landen in intrinsiek valrisico?
- Wat zijn de effecten van een gecoördineerde preventieve zorgaanpak op de leefstijl, gezondheid en kwaliteit van leven onder ouderen in Europa, en hoe wordt deze aanpak uitgevoerd wat betreft procescomponenten?

Data van 'The Older Persons and Informal Caregivers Survey Minimum DataSet' (TOPICS-MDS) zijn geanalyseerd om het verband tussen sociaaleconomische status en etnische achtergrond en kwetsbaarheid in Nederland te onderzoeken. Kwetsbaarheid is gemeten met een gevalideerde kwetsbaarheidsindex, die bestond uit zes componenten:

aandoeningen en ziektes, activiteiten van het dagelijks leven, instrumentele activiteiten van het dagelijks leven, kwaliteit van leven, psychosociale gezondheid en zelf-gerapporteerde gezondheid. In **Hoofdstuk 2** werd het verband onderzocht tussen sociaaleconomische status (opleidingsniveau en sociaaleconomische status van de buurt) en kwetsbaarheid en kwetsbaarheidscomponenten onder zelfstandig wonende ouderen in Nederland. De resultaten toonden aan dat ouderen met een primair of secundair opleidingsniveau kwetsbaarder waren vergeleken met ouderen met een tertiair opleidingsniveau. In alle leeftijdsgroepen hadden ouderen met een lager opleidingsniveau een hogere mate van kwetsbaarheid, meer aandoeningen en een slechtere zelf-gerapporteerde gezondheid vergeleken met ouderen met een hoger opleidingsniveau. Het aantal aandoeningen van ouderen was een gemiddeld tot sterk wegende factor in de opleidingsgerelateerde ongelijkheden in kwetsbaarheid. Ouderen die in buurten woonden met de laagste sociaaleconomische status (het laagste kwartiel) waren kwetsbaarder dan ouderen in buurten met de hoogste sociaaleconomische status (hoogste kwartiel). Er waren echter minder buurtgerelateerde ongelijkheden dan opleidingsgerelateerde ongelijkheden.

In **Hoofdstuk 3** werd het verband onderzocht tussen etnische achtergrond (Nederlands, Indonesisch, Surinaams, Marokkaans of Turks) en kwetsbaarheid en kwetsbaarheidscomponenten onder zelfstandig wonende ouderen in Nederland. Ouderen met een Turkse, Marokkaanse of Surinaamse achtergrond waren kwetsbaarder vergeleken met ouderen met een Nederlandse achtergrond. Er waren geen verschillen in kwetsbaarheid tussen ouderen met een Indonesische achtergrond en ouderen met een Nederlandse achtergrond. Alle ouderen met een niet-Nederlandse achtergrond hadden meer beperkingen in instrumentele activiteiten die nodig zijn om zelfstandig te wonen.

Om de variatie in vallen en valrisico tussen Europese landen te onderzoeken werd data gebruikt van de 'Survey of Health, Ageing and Retirement in Europe' (SHARE). Dit onderzoek is beschreven in **Hoofdstuk 4**. De resultaten van deze studie lieten een aanzienlijke variatie in vallen tussen Europese landen zien. Ouderen in Zwitserland, Denemarken, Zweden en Oostenrijk rapporteerden relatief weinig vallen vergeleken met de andere landen, en ouderen in Estland, Frankrijk, Spanje en Tsjechië rapporteerden de meeste vallen. Er was een sterke variatie in intrinsieke valrisicofactoren zoals mobiliteitsbeperkingen, zelf-gerapporteerde gezondheid en visusbeperkingen. De variatie tussen landen in vallen kon inderdaad grotendeels verklaard worden door de variatie tussen landen in intrinsiek valrisico en niet door de variatie tussen landen in sociaal-demografische factoren: leeftijd, sekse, opleidingsniveau en leefsituatie. De verbanden tussen oudere leeftijd en vallen en tussen vijf intrinsieke valrisicofactoren en vallen – minder dan goede zelf-gerapporteerde gezondheid, mobiliteitsbeperkingen, beperkingen in activiteiten van het dagelijks leven, duizeligheid en depressie – waren kleiner in landen met een hoog valpercentage vergeleken met landen met een laag valpercentage.

