Determinants of Disability in the Elderly

Ümit Taş

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Determinants of Disability in the Elderly

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CHAPTER 1

General introduction; research questions

INTRODUCTION

A person who suffers disability experiences difficulty or inability in performing the basic activities with regard to daily living. In general the risk of disability increases with age and constitutes a common health problem among the elderly [1]. Incidence rates in the literature for disability range from 4.6% to 46% depending on the length of follow-up and population characteristics [1-6].

Moreover, physically disabled elderly have a higher risk of dying or being institutionalised [7]. Maintenance of physical function, which represents the absence of disability, has been mentioned by researchers as one of the criteria of successful aging [8]. Disability is also to some extent inversely proportional to quality of life (QoL). The phenomenon that still a large proportion of elderly with a disability perceive their QoL as good, which is called the disability paradox , may be explained by the influence of other factors like lower disease burden and greater levels of psychosocial resources [9].

Disability, in most cases a chronic condition, also yields economical and logistical challenges for society. As the older persons, most likely women, caring for their impaired spouse, become disabled themselves more people will need extended health care comprising the use of assistive technology, professional care givers and nursing homes.

Conceptual framework

The conceptual framework in which disability is defined is dynamic. In 1980 the International Classification of Impairments, Disabilities and Handicap (ICIDH) was developed on initiative of the WHO in order to offer a theoretical basis for research [10]. In this model disorders may lead to impairments of psychological, physiological or anatomical structures. Impairments may lead to disability, inability or difficulty with respect to an activity. Experiencing disadvantage in life due to an impairment or disability results in handicap. In 2001 the ICIDH was revised into the International Classification of Functioning, Disability and Health (ICF), shifting the focus from cause to impact [11]. The ICF comprises body functions and structures, activities and participation and environmental factors (figure 1).

There are many ways of assessing disability as indicated by the large number of disability indices that have become available in time. The best known instrument is probably Katz' Index of Activities of Daily Living (ADL) by which performance is assessed in six functions: bathing, dressing, toileting, transfer, continence and feeding [12].

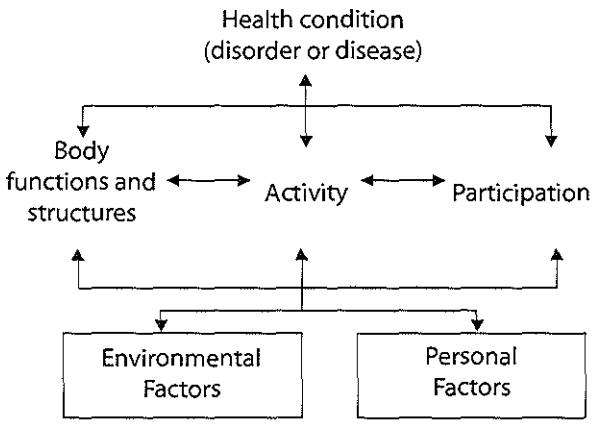

Figure 1. The conceptual framework of ICF (source: WHO 2001, International Classification of Functioning, Disability and Health).

In this thesis we use the Health Assessment Questionnaire Disability Index (HAQ DI) for assessment of disability. The HAQ DI comprises twenty four questions in the following eight domains: dressing and grooming, rising, reach, hygiene, eating, walking, grip and activity [13]. Most of these questions correspond to items of the ICF domains of mobility, self care and domestic life within the 'activities and participation' section. The HAQ therefore can be placed in the conceptual framework of the ICF.

Aim and outline of this thesis

The main objective of this thesis is to identify risk factors and prognostic factors of disability and to study possible secular changes of disability in community-dwelling elderly. The factors that were considered comprise mainly determinants that can be easily obtained in a primary care setting by history taking, physical examination or exploratory laboratory studies.

In chapter 2 existing evidence for the risk factors of incident disability is studied by means of a systematic review of the literature. Chapter 3 comprises the description of our study on risk factors of disability using original data from the Rotterdam Study. In chapter 4 a systematic review on the course and prognostic factors of prevalent disability is presented followed by our findings on prognostic factors of disability from the Rotterdam Study in chapter 5. In chapter 6 prevalence of disability and other health outcomes are compared between the two consecutive cohorts of the Rotterdam Study. Chapter 7 describes the development of a prediction model for disability. In chapter 8 finally the main findings of chapters 2 to 7 and their implications are discussed.

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CHAPTER 2

Risk factors of incident disability in the elderly: a systematic review

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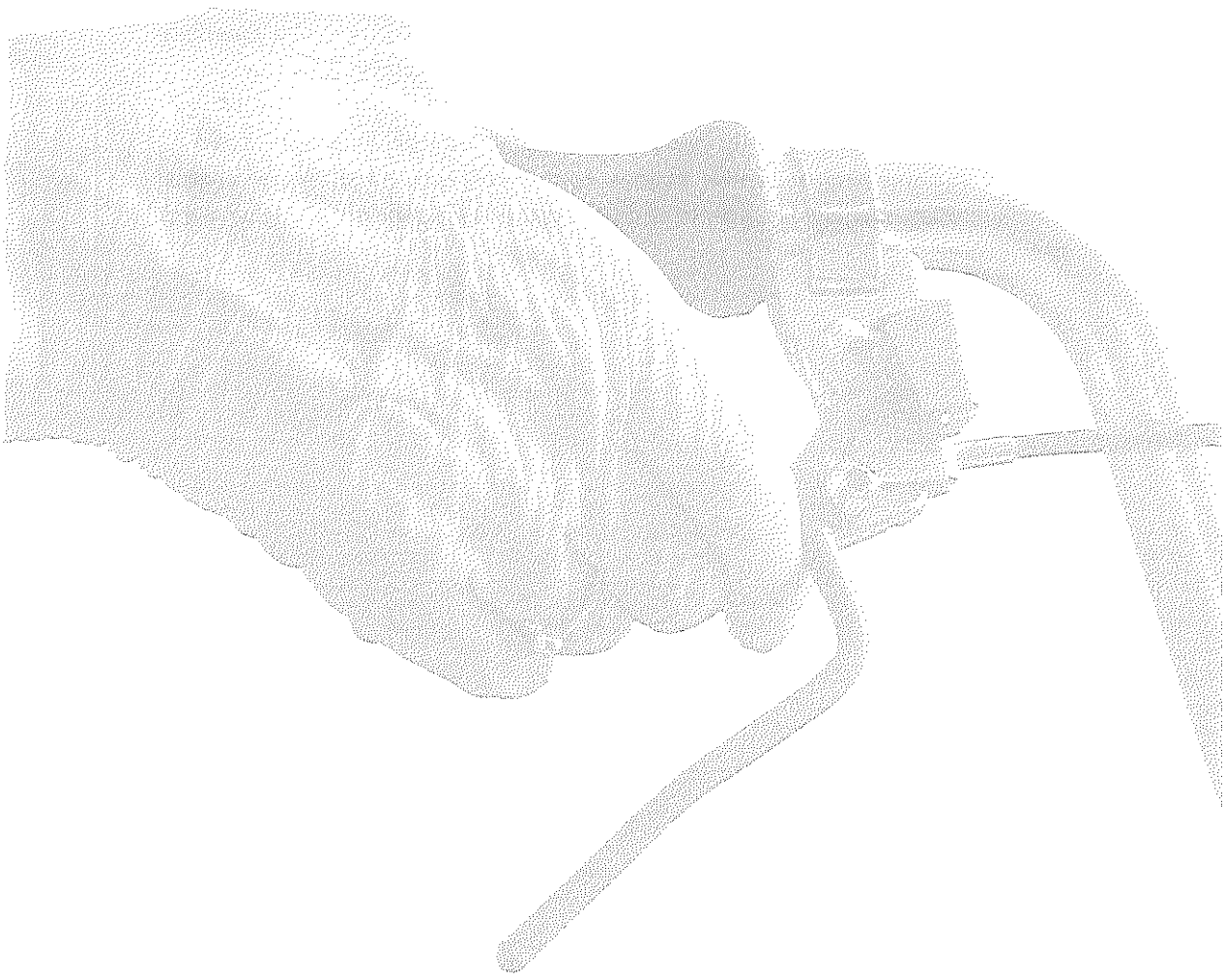
Submitted



ABSTRACT

Objective: To systematically review the evidence on the impact of sociodemographic and (bio)medical variables on incident disability in community-dwelling elderly people.