Om gezond ouder worden te bevorderen onder ouderen is een gecoördineerde preventieve gezondheids- en sociale zorgaanpak 'Urban Health Centres Europe' (UHCE) ontwikkeld en geïmplementeerd in vijf Europese steden (Greater Manchester, Verenigd Koninkrijk; Pallini, Griekenland; Rijeka, Kroatië; Rotterdam, Nederland en Valencia, Spanje). Een pre-post gecontroleerde studie is uitgevoerd om de effecten te onderzoeken van de UHCE-aanpak op de leefstijl, gezondheid en kwaliteit van leven van ouderen in deze steden. Procescomponenten werden geëvalueerd naast de effecten van de UHCE-aanpak. Deelnemers in de interventiegroep kregen zorg volgens de UHCE-aanpak en deelnemers in de controlegroep kregen zorg zoals gewoonlijk. De UHCE-aanpak bestond uit een multidimensionale gezondheidsbeoordeling, en wanneer de persoon een verhoogd risico had, ook uit gecoördineerde zorgpaden gericht op valrisico, adequaat medicatiegebruik, eenzaamheid en kwetsbaarheid. Het ontwerp en de evaluatie van deze aanpak zijn beschreven in **Hoofdstuk 5, 6 en 7**. De UHCE-aanpak zorgde voor kleine positieve effecten in het tegengaan van herhaald vallen en kwetsbaarheid en het bevorderen van fysieke kwaliteit van leven en mentaal welzijn vergeleken met zorg zoals gewoonlijk. Deze effecten leken sterker in de subgroep van ouderen die een zorgpad volgden. De context van uitvoering verschilde sterk tussen de Europese steden. Ouderen die beperkingen hadden in functioneren volgden minder vaak de valrisico- of eenzaamheidszorgpaden vergeleken met ouderen met beter functioneren. Ouderen noemden als voordeel van de UHCE-aanpak zich gesteund te voelen door een zorgprofessional. Wantrouwen tegenover onbekende zorgprofessionals en gebrek aan zelfvertrouwen om deel te nemen aan bepaalde zorgactiviteiten werden genoemd als barrières.

In **Hoofdstuk 8** zijn de hoofdbevindingen van de studies in deze thesis beschreven in het licht van bestaande literatuur. Daarna zijn de methodologische kwesties die deze bevindingen mogelijk hebben beïnvloed beschreven. Uiteindelijk zijn aanbevelingen voor toekomstig onderzoek en implicaties voor beleid en praktijk uiteengezet en is een conclusie geformuleerd. Toekomstig onderzoek is aan te bevelen naar de rol die ziektes, aandoeningen en andere factoren spelen in de aanloop naar en progressie van kwetsbaarheid onder sociaal achtergestelde groepen. Daarnaast zijn gecoördineerde preventieve zorginterventies nodig met een langere follow-up tijd die tevens een gedegen procesevaluatie bevatten. In conclusie, gecoördineerde preventieve zorg strategieën moeten verder worden ontwikkeld, en zouden gunstig kunnen zijn voor Europees beleid gericht op het actief en gezond ouder worden.

List of publications

This thesis

Franse CB, van Grieken A, Qin L, Melis RJF, Rietjens JAC, Raat H. Socioeconomic inequalities in frailty and frailty components among community-dwelling older citizens. PLoS One 2017;12(11):e0187946.

Franse CB, van Grieken A, Qin L, Melis RJF, Rietjens JAC, Raat H. Ethnic differences in frailty: a cross-sectional study of pooled data from community-dwelling older persons in the Netherlands. BMJ Open 2018;8(8):e022241.

Franse CB, Rietjens JA, Burdorf A, van Grieken A, Korfage IJ, van der Heide A, Mattace Raso F, van Beeck E, Raat H. A prospective study on the variation in falling and fall risk among community-dwelling older citizens in 12 European countries. BMJ Open 2017;7(6):e015827.

Franse C B, Voorham AJJ, van Staveren R, Koppelaar E, Martijn R, Valia-Cotanda E, Alhambra-Borras T, Rentoumis T, Bilajac L, Marchesi VV, Rukavina T, Verma A, Williams G, Clough G, Garces-Ferrer J, Mattace Raso F, Raat H. Evaluation design of Urban Health Centres Europe (UHCE): preventive integrated health and social care for community-dwelling older persons in five European cities. BMC Geriatr 2017;17(1):209.

Franse CB, van Grieken A, Alhambra-Borrás T, Valia-Cotanda E, van Staveren R, Rentoumis T, Markaki A, Bilajac L, Marchesi VV, Rukavina T, Verma A, Williams G, Koppelaar E, Martijn R, Voorham AJJ, Mattace Raso F, Garces-Ferrer J, Raat H. The effectiveness of a coordinated preventive care approach for healthy ageing (UHCE) among older persons in five European cities: a pre-post controlled trial. Int J Nurs Stud 2018; 88, pages 153-162.

Franse CB, Zhang X, van Grieken A, Rietjens J, Alhambra-Borrás T, Durá E, Garcés-Ferrer J, van Staveren R, Rentoumis T, Markaki A, Bilajac L, Marchesi VV, Rukavina T, Verma A, Williams G, Clough G, Koppelaar E, Martijn R, Mattace Raso F, Voorham AJJ, Raat H. A coordinated preventive care approach for healthy ageing (UHCE) in five European cities: a mixed-methods study of process evaluation components. [submitted]

Other

Franse CB, Kayigamba FR, Bakker MI, Mugisha V, Bagiruwigize E, Mitchell KR, Asiimwe A, Schim van der Loeff MS. Linkage to HIV care before and after the introduction of provider-initiated testing and counselling in six Rwandan health facilities. AIDS Care 2017;29(3):326-34.

Franse CB, Wang L, Constant F, Fries L, Raat H. Factors associated with water intake among children: a systematic review. [submitted]

Feng Z, Lugtenberg M, Franse CB, Fang X, Hu S, Jin C, Raat H. Risk factors and protective factors associated with incident or increase of frailty among community-dwelling older adults: A systematic review of longitudinal studies. PLoS One 2017;12(6):e0178383.

Zhang X., Tan SS, Franse CB, Alhambra-Borras T, Durá-Ferrandis E., Bilajac L., Markaki A., Verma A., Mattace-Raso F., Voorham A.J.J., Raat H. Association between physical, psychological and social frailty and health-related quality of life (HRQoL) [submitted]

About the author

Carmen Betsy Franse was born on May 21st 1985 in Amsterdam, the Netherlands. In 2003 she completed secondary school at Vossius Gymnasium in Amsterdam. After travelling and doing volunteer work in Australia and New Zealand she started the interdisciplinary Natural and Social Sciences bachelor (Dutch: 'Bèta-Gamma') with a major in Biomedical Sciences at the University of Amsterdam. As part of her bachelor she studied at the Complutense University in Madrid, Spain in 2007-2008 as an Erasmus exchange student. She obtained her bachelor's degree in 2008. In 2011, she obtained a master's degree in Biomedical Sciences at the VU University in Amsterdam, with a specialization in International Public Health. For her master's internship she went to Rwanda where she did research on factors affecting timely enrolment in care among persons with HIV. For this study she wrote a peer-reviewed international publication. After her studies she worked as a project manager for an international non-governmental organisation specialized in e-health education. In 2014, she started working as a junior researcher for the European Urban Health Centres Europe (UHCE) project at the Department of Public Health of the Erasmus Medical Centre in Rotterdam. While working for the UHCE project, she obtained a grant from The Netherlands Organisation for Health Research and Development (Dutch: 'ZonMw') to study socio-economic and ethnic inequalities in frailty among older persons in the Netherlands. Her PhD research of these studies is presented in this thesis.

PhD portofolio

Name: Carmen Betsy Franse
Erasmus MC Department: Public Health
Research School: Netherlands Institute for Health Sciences (NIHES)
PhD period: 2014 - 2018
Promotor: Prof. dr. Hein Raat
Copromotors: dr. Amy van Grieken and dr. Judith Rietjens