Methods: Articles were identified through searches of PubMed, Embase and PsycINFO databases and reference lists of relevant articles up to June 2009. Prospective studies investigating elderly with a disability free baseline that reported on associations between sociodemographic or (bio)medical independent variables and disability were included. Methodological quality of studies was assessed by standardised criteria after which relevant data were extracted. Finally a synthesis of the available evidence was made.

Results: Nineteen studies representing 16 different cohorts were included. There was heterogeneity among studies in definition and assessment of disability. Incidence rates for disability varied from 4.6 to 46%. Higher age, depression and comorbidity, especially arthritis were identified as moderate to strong predictors of disability.

Conclusions: Risk factors, partly modifiable, are identified that should be taken into account in developing preventive policies. Further conceptual and methodological standardisation is required in order to perform a meta-analysis and obtain higher levels of evidence.

INTRODUCTION

The increase of life expectancy due to socioeconomic and medical progress in the 20th century has yielded a population of elderly people that is growing in size and proportion. At present many Western populations are aging. In the Netherlands for instance, people aged 65 and older constitute 13% of the total population, ranging from 6% to 27% in different regions. As by 2010 the generation of the post-war baby boom will pass the age of 65, this proportion will increase further. It is estimated that by the year 2040 23% of the Dutch population will be 65 years or older. This proportion is then expected to remain stable and reach a new equilibrium [1].

Although the prospect of a longer life may rejoice many of us, the absolute and proportional increase of the older population entails troubling medical and economical consequences for the individual and society. In general the risk of disability increases with age [2]. In most cases disability is a chronic condition raising health care costs for society and reducing the quality of life of elder individuals. There are studies that have shown recovery from disability in prospective cohorts though for an overall small percentage and short lasting with recovery percentages of around 14% [3]. Furthermore physically disabled elderly have a higher risk of dying or being institutionalised [4].

Prevention of disability may therefore yield substantial profit for both individuals and society. For effective preventive interventions knowledge of risk factors is a prerequisite. No systematic approach to evaluate the impact of several risk factors on disability has been performed so far. Therefore in this paper a systematic review of the evidence for risk factors of disability based on prospective, longitudinal studies in people with a disability free status at baseline is presented.

METHODS

Search strategy and selection criteria

Through searches of MEDLINE (1966-June 2009), EMBASE (1980- June 2009) and PsycINFO (1975- June 2009) an initial set of publications were identified. The main search terms (and MESH term) were 'elder#', 'old age', 'old people', 'frail' and 'disab#' where # denotes all words starting with the preceding characters. This search was combined with the terms 'incidence', 'mortality', 'follow-up studies', 'prognos#', 'predict#' and 'course' in order to identify longitudinal studies. In addition reference lists included studies were screened for relevant publications.

Study population

Table 1 gives a description of the cohorts included in this review. In most studies baseline age was 60 years and older, only in two cohorts baseline age was 55 years [6, 7]. In total 28,103 people were included in 16 cohorts with a cohort size varying between 545-5355 people. Seven cohorts were considered large, meaning over 1000 participants. Half of the included studies were conducted in the United States (n=8), including four large cohorts based on data from the Established Populations for Epidemiological Studies of the Elderly (EPESE) or the Longitudinal Study of Aging (LSOA) [7-14] and four smaller cohorts [6; 15-17]. We also included four French studies [18-21] including one large cohort [20], one Finnish cohort [22], one large Japanese cohort [23], one large Italian cohort [24] and one large Dutch study [7]. Two studies reported on women only [15, 21], and three presented data separately for women and men [7, 11, 23].The follow-up period ranged from 1-7 years, with a mean of 4 years.

Determinants

Independent variables

The independent variables measured varied considerably over the different cohorts. When possible, cohorts used validated questionnaires (such as the Mini-Mental State Examination (MMSE) for cognition) for measuring independent variables. Most cohorts included sociodemographic determinants such as age, gender and educational level, and health conditions such as smoking, body mass index (BMI), physical activity, comorbidities, cognitive status and depression.

Dependent variable

Disability as outcome was defined dissimilarly among studies, as impaired Activities of Daily Living (ADL), Instrumental ADL (IADL), impaired walking ability, mobility disability, lower extremity disability or homeboundness. In seven cohorts a valid instrument to assess disability was used; meaning the questionnaire of Katz et al [8-11, 20, 24], or the Health Assessment Questionnaire (HAQ) [7, 15]. Incidence rates for disability varied from 4.6 to 46% [8, 17] and in four studies the disability incidence is unknown.

Associations between disability and its determinants were most often presented as odds ratios (OR's) and nine cohorts presented multivariate results (see table 1).

Table 1. Characteristics of included studies on incident disability

Cohort (authors)	Population	Independent variable	Dependent variable	Results univariate	Results multivariate	Methodol score
USA Established Populations for Epidemiologic Studies in the Elderly (EPESE) (Guralnik '01; Penninx '99) *	Community living (East Boston, Massachusetts, Iowa, New Haven); n=5355; age: > 65 years; follow-up: 7 years	Age, gender, education (< 12 years), self-rated health (poor), BMI (>30), smoking (no), mental status, number of chronic conditions (>2), stroke, diabetes mellitus	ADL Mobility disability (Katz) Incidence: 4.6%	Age (RR=3.5; 2.5-5.0) Female (RR=1.2; 0.7-2.1) Education (RR=1.3; 0.9-1.8) Self-rated health (RR=1.7; 1.2-2.3) Smoking (RR=0.9; 0.5-1.5) BMI (RR=0.8; 0.5-1.2) Mental status (RR=2.5; 1.7-3.7) Chronic conditions (RR= 5.3; 3.8-7.3) COPD (RR=1.4; 0.8-2.6) Dyspnea (RR=1.4; 1-1.9) Incontinence (RR=1.2; 0.8-1.7) Claudication (RR=1.4; 0.3-6.3)		13
Dutch Rotterdam Study (Tas '07)	Community-dwelling elderly; n=4258; age: > 55 years; follow-up: 6 years	Age, gender, education, marital status (life companion), smoking (yes), alcohol use (yes), medications, depression, cognitive function, BMI (>30), comorbidity (>2), self-rated health (worse), chronic conditions (no)	ADL (HAQ) Incidence 26.7%	All variables univariately significantly related to mild disability (not presented)	Age (OR=1.1; 1.1-1.1) Life companion (women OR=1.4; 1.1-1.9) Cognitive function (women OR=1.9; 0.9-2.8) Self rated health (men OR=1.3; 0.7-2.7; women OR=1.6; 0.8-3.2) Smoking (men OR=1.8; 1-3.2; women OR=0.9; 0.6-1.3) Alcohol use (women OR=0.9; 0.3-2.5) BMI (men OR=2.0; 1.1-3.4; women OR=1.6; 1.1-2.3) Depression (men OR=0.9; 0.6-1.3; women OR=1.2; 1-1.6) Comorbidities (men OR=2.2; 1.4-3.5) Medication use (men OR=1.1; 0.8-1.7; women OR=1.6; 1.2-2.1)	13

Cohort (authors)	Population	Independent variable	Dependent variable	Results univariate	Results multivariate	Methodol score
USA Longitudinal Study of Ageing (LSOA) (Dunlop '02; Boult '91; Lawrence '96) **	Community-dwelling elderly; n=4205; age: > 70 years; follow-up > 2 years	Age, gender, education, BMI (>30), hearing or vision impairment, chronic conditions (arthritis, cancer, diabetes mellitus, cardiovascular disease)	ADL Incidence: 10.2%	Age (β=0.12; 0.1-0.13) Arthritis (β=0.27; 0.11-43) Diabetes (β=06; 0.37-0.83) Incontinence (β= 0.46; 0.19-0.73) Vision impairment (β=0.38; 0.2-0.55) Female, education, race, cancer, cardiovascular, hearing impairment, obesity not significant		12
Italian Longitudinal Study on Aging (ILSA) (diCarlo '03)	Community-dwelling elderly; n=2639; age: >65 years; follow-up: 3 years	Age (years), gender, education (years), smoking, osteoarthritis, hypertension, heart failure, angina pectoris, myocardial infarction, diabetes, Parkinson, peripheral artery disease, dementia, stroke (first), neuropathy	ADL (Katz) Incidence: ?		Age (OR=1.07; 1.04-1.11) Education (OR=0.96; 0.92-0.99) Dementia (OR=5.62; 2.54-12.4) Stroke (OR=4; 1.39-11.46) Parkinson (OR=3.21; 1.3-7.91) Heart failure (OR=2.58; 1.44-4.61) Osteoarthritis (OR=1.98; 1.37-2.87) Gender, smoking, hypertension, angina pectoris, myocardial infarction, diabetes, peripheral artery disease, neuropathy not significant	12
USA Hispanic Established Populations for Epidemiologic Studies in the Elderly (H-EPESE) (AlSnih '01)	Community living (Texas, New Mexico, Colorado, Arizona, California); n=2108; age: > 65 years; follow-up: 2 years	Age, gender marital status, education (< 12 years), pain, depression, chronic diseases (arthritis, diabetes, stroke, cancer), BMI (>30)	ADL (Katz) Incidence: ?		Age (OR=2.09; 1.48-2.94) Female (OR=1.2; 0.84-1.72) Education (OR=1.38; 0.72-2.61) Unmarried (OR=1.09; 0.77-1.55) Any pain (OR=2.51; 1.78-3.54) Arthritis (OR=1.57; 1.14-2.17) Depression (OR=2.64; 1.68-4.15) BMI (OR=1.18; 0.77-1.8) Diabetes (OR=1.84; 1.22-2.97) Stroke (OR=1.48; 0.69-3.17) Heart attack (OR=1.7; 0.99-2.91) Cancer (OR=1.42; 0.65-3.14)	13

Cohort (authors)	Population	Independent variable	Dependent variable	Results univariate	Results multivariate	Methodol score
French Personnes Âgées Quid (PAQUID) cohort (Sauvel '94)	Community-dwelling elderly; n=1850; age: > 65 years; follow-up: 12 months	Age (years), gender (female), education (low), vision impairment, hearing impairment, dyspnea, cognitive performance, depression, joint pain	ADL (Katz) Incidence: 5.6%	Age (OR=1.07; 1.04-1.11) Female (OR=1.72; 1.17-2.54) Education (OR=1.24; 0.76-2.03) Vision impairment, (OR=1.03; 0.58-1.84) Hearing impairment (OR=1.36; 0.87-2.13) Dyspnoea (OR=1.33; 0.81-2.16) Cognitive performance (OR=0.91; 0.85-0.97) Depression (OR=2.44; 1.41-4.23) Joint pain (OR=1.31; 0.86-1.97)		12
Japanese (Okochi '05)	Community-dwelling elderly; n=786; age: > 65 years; follow-up: 7 years	Age (10 years), gender, chronic conditions	Disability Incidence: 10% male; 23% female	Age: (men RR=2.5; 1.4-4.5; women RR= 4.9; 3.4-7.1) Arthritis (men RR=1.9; 0.6-6.2; women RR=2.8; 1.5-5.2) Diabetes (men RR=1.2; 0.4-3.1; women RR=2.6; 1.2-5.9) All other diseases were not significant		12
USA McArthur study (part of EPESE) (Seeman '96)	Community living (Durham, North Carolina, East Boston, Massachusetts, New Haven); n=1031; age: > 70 years; follow-up: 2 years	Age, BMI (>27), marital status, mental status, number of chronic conditions (>3), blood pressure, depressive symptoms, social networks, emotional support, instrumental support	ADL Mobility disability (Katz) Incidence: 4.8%		Age (men OR=1.09; 0.93-1.29; women OR=1.16; 0.99-1.37) BMI (men OR=0.99; 0.88-1.11; women OR=1.12; 1.03-1.23) Physical performance (men OR=0.66; 0.23-1.89; women OR=1.64; 0.6-4.45) Cognitive performance (men OR=0.93; 0.89-0.99; women OR=1; 0.95-1.05) Depression (men OR=4.68; 1.26-17.41; women OR=5.46; 1.65-18.09) Instrumental support (men OR=4.72; 1.71-13.02; women OR=1.04; 0.59-1.84) Emotional support (men OR=1.45; 0.41-5.11; women OR=1.28; 0.48-3.44)	13

Cohort (authors)	Population	Independent variable	Dependent variable	Results univariate	Results multivariate	Methodol score
USA (Oman '99)	Community-dwelling elderly; n=997; age: > 55 years; follow-up: 4 years	Demographic (e.g. age (decade), gender, education), health status (e.g. diabetes, hypertension), health habits (e.g. smoking, BMI (>26), alcohol (high)), social functioning and support (e.g. living alone, religious), psychological (e.g. depression, self-reported health)	Disability Incidence: ?		Age (OR=2.62; 2.03-3.38) Female (OR=0.92; 0.6-1.4) Chronic illnesses (OR=1.58; 1.17-2.12) Vision problems (OR=1.56; 1.06-2.28) Exercise (OR=0.97; 0.94-0.99) BMI (OR=1.89; 1.2-2.97) Social activities (OR=0.86; 0.77-0.95) Memory (OR=1.51; 1.02-2.24) Depression (OR=1.05; 1.01-1.08)	13
Finnish (Kivela '01)	Community-dwelling elderly; n=786; age: > 60 years; follow-up: 5 years	Gender (male), age (high), education (low) occupation, marital status, self-perceived health (poor), comorbidity (yes), physical disease (yes), depression (yes), medication, smoking (yes), exercise (low), alcohol (no), social participation	ADL Incidence: 14%	Male (RR=1.0; 0.96-1.08) Exercise (RR=1.1;0.7-1.77) Smoking (RR=1.1; 0.64-1.86) Alcohol (RR=1.1; 1.01-1.14) Depression (RR=1.2; 0.78-1.8) Comorbidity (RR=1.9; 1.16-3.03)	Age (OR=6.1; 3.76-9.85) Education (OR=1.5; 0.93-2.48) Perceived health (OR=1.8; 0.91-3.49) Physical disease (OR=1.9; 1.06-3.34) Comorbidity (OR=1.9; 1.06-3.34)	13
USA (Gill '04)	Hispanics and non-Hispanic whites; n=754; age: > 70 years; follow-up: 3 years	Age, gender (female), non-Hispanic, education (years), living alone, cognitive status, depressive symptoms, chronic diseases (number), physical frailty	Disability Incidence: 46%	Age (OR=1.0; 0.8-1.3) Female (OR=1.5; 0.8-2.6) Non-Hispanic (OR=1.4; 0.6-3.1) Living alone (OR=0.9; 0.5-1.5) Education (OR=1.0; 0.9-1.1) Chronic diseases (OR=1.5; 0.8-1.1) Cognition (OR=1.5; 0.8-2.8) Depression (OR=0.9; 0.5-1.6) Frailty (OR=2.4; 1.4-4.1)		10

Cohort (authors)	Population	Independent variable	Dependent variable	Results univariate	Results multivariate	Methodol score
USA San Luis Valley Health & Aging Study (Bryant '02)	Hispanics and non-Hispanic whites; n=751; age: > 60 years; follow-up: 22 months	Age (5 years); sex; ethnicity; education level; cognitive function; comorbidity; smoking; nutrition; physical activity; falls	ADL IADL Incidence: 23%	Ethnicity, cognitive function, education not significant	Age (OR=1.58; 1.38-1.83) Female (OR=1.58; 1.07-2.32) Comorbidities (OR=1.31; 1.16-1.48) Nutrition (OR=1.65; 1.07-2.55) Smoking (OR=1.93; 1.16-3.29) Falls (OR=1.51; 1.01-3.21) Physical inactivity (OR=1.69; 1.02-2.8)	11
French (Colvez '87)	Community-dwelling elderly; n=736; age: > 65 years; follow-up: 5 years	Education, activity level, cognitive impairment, depression, anxiety, respiratory dysfunction, digestive tract disease, locomotor impairment, vascular disease, hospitalisation	Home boundness Incidence: 17%	Education (RR=3.2; non-sign) Activity level (RR=0.5; non-sign) Depression/anxiety (RR=1.5; non-sign) Cognitive impairment (RR=3.8; sign) Digestive tract disease (RR=2.1; non-sign) Respiratory dysfunction (RR=3.6; sign) Vascular disease (RR=1.8; non-sign) Locomotor impairment (RR=2.1; sign) No diseases/impairments (RR=0.2; sign)		8
USA Study of Ostoporotic Fractures (Sarkisian '01)	Women; n=657; age: > 67 years; follow-up: 4 years	High age, education, comorbidity, cognition, BMI (>29), gait speed, physical activity, social network, smoking, grip strength, vision impairment, depression	ADL (HAQ) Incidence: 20%		Age (OR=5.5; 2.1-14.7) Grip strength (OR= 0.92; 0.84-1.0) Vision (OR=0.97; 0.89-1.1) Smoking (OR=1.4; 0.81-2.4) Social network (OR=1.0; 0.93-1.1)	13