1. PhD training	Year	Workload (Hours/ ECTS)
General courses		
- Systematic literature review in Pubmed I and II, literature review in other databases and EndNote	2014	1.0 ECTS
- Biostatistical Methods I: Basic Principles	2014	5.7 ECTS
- Scientific integrity	2017	0.3 ECTS
Specific courses		
- Principles of research in medicine	2014	0.7 ECTS
- Clinical trials	2014	0.7 ECTS
- Methods of Public Health research	2014	0.7 ECTS
- Health Economics	2014	0.7 ECTS
- CPO course (Patient Oriented Research: design, conduct, analysis and clinical implications)	2015	0.3 ECTS
- Social epidemiology	2015	0.7 ECTS
- Causal mediation Analysis	2015	0.7 ECTS
- Conceptual foundation of epidemiologic study design	2015	0.7 ECTS
- Didactic skills (deel-BKO): Teach the teacher & Handling groups	2017	0.7 ECTS
Presentations		
- Oral presentation, UHCE consortium meeting, Rijeka, Croatia	2014	8 hours
- Oral presentation, ouderenzorg overleg, Rotterdam	2014	4 hours
- Oral presentation, Innovation in Healthy Ageing Summit, Brussels	2015	12 hours
- Oral presentation, Public Health festival, Manchester, United Kingdom	2015	12 hours
- Oral presentation, UHCE consortium meeting, Valencia, Spain	2015	8 hours
- Oral presentation, TOPICS diversity working group, Utrecht	2015	8 hours
- Oral presentation, TOPICS-MDS kick-off workshop, Nijmegen	2015	8 hours
- Oral presentation, Seminar department MGZ, Rotterdam	2015	8 hours
- Preparation oral presentation, UHCE final conference, Brussels, Belgium	2017	4 hours
- Poster presentation, EUGMS, Nice, France	2017	8 hours
- Oral presentation, EUGMS, Nice, France	2017	8 hours
- Oral presentation, diversity meeting, department MGZ, Rotterdam	2017	8 hours
- Oral presentation, Geriatriedagen, Den Bosch	2018	8 hours

Symposiums and workshops		
- Seminars at the department of Public Health, Erasmus MC, Rotterdam	2014-2018	50 hours
- Journal clubs and research meetings of the Youth section at the department of Public Health, Erasmus MC, Rotterdam	2014-2018	50 hours
- GENERO symposium, Ondersteuning mantelzorgers van mensen met dementie, Rotterdam	2016	4 hours
- GLOBE symposium; over kansen keuzes en omstandigheden, sociaaleconomische verschillen in ongezond gedrag verklaard, Rotterdam	2017	4 hours
- Expertmeeting van kennisnetwerk “Diversiteit in zorg”, Amsterdam	2018	4 hours
- Smarter choices for better health, Rotterdam	2018	4 hours
(Inter)national conferences		
- EUGMS, Rotterdam, The Netherlands	2014	16 hours
- CHAFEA, The Hague, The Netherlands	2015	16 hours
- Innovation in Healthy Ageing Summit, Brussels, Belgium	2015	16 hours
- Urban Heart pre-conference, Manchester, United Kingdom	2015	8 hours
- Public Health festival, Manchester, United Kingdom	2015	8 hours
- UHCE final conference, Brussels, Belgium	2017	8 hours
- EUGMS, Nice, France	2017	16 hours
- Geriatriedagen, Den Bosch, The Netherlands	2018	8 hours

2. Teaching	**Year**	**Workload (Hours/ ECTS)**
Revising		
- Second year pleas	2015	16 hours
- Bachelor essays	2015	16 hours
Supervising		
- SPSS computer practicals Biostatistical methods I	2015	16 hours
- Advise, aid with methodology and co-author visiting fellow with systematic review	2016	28 hours
- Community project students minor Public Health	2017	28 hours
- Advise, aid with methodology and co-author colleague PhD student	2017-2018	28 hours

3. Other activities		Year	Workload (Hours/ ECTS)
-	Member of the junior representatives consultation, department of Public Health, Erasmus MC	2014-2015	14 hours
-	Secretary of the 'care for older persons' consultation, department of Public Health, Erasmus MC	2014-2015	16 hours
-	Site visits within UHCE to Manchester, Pallini, Rijeka and Valencia	2014-2015	28 hours
-	Contributions to EU proposals in the area of preventive elderly care	2014-2015	16 hours
-	Writing accepted personal Zon-mw grant: 'Socioeconomic and ethnic inequalities in frailty among older persons'	2015	28 hours
-	Project leader of the Zon-mw funded project: 'Socioeconomic and ethnic inequalities in frailty among older persons'	2015-2017	16 hours
-	Member of the TOPICS-MDS Special Interest Group on Diversity among older persons	2015-2016	8 hours
-	Peer-review for journals BMJ Open, PLOS One, Quality of Life Research, and The journal of nutrition, health and aging	2015-2018	20 hours
-	Pitching of and advise on accepted Zon-mw grant: 'E-health voor gezond en actief ouder worden.'	2017	4 hours

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