Cohort (authors)	Population	Independent variable	Dependent variable	Results univariate	Results multivariate	Methodol score
French (Bocquet '89)	Community-dwelling elderly; n=645; age: > 60 years; follow-up: 4 years	Age (>75), gender (female), comorbidities (>2), perceived health (low), poverty, feeling useless	Disability Incidence: ?	Age (OR=4.5; sign) Feeling useless (OR= 4.7; sign) Poverty (OR=3.0; sign) Female, comorbidities, perceived health not significant		7
French EPIDOS study (Carriere '05)	High functioning women; n=545; age: >75 years; follow-up: 7 years	Education; physical activity; mobility (gait speed, steps to walk, time); balance (time to complete, time to stand, difficulty); strength (grip, quadriceps); body composition (weight, body mass, BMI, waist circumference); visual acuity; perceived health, fear of falling	IADL Incidence: 33.8%	All variables univariate significant except visual acuity and waist circumference	Education (OR=1.57; 1.02-2.44) BMI (OR=2.43; 1.48-3.98) Self rated health (OR=3.47; 1.07-11.33) Physical activity (OR=1.67; 0.99-2.82) Grip strength (OR=1,78; 1.07-2.95) Gait speed (OR=1.76; 1.04-2.98) Time to complete chair stands (OR=3.41; 1.74-6.67) Fear of falling (OR=1.58; 1.01-2.46) Time to stand tandem (OR=3.04; 1.49-6.21) Predictive score	15

*data from Guralnik 2001; ** data from Dunlop et al 2002; ADL = activities of daily living; IADL = instrumental ADL; BMI = body mass index; OR = Odds Ratio; RR = relative risk.

Methodological Quality Assessment

The methodological quality differed among studies ranging from 46,7% to 100% of the obtainable 15 points. The mean methodological quality score was 79.3%.

Strength of evidence

As there was considerable heterogeneity in the way disability and independent variables were defined and assessed, the data were not pooled statistically. Instead, a best evidence synthesis was performed. In table 2 the evidence is summarised for determinants measured by two or more cohorts. Determinants only measured in one cohort are not presented here.

There is strong evidence that age, arthritis and depression are predictors of disability. There is also strong evidence that low education and smoking are not associated with incident disability.

There is moderate evidence for an association between comorbidity and disability and for no association between hearing impairment and myocardial infarction and disability. Lastly we found limited evidence for no association between race and disability.

For all other determinants we conclude that there is conflicting evidence whether there is an association or not. Concerning gender it is difficult to draw a firm conclusion, because two cohorts evaluated only a female population and in three cohorts data were presented for males and females seperately, indicating there was a different association between males and females. All other cohorts provided strong evidence for no association of gender with incident disability.

DISCUSSION

In this systematic review we summarised the evidence that is at our disposal in the literature on incident disability in the community-dwelling elderly. We found that age, arthritis, depression and comorbidity are predictors of incident disability, and that education, smoking, hearing impairment, myocardial infarctions and race were not associated with disability.

To our knowledge this is the first systematic review examining prospective studies that comprised people with a disability free status at baseline only. One systematic review

Table 2. Summary of the evidence

Independent variable	Univariable				Multivariate			
	Significant		Non-sign		Significant		Non-sign	
	Large cohorts	*Small cohorts*	*Large cohorts*	*Small cohorts*	*Large cohorts*	*Small cohorts*	*Large cohorts*	*Small cohorts*
Age	4	1		1	3	2+1f	1	1f
Female	1		2	3		1	2	1
Education (low)			3	3		1f	2	1
Smoking (no)			1	1	1m	1	1+1f	1f
Mental/cognitive impairment	1	1	1	2	1	1	1+1f	
Comorbidity (yes)	1	2		2	1m	3		
Self-rated health (poor)	1			1		1f	1	1
Depression (yes)	1			3	2+1f	1	1m	
BMI (high)			2		1+1f	1+1f	1+1m	
Physical inactivity				2		2	1	1f
Arthritis	1+1f	1	1m		2			
Diabetes	1+1f		1m		1		1	
Vision impairment	1		1			1		1f
Marital status (yes)				1	1		1	
Alcohol (yes)		1					1f	
Medication (yes)					1f		1m	
Incontinence	1		1					
Race			1	2				
Hearing impairment			2					
Dyspnea	1		1					
Cancer			1		1		1	
Stroke					1		1	
Myocardial infarction							2	
Pain				1	1			
Social activities						1		1

f means only female; m means only male participants.

has been published before on functional decline as outcome, in which samples with prevalent disability (functional impairment) at baseline were included as well, although this was reckoned with in rating the evidence [25]. Even though there is some conceptual overlap in outcome and therefore in study selection between these reviews, they represent two different approaches in accordance with the complexity of the concept of disability. While Stuck et al. defined the outcome as 'functional status decline' includ-

ing disability and/or physical function limitation in this study outcome was defined as disability only. Another difference between the studies is that this review included only studies that comprised people older than 50 years at baseline. Finally, in contrast with Stuck et al., we included sociodemographic variables in the synthesis of the evidence.

Strength and limitations of this review

Although we tried to be sensitive in our initial search, that produced over 3,000 titles on disability, the possibility exists that relevant publications or unpublished studies that would have added to the evidence may have been missed. Large cohort studies with multiple publications on single factor associations are easier to be found compared to smaller cohort studies, which might have lead to publication bias. Nevertheless we performed a rather sensitive search strategy to be able to minimise the risk of publication bias.

Notwithstanding that different countries are represented in our sample, studies published in languages other than English, Dutch, German, Turkish, French, Danish, Norwegian and Swedish were excluded which again might have caused loss of evidence. Based on language, only two -Japanese - cohorts were excluded that met the inclusion criteria after title and abstract assessment.

This review focuses on prediction models or risk models instead of single factor analysis. This way the relative attribution of multiple factors can be evaluated. Given the variability of patients a single factor rarely provides an adequate estimate on the overall risk of the patients. Furthermore general practitioners implicitly use multiple factors to estimate the risk of a patient to become disabled. An overall risk score better enables the general practitioner to estimate this risk of disability.

Methodological quality score

The quality of all included studies were high with a quality score ranging from 7 to 15 with a mean of 11.9. This could imply that either the studies were indeed of a high methodological quality or that our instrument was not sensitive enough to differentiate between studies with high or low risk of biased estimates. Another explanation could be that some of the criteria that were used for study inclusion, like relevant outcome measures, causative factors and prospective design, were also represented in the methodological criteria list, although these would only account for 3 points out of 15, leaving sufficient possibility for difference in fulfillment of other criteria. Most included

studies represented large cohorts. The idea that the quality was indeed high in general is conceivable because of the effort that is put in designing studies of this scale.

Strength of evidence

The definition of disability varies extensively across the studies included. This heterogeneity in defining disability reflects the conceptual complexity, which is discussed elaborately in the literature [26]. Despite this heterogeneity in the definition and assessment of disability in different studies we deemed it necessary to combine these outcomes. Although it would be sounder to compare measures of association using more homogenous definitions of outcome this would be at the expense of reducing the strength of evidence for these associations. Therefore we chose to combine these different definitions of disability.

In some of the studies, association measures for subsamples based on age or gender were presented separately because previous studies had shown differences in association for different gender or age groups [15, 21]. Although these studies fulfilled the inclusion criteria for this review, the results were presented in a way that makes accumulation with evidence from other studies, in which gender was introduced in the multivariate model as a covariate, troublesome.

To some extent there was analytical heterogeneity in our sample of studies. Although most studies reported multivariate odds ratios, several presented relative risks of which some were adjusted for age and gender. In some studies there was a low incidence rate of disability which resulted in low numbers of people with incident disability. In none of these studies however the authors stated to limit their number of independent variables in the multivariate analysis according to the rule of one variable per 10 cases [27]. This might have resulted in overestimation of the associations found.

Independent variables

Age is the most prominent independent variable contributing to the onset of disability. Although age cannot be modified, it may be considered in effectively targeting interventions preventing future disability. Other risk factors that may, to some extent, be influenced are depression and comorbidity, in particular arthritis.

In our sample there were only two studies that examined pain as an independent variable. Although pain may often be based on a medical condition it still may have merit as

an independent predictor of disability and be worthy of analysing. This should be taken into account in future research activities.

In general, the magnitude of the association measures in our sample of studies was low, most OR's or RR's being lower than 2. This may be due to the selection of people with a disability free baseline and the outcome of incident disability over a longer period. Strong risk factors that would have shown higher measures of association might have produced disability in an earlier period of life and thus would have given prevalent disability at the age of 50. Because prevalent disability at baseline was excluded, the association of those risk factors and disability might have been weakened.

This low magnitude of association also implies that disability is a complex phenomenon and may not easily be attributed to a single risk factor. A combination of risk factors with the strongest associations might foretell future disability more effectively.

CONCLUSION

In conclusion higher age, depression and comorbidity were identified as predictors of disability. These findings should be taken into account in targeting future preventive strategies. The necessity of further standardisation of both dependent and independent variables across studies remains in order to make pooling of the data possible. The next level of research on disability may be the creation of a prediction model based on multiple risk factors, for the benefit of the individual and society.

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CHAPTER 3

Incidence and risk factors of disability in the elderly: the Rotterdam Study

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ABSTRACT

Background: This study analysed the incidence of disability and its risk factors in multiple dimensions in community-dwelling women and men of older age, between 1990 and 1999, in Rotterdam, The Netherlands.

Methods: For this community-based prospective longitudinal study, data were obtained from the Rotterdam Study that comprised a cohort of 7983 elderly aged 55 and over. The study sample for incident disability consisted of 4258 subjects who were disability free at baseline and had complete outcome data at follow-up, six years later.

Sociodemographic factors, lifestyle variables, health conditions and disability status were assessed at baseline and follow-up. Disability was defined as a Disability Index (DI) ≥ 0.50 according to the Health Assessment Questionnaire.

Results: Multivariate analyses, performed separately due to gender differences, revealed that age, self-rated health, overweight, depression, joint complaints and medication use were predictors of disability for both men and women. Stroke, falling and presence of comorbidities predicted disability in men only while having a life companion, poor cognitive functioning, osteoarthritis and morning stiffness only predicted disability in women.

Conclusion: Identified risk factors in this study are to some extent modifiable, enabling interventive strategies, reckoning with gender differences in risk profile, in order to prevent disability.

INTRODUCTION

The increase of life expectancy due to socioeconomic and medical progress in the 20th century has yielded a population of elderly people that is growing in size and proportion. At present many Western populations are aging. In the Netherlands for instance, people of age 65 and older constitute 13% of the total population, ranging from 6% to 27% in different regions. As by 2010 the generation of the 'post-war baby boom' - referring to the increased birth rate after the end of the Second World War - will pass the age of 65, this proportion will increase further. It is estimated that by the year 2040 23% of the Dutch population will be 65 years or older. This proportion is then expected to remain stable and reach a new equilibrium [1].

Although the prospect of a longer life may rejoice many of us, the absolute and proportional increase of the older population entails troubling medical and economical consequences for the individual and society. In general the risk of disability for Activities of Daily Living (ADL), comprising bathing, dressing, toileting, transfer and feeding, increases with age [2]. In most cases disability is a chronic condition, raising health care costs for society and reducing the quality of life of elder individuals. Furthermore physically disabled elderly have a higher risk of dying or being institutionalised [3].

Incidence rates in the literature for ADL disability with different lengths of follow-up and within different age groups range from 4.6% to 46% [2, 4-7]. Kivela and colleagues report an incidence rate of 14% over five years while Penninx and colleagues report 25% over six years [8, 9]. Furthermore several studies show different levels of statistical significance for the association of certain determinants of disability among which gender, body mass index, cognitive functioning and stroke [4, 6, 7, 9-12]. A proper understanding of the contribution of determinants to the onset of disability is a prerequisite for preventive interventions in this field.

In this paper we present the incidence of disability in the Rotterdam Study. In addition we present the independent contribution of the main factors that, according to literature, may lead to disability. Other studies have addressed this subject often focusing on one determinant or a distinct group of determinants and correcting for other factors [6, 9, 11-13]. In this study we considered all plausible determinants as potential risk factors and treated them as such in the multivariate analyses.

METHODS

Study population

Data for this study were obtained from the Rotterdam Study; a population based prospective cohort study of neurological, cardiovascular, locomotor and ophthalmological diseases in the elderly. Detailed information on the Rotterdam Study has been published previously [14]. Informed consent was obtained from the participants and the Medical Ethics Committee of the Erasmus Medical Center approved the study. All 10.275 inhabitants of age 55 and older living in the Ommoord district, a district of Rotterdam, the Netherlands, were invited. Of these 7983 subjects (78%) agreed to participate. For this study we excluded 482 respondents who were diagnosed with dementia at baseline. Another 133 persons were excluded because of missing data on disability at baseline.

Comprehensive interviews were conducted at baseline (first wave), between 1990 and 1993; at the first follow-up (second wave), between 1994 and 1996; and at the second follow-up (third wave), between 1997 and 1999. The interviews covered among others the following fields that were relevant to our study: general information, activities of daily living, Rose questionnaire of cardiovascular disease, joint complaints, ophthalmology, medical history, medical consumption and life events, smoking, socioeconomic status, medication, family history and hypertension [15]. Anthropometrical and biochemical variables were measured at the research centre. The present study is based on data from the first and third waves of the Rotterdam Study as no information was collected on disability during the second wave. The follow-up period is six years. For the cross- sectional analysis of determinants of prevalent disability at baseline we used available data from the total sample of 7368 persons while for the longitudinal analysis of risk factors of incident disability at six years we used data from a sub sample comprising only 5024 persons who were disability free at baseline.

Outcome

The dependent variable in this study was disability. For the assessment of disability the Stanford Health Assessment Questionnaire (HAQ) was used [16]. The Health Assessment Questionnaire has proven to be reliable, valid and sensitive to change in both general populations and populations with a specific disease [17]. The HAQ measures disability in eight fields (dressing and grooming, rising, reach, hygiene, eating, walking, grip and activity). Each field comprises two to four items. Per item the status of the respondent is scored as able to do without difficulty (0), with some (1) or much (2) difficulty or unable to do with or without assistance (3). The highest item score determines the final

field score. The mean score of all fields constitutes the Disability Index (DI) ranging from 0.00 to 3.00. A person, for example, who experiences only some difficulty in dressing and rising without needing assistance, would be given 2 points. Dividing this by the number of fields with complete information, usually all eight, would give a DI of 0.25. If someone would be unable to perform one item in six fields that person would have a DI of (3*6)/8=2.25. In the present study respondents with a DI lower than 0.50 were considered not disabled. A DI from 0.50 to 1.00 was considered as mild disability while a DI of 1.00 or higher was regarded as severe disability [18].

Determinants

The selection of determinants was based on preliminary findings of a review of the literature and on the availability of data in our sample. All determinants were assessed at baseline.

Age and gender were assessed. Education was based on the highest level attained. Income was assessed as nett income per year and household income. Type of health insurance was assessed as private or public insurance. Marital status was based on whether or not having a life companion at baseline.

Smoking status was assessed as never, former and current smoker. Self-report of alcohol intake was approximated in grams per day. The number of medications was based on a pharmacological database.

Weight and height were measured. Body mass index (BMI) was defined as weight/height^2 (kg/m^2). Serum levels of total cholesterol and HDL-cholesterol (mmol/l) were measured. Diastolic and systolic blood pressures were measured by hand using a 'random zero' sphygmomanometer.

Cognitive status was assessed using the Folstein Mini-Mental State Examination (MMSE) [19]. Stroke was assessed as part of the Rose questionnaire [15]. Assessment of depression, Parkinson's disease, myocardial infarction, diabetes mellitus, osteoarthritis, joint complaints, morning stiffness, falls and dizziness was based on self-report (yes/no) to questions on these conditions formulated as "Do you have...?" or "Did you ever experience...?". Because of lacking direct data on pulmonary disease, use of anti-asthmatics was used as a proxy variable.

Hypertension was defined as a systolic blood pressure equal to or higher than 160 mmHg and/or a diastolic blood pressure equal to or higher than 100 mmHg. Receiving an anti-hypertensive treatment was also considered as having hypertension.

Self-rated health was defined as self-report of the perception of one's own health compared to contemporaries.

Data on vision and hearing were based on observations during the interview.

Statistical analysis

Differences in baseline characteristics were compared using Student's t-test for continuous variables, Pearson's χ^2 for categorical variables and Mann-Whitney U test for not normally distributed continuous variables.

Using SPSS10, frequencies of disability were estimated. Prevalence at baseline and incidence at six years were calculated for men and women separately.

In the analyses age was entered as a continuous variable. Dichotomised variables (with their cut-off points) were gender, marital status (life companion/ no life companion), health insurance (public/private), cognitive impairment (MMSE < 26), specific chronic conditions (present/not present), dizziness (once a month or more frequently), comorbidities (presence of two or more conditions out of eight: depression, Parkinson's disease, diabetes mellitus, hypertension, myocardial infarction, stroke, pulmonary disease and osteoarthritis), hearing and vision (impaired/not impaired), number of medications (more than two), total cholesterol (> 7.4 mmol/l) and HDL (< 1.1 mmol/l), Variables with three or more categories were education (primary, secondary, higher), household equivalent income (25^{th} and 75^{th} percentiles), smoking (never, former, current), alcohol consumption (none, 0.1-20.0, 20.0-40.0, > 40.0 gr/day), BMI (< 25, 25-30, >30) and self-rated health (better, same, worse).

After univariate analysis two logistic regression models were run to examine multivariately the contribution of each determinant to the prevalence of disability at baseline and in the disability free sub sample to the presence of disability at six years. In the analyses of prevalence, multinomial categories for the outcome variable were mild and severe disability, with no disability as reference. In the analyses for incidence these categories were mild disability, severe disability and death versus no disability. Threshold for entry and removal of independent variables in the logistic models was respectively $p < 0.05$ and $p > 0.05$. Odds ratios (OR) with confidence intervals were thus obtained.

Table 1. Baseline characteristics for total sample, completers and non-completers

Baseline characteristic	Total sample (n=7368)	Completers (n=6184)	Non-completers (n=1184)	P Value
Age, y	69.7 ± 9.2	69.4 ± 9.2	71.2 ± 8.9	.000 †
Women	60.1	58.6	68.1	.000
Life companion	63.0	64.0	58.1	.000
Educational level				.000
Low	24.7	23.2	32.7	
Intermediate	67.0	68.0	61.3	
High	8.3	8.8	6.0	
Income level				.000
Low	24.7	23.6	30.3	
Intermediate	51.5	51.6	51.0	
High	23.9	24.9	18.7	
Insurance (public)	56.0	55.0	61.3	.000
Smoking				.001
Never	35,9	35.1	39.6	
Former	41,1	42.0	36.5	
Current	23,0	22.8	23.9	
Alcohol use, g/day	10.4 ± 15.2	10.7 ± 15.4	8.6 ± 14.0	.000 †
Body mass index, kg/m^2	26.3 ± 0.5	26.3 ± 3.7	26.6 ± 3.9	.006 ‡
Self-rated health				.671
Same as contemporaries	38,2	38.2	38.5	
Better than contemporaries	51,4	51.6	50.5	
Worse than contemporaries	10,3	10.2	11.0	
MMSE	27.6 ± 1.9	27.7 ± 1.9	27.2 ± 2.0	.000 †
Depression	33.8	33.9	33.5	.798
Parkinson's disease	0.8	0.7	1.2	.080
Diabetes mellitus	6.5	6.5	6.2	.665
Hypertension	35.9	34.9	41.9	.000
Myocardial infarction	9.3	9.3	9.0	.721
Stroke	4.1	4.0	4.3	.642
Respiratory disease	5.7	5.9	4.4	.041
Osteoarthritis	24.5	24.2	26.1	.185
Joint complaints	51.5	51.5	51.5	.978
Morning stiffness	32.8	33.2	30.9	.122
Falls	16.8	16.4	18.9	.031
Hearing impairment	6.2	5.9	8.1	.005
Vision impairment	3.0	3.0	3.0	.878
Dizziness	12.4	12.2	13.2	.325
Comorbidities	20.6	20.6	21.0	.750
Medication	33.3	33.1	34.1	.529
Total cholesterol (mmol/l)	6.7 ± 1.2	6.6 ± 1.2	6.7 ± 1.2	.010 †
HDL (mmol/l)	1.4 ± 0.1	1.3 ± 0.4	1.4 ± 0.4	.031 †

Data are means with standard deviations for continuous variables and percentages for categorical variables; p values are for differences between completers and non-completers: † Mann-Whitney U test, ‡ Student's t-test, all other p values are based on χ^2 for categorical variables.

RESULTS

Of the 7368 subjects who were included at baseline 5024 (68%) were disability free. Seventy-three percent (n=3642) of those who were disability free at baseline participated in the follow-up while 715 (14.2%) refused, 51 (1.0%) were not able to complete the follow-up and 616 (12.3%) died.

In Table 1 baseline prevalence's and means of independent variables are presented for the total sample, completers and non-completers separately. Non-completers comprise persons who refused or were alive but not able to participate. Completers were those who participated or those who died, as death is included as an outcome category in the analyses.

The mean age of non-completers was higher. Compared to men, proportionally more women refused or were not able to participate to follow-up. Among non-completers there were more persons with a lower socioeconomic status. Also higher were the proportions of people with hypertension and hearing impairment among non-completers. Average alcohol consumption and cognitive functioning were higher among completers. BMI, total cholesterol and HDL were slightly lower among completers. For the majority of chronic conditions there were no significant differences between completers and non-completers.

Prevalent disability

At baseline 31.8% (n=2344) of the study population had disability. Prevalence of disability was higher for women (38.9%, n=1717) then for men (21.2%, n=627). Of those who were disabled 52.4% (n=1228) had severe disability. The proportion of severe disability was higher for women (55.5%) than for men (43.9%).

Univariate analysis showed that all variables but HDL were associated with the presence of mild or severe disability at baseline in men, cross-sectionally. After logistic regression eight of them remained associated with disability at a statistically significant level (Table 2). Higher age, self-rated health as worse than contemporaries, respiratory disease, joint complaints, morning stiffness and falling were associated with both prevalent mild and severe disability. Overweight and osteoarthritis were associated with mild disability while public health insurance, cognitive impairment, stroke and medication use were associated with severe disability. Self-rated health as better than contemporaries was associated with the absence of disability.

In women, all studied variables were univariately associated with prevalent disability at baseline. Logistic regression revealed that age, self-rated health as worse than contemporaries, overweight, osteoarthritis, joint complaints, morning stiffness, falling, medication use, vision impairment and dizziness were all associated with the presence of both mild an severe disability at baseline (Table 2). Stroke was only associated with severe disability in women as well although at a less significant level than in men. In addition depression and hearing impairment were associated too with severe disability in women. Self-rated health as better than contemporaries was associated with the absence of disability.

Table 2. Associated factors with prevalent disability: multinomial regression analysis with odds ratios (95% confidence intervals)

Independent variable	**Men**		**Women**	
	Mild disability	**Severe disability**	**Mild disability**	**Severe disability**
Age	1.1 (1.1-1.1)**	1.2 (1.2-1.2)**	1.1 (1.1-1.1)**	1.2 (1.2-1.3)**
Insurance	1.0 (0.8-1.3)	1.9 (1.2-2.9)**	-	-
Cognitive impairment	1.2 (0.7-1.9)	2.2 (1.2-3.8)**	-	-
Self-rated health†				
Same	1.0	1.0	1.0	1.0
Better	0.6 (0.4-0.8)**	0.5 (0.3-0.8)**	0.5 (0.4-0.6)**	0.4 (0.3-0.6)**
Worse	3.8 (2.5-5.9)**	7.0 (4.1-12.1)**	3.2 (2.3-4.6)**	10.3 (6.8-15.5)**
Body mass index				
Lower than 25	1.0	1.0	1.0	1.0
25 to 30	1.2 (0.9-1.5)	0.7 (0.4-1.0)	1.0 (0.8-1.2)	1.0 (0.8-1.4)
30 or higher	1.8 (1.1-3.0)*	1.6 (0.8-3.2)	1.4 (1.1-1.9)*	1.5 (1.1-2.2)*
Depression	-	-	1.2 (0.9-1.4)	1.4 (1.1-1.9)**
Stroke	1.2 (0.6-2.2)	4.2 (2.3-7.6)**	1.2 (0.6-2.3)	1.9 (1.0-3.8)*
Respiratory disease	2.1 (1.3-3.4)**	1.9 (1.1-3.5)*	-	-
Osteoarthritis	1.5 (1.1-2.2)*	1.4 (0.8-2.2)	1.8 (1.4-2.2)**	1.6 (1.2-2.2)**
Joint complaints	2.4 (1.8-3.2)**	2.2 (1.5-3.5)**	2.0 (1.6-2.5)**	2.9 (2.1-4.0)**
Morning stiffness	2.7 (2.1-3.7)**	3.7 (2.5-5.6)**	2.4 (1.9-2.9)**	5.3 (4.0-7.0)**
Falls	2.0 (1.3-3.0)**	4.3 (2.7-6.9)**	1.4 (1.1-1.7)*	1.7 (1.3-2.3)**
Medication use	1.2 (0.9-1.6)	1.7 (1.1-2.6)*	1.4 (1.1-1.8)**	1.9 (1.5-2.5)**
Hearing impairment	-	-	1.3 (0.8-2.2)	2.3 (1.3-3.8)**
Vision impairment	-	-	2.1 (1.0-4.2)*	2.9 (1.4-6.1)**
Dizziness	-	-	1.4 (1.1-1.9)*	1.5 (1.1-2.1)*
Explained variance ‡	38.6%		50.4%	

* $p < 0.05$, ** $p < 0.01$; † health compared to contemporaries; ‡ Nagelkerke R^2.

Incident disability

Of those who were disability free at baseline 26.7% (n=1129) had disability at follow-up after six years. Incidence of disability was higher for women (33.2%, n=732) then for men (19.7%, n=397). Of those with new disability at follow-up 33.0% (n=756) had severe disability. The proportion of severe disability was again higher for women (35.9%) than for men (27.7%). Nearly fifteen percent of the persons who were disability free at baseline had died at follow-up. Relatively more men (19.2%) died than women (10.3%).

All variables were univariately associated with the outcome at six years in men at a statistically significant level. After logistic regression age proved strongly predictive of both disability and death (Table 3). Self-rated health as worse than contemporaries and medication use were predictors of severe disability and death while a higher BMI was predictive of any disability. Depression and stroke emerged as risk factors of severe disability. Hypertension and current smoking were predictors of death. Joint complaints and the presence of more than one chronic condition were associated with mild disability. Falling was predictive of both mild disability and death.

Univariately, all variables except for falling and respiratory disease were significantly associated with disability and death in women at six years. Logistic regression revealed that age and medication use constituted predictors for disability and death. Living with spouse at baseline was related with mild disability and death at follow-up. Cognitive impairment, health rated as worse and depression were predictive of both severe disability and death. Current smoking and only alcohol consumption of 20 to 40 grams per day were associated with death. Overweight and osteoarthritis were predictors for both mild and severe disability. In women joint complaints were associated with severe disability and morning stiffness with mild disability though only borderline significant.

DISCUSSION

Although it is difficult to compare incidences of disability between studies due to different follow-up length, study populations and definitions of disability, we can conclude that our findings are within the range of incidences that are found in literature [8, 9]. A substantial proportion, a quarter, of our study population developed disability within 6 years. Both prevalence and incidence of disability were higher for women than for men. The present study identifies age, self-rated health, overweight, depression, joint complaints and use of more than two medications as predictors of disability for both men and women. Both male and female smokers and hypertensives had a higher likelihood

Table 3. Risk factors of disability: multinomial regression analysis with odds ratios (95% confidence intervals)

	Men			Women		
Independent variable	**Mild disability**	**Severe disability**	**Death**	**Mild disability**	**Severe disability**	**Death**
Age	1.1 (1.1-1.1)**	1.2 (1.1-1.2)**	1.2 (1.2-1.2)**	1.1 (1.1-1.1)**	1.2 (1.2-1.2)**	1.2 (1.2-1.2)**
Life companion	-	-	-	1.4 (1.1-1.9)**	1.3 (0.9-1.9)	1.6 (1.0-2.3)*
Cognitive impairment	-	-	-	1.9 (0.9-2.8)	2.6 (1.3-5.0)**	2.1 (1.0-4.4)*
Self-rated health†						
Same	1.0	1.0	1.0	1.0	1.0	1.0
Better	0.8 (0.6-1.0)	1.0 (0.6-1.6)	0.8 (0.6-1.1)	1.0 (0.8-1.3)	0.9 (0.6-1.2)	0.8 (0.5-1.2)
Worse	1.3 (0.7-2.7)	3.6 (1.5-8.7)**	2.7 (1.4-5.2)**	1.6 (0.8-3.2)	2.7 (1.2-5.8)*	2.7 (1.2-6.1)*
Smoking						
Never	1.0	1.0	1.0	1.0	1.0	1.0
Former	1.0 (0.6-1.8)	1.0 (0.4-2.3)	1.0 (0.6-1.7)	1.0 (0.8-1.3)	1.0 (0.7-1.5)	1.3 (0.8-2.0)
Current	1.8 (1.0-3.2)	1.9 (0.7-4.7)	2.1 (1.1-3.7)*	0.9 (0.6-1.3)	1.5 (0.9-2.3)	3.5 (2.1-5.6)**
Alcohol use						
None	-	-	-	1.0	1.0	1.0
1-2 drinks	-	-	-	0.8 (0.6-1.0)	1.2 (0.8-1.8)	0.8 (0.5-1.3)
3-4 drinks	-	-	-	0.7 (0.4-1.2)	1.0 (0.5-1.9)	0.3 (0.1-0.7)**
> 4 drinks	-	-	-	0.9 (0.3-2.5)	1.7 (0.5-5.9)	1.7 (0.5-5.6)
Body mass index						
Lower than 25	1.0	1.0	1.0	1.0	1.0	1.0
25 to 30	1.2 (0.9-1.6)	1.9 (1.2-3.1)*	0.8 (0.6-1.1)	1.3 (0.9-0.7)	1.5 (1.0-2.2)*	1.2 (0.8-1.9)
30 or higher	2.0 (1.1-3.4)*	2.1 (0.8-5.6)	1.3 (0.7-2.5)	1.6 (1.1-2.3)*	2.8 (1.7-4.4)**	0.7 (0.3-1.3)
Depression	0.9 (0.6-1.3)	2.4 (1.4-4.1)**	1.2 (0.8-1.8)	1.2 (1.0-1.6)	1.7 (1.2-2.5)**	1.5 (1.0-2.2)*
Hypertension	1.2 (0.9-1.7)	0.8 (0.5-1.4)	1.6 (1.2-2.2)**	1.2 (0.9-1.6)	1.1 (0.8-1.6)	2.3 (1.5-3.4)**
Stroke	0.6 (0.2-2.0)	4.6 (1.6-13.5)**	2.2 (0.9-5.4)	-	-	-
Osteoarthritis	-	-	-	1.6 (1.2-2.2)**	1.5 (1.0-2.2)*	1.3 (0.8-2.1)
Joint complaints	1.6 (1.2-2.2)**	1.6 (1.0-2.5)	1.0 (0.7-1.3)	1.3 (1.0-1.7)	1.8 (1.2-2.6)**	1.2 (0.8-1.9)
Morning stiffness	-	-	-	1.4 (1.0-1.8)*	1.3 (0.9-1.9)	1.1 (0.7-1.8)
Falls	1.7 (1.0-2.9)*	0.3 (0.1-1.2)	1.7 (1.0-2.9)*	-	-	-
Comorbidities	2.2 (1.4-3.5)**	1.0 (0.5-1.9)	1.1 (0.7-1.8)	-	-	-
Medication use	1.1 (0.8-1.7)	1.8 (1.1-3.2)*	1.8 (1.3-2.6)**	1.6 (1.2-2.1)**	2.0 (1.3-2.9)**	1.8 (1.2-2.7)**
Explained variance ‡	31.5%			28.7%		

* $p < 0.05$, ** $p < 0.01$; † health compared to contemporaries; ‡ Nagelkerke R^2.

of dying but the odds ratios for incident disability were not statistically significant. Living with spouse, poor cognitive functioning, osteoarthritis and morning stiffness predicted disability in women only while stroke, falling and the presence of more than one chronic condition predicted disability in men only.

Higher age is a major predictor with the strongest association in our study as well as in other studies. Impaired cognitive functioning, depression, stroke and osteoarthritis are well-known significant risk factors of disability in the literature and were highly significant in our study as well, although with different risk profiles for men and women [4, 9, 20-23]. We identified overweight, defined as a high BMI, as a risk factor for both men and women. In one other study in which risk factors were analysed for men and women separately no significant association was found for men [11].

Little is known about the longitudinal relation of dizziness with disability. To our knowledge there is only one other study with a prospective design exploring this relation multivariately, in which no statistically significant association was found [24]. Although in our study dizziness was associated with prevalent disability in women, we too did not find any evidence for a longitudinal influence. Socioeconomic variables, diabetes mellitus, hypertension and myocardial infarction were not identified as statistically significant risk factors of disability in this study although other prospective studies have presented evidence for their contribution to incident disability [9, 13, 25].

More chronic conditions were significantly associated with prevalent disability at baseline than with incident disability in six years. This may be because, in this study, people with disability at baseline were excluded from the longitudinal analyses therefore identifying mainly slowly disabling diseases and impairments. Furthermore the explained variance in this study for incident disability was relatively low (32% for men, 29% for women). This could imply that other conditions have emerged during follow-up that contributed rather to the onset of disability than baseline conditions.

In our sample, relatively, men had a higher education, smoked more often, consumed more alcohol, and suffered more adverse cardiovascular conditions than women. Women on the other hand suffered more conditions of the locomotor tract. To some extent this difference in exposure distribution may have a sociocultural and historical background. We hypothesise that in this generation men were more likely to have a higher education and work outdoors having more physical and social activity accompanied by smoking and alcohol consumption while women were probably raising children, having less physical exercise, gaining weight and suffering more locomotor conditions.

The difference between mild and severe disability is determined by the *level* of difficulty experienced in a field and the *number* of fields in which the respondent's ability is compromised. The impact of each determinant may therefore be qualitative and/or quantitative. In our longitudinal analyses morning stiffness was associated with mild disability while stroke and depression were associated with severe disability. One could

hypothesize that a person with chronic or recurrent morning stiffness is more likely to experience some difficulty in few fields corresponding with mild disability while someone who has remained hemiplegic after his third stroke will experience severe difficulties in many fields representing severe disability. Depression may lead to real severe disability through physical and social inactivity or to a sense of disability based on psychological aspects of the depression.

Strengths and limitations

Although many determinants of disability have been studied frequently, the majority of research is still cross-sectional in design or presentation. A major advantage of this study lies in its longitudinal design and six year follow-up, the latter being suitable for the study of disability of a more chronic nature and determinants with a lasting impact. The independent variables were all assessed prior to the onset of disability making the estimation of the incidence of disability possible. The determinants analysed in this study constitute therefore risk factors. Furthermore a large number of independent variables, which have been analysed separately in different studies, were analysed jointly in this study population revealing the independent contribution of each variable to the onset of disability. Another merit is the large population size, which was likely to contribute to the significance of identified associations.

In this study data on chronic conditions were based on self-reports. We know from literature that the agreement between self-report of diseases and other methods of assessment may vary and is determined by some patient characteristics and the nature of the condition itself. For our selection of diseases the agreement appears to be fair to good except for arthritis which may have been subject to over-reporting in especially women [26, 27].

A drawback of our study is the proportion of non-completers probably due to a longer follow-up period. Baseline characteristics differed significantly between completers and non-completers for age, socioeconomic status, lifestyle variables and certain chronic conditions. We also performed a logistic regression analysis, which showed less variables to be significantly associated with completion status compared to the p-values as presented in Table 1, indicating the differences between these two groups might not be that dramatic. Attrition was nevertheless selective with respect to baseline determinant status. This partially selective attrition has probably influenced our point-estimates and strength of relations in a way that less strong associations have been found.

Altough we did not include interaction terms in our statistical model there may have been some interaction between independent variables. The adverse disability effect of falling may for instance be higher in the depressed than in the non-depressed due to unfavourable coping mechanisms. Hypothesizing on interactions however remains difficult.

Conclusions

Our findings corroborate some of the associations between determinants and disability that were published previously by others. In addition this study explores some of the determinants that yet have been studied insufficiently, thus contributing to the knowledge and insight that are required for primary prevention of disability. Identified determinants in this study are, to some extent, modifiable. This implies that incidence of disability and treating these conditions may still reduce related individual and societal burden. However, in order to acquire a better and more accurate understanding of the incidence, transition and risk factors of disability, more longitudinal research is required, with particular consideration of gender differences.

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CHAPTER 4

Prognostic factors of disability in older people: a systematic review

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ABSTRACT

Objective: To systematically review the evidence on the influence of sociodemographic, lifestyle and (bio)medical variables on the course of prevalent disability and transition rates to different outcome categories in community-dwelling elderly people.

Methods: Articles were identified through searches of PubMed, EMBASE and PsycINFO databases and reference lists of relevant articles. Prospective population studies that assessed disability at baseline and reported on associations between potential prognostic variables and disability were included. Methodological quality of studies was assessed by standardised criteria after which relevant data were extracted. A synthesis of the available evidence was carried out.

Results: Nine cohort studies reported transition rates and eight cohort studies presented multivariate analyses on prognostic factors. There was some heterogeneity among studies in definition and assessment of disability. There is moderate to strong evidence that higher age, cognitive impairment, vision impairment and poor self-rated health are prognostic factors of disability.

Conclusions: Prognostic factors, partly modifiable, are identified that should be taken into account in targeting treatment and care for the disabled elderly. Further conceptual and methodological standardisation is required in order to enable a meta-analysis and obtain higher levels of evidence.

INTRODUCTION

Due to demographic changes and improved socioeconomic and medical achievements, many populations, especially those in the West, are aging.

As the population gets older, disability becomes one of the greater individual and societal burdens. For mobility disability Leveille *et al* reported a prevalence of 18.8% for women and 13.3% for men aged 65 to 69 years. The prevalence in the highest age category (90 to 95 years) was 83% and 63.4% for women and men respectively [1].

The pathway of disability has a complex nature comprising aging, lifestyle factors and medical conditions. Although the benefits of improved socioeconomic conditions and medical care have prolonged total life expectancy this is not the case for active life expectancy. In the absence of widespread preventive strategies, occurrence of precursors of disability and therefore disability itself will as yet remain unaltered [2]. Hence it is important to study prognosis of disability as the dynamic nature of disability may enable intervention on modifiable (prognostic) factors to alter its course to a more favourable outcome. Recovery from disability has been reported to occur. A better understanding of the disability process may help in targeting effective treatment by defining risk groups for adverse outcomes.

While a systematic review on risk factors of incident disability or functional decline in the older population has been published, [3] prognostic factors have not been reviewed. The study aim was to review systematically and summarise the evidence on prognostic factors of disability in older people to guide clinical decision processes and future research.

METHODS

Search strategy and selection criteria

Through searches of PubMed (1966-2006), EMBASE (1980- 2006) and PsycINFO (1975-2006) an initial set of publications was identified. The main search terms were 'elder#', 'old age', 'old people', 'frail' and 'disab#' where # denotes truncated terms. This search was combined with the terms 'incidence', 'mortality', 'follow-up' 'studies', 'prognos#', 'predict#' and 'course' in order to identify longitudinal studies. In addition reference lists of included studies were screened for relevant publications.

Based on title and abstract information two reviewers independently included references in accordance with the inclusion criteria: disability as outcome, longitudinal study design and population older than 50 years. Full texts of the remaining articles were assessed. For this review only prospective studies with a population that was disabled at baseline were included. Disagreement of reviewers was solved by consensus. Only English, Dutch, German, French, Danish, Norwegian, Swedish and Turkish articles were considered.

Data extraction and methodological quality assessment

a standard form frequently applied in other systematic reviews of prognostic factors for patients with musculoskeletal disorders was used [4]. Relevant data were extracted from the final set of articles concerning sample characteristics, design characteristics, attrition, assessment of disability, assessment of determinants, and their association measures.

Finally, the methodological quality of each study was scored based on 15 criteria of internal and external validity. The criteria for internal validity were: prospective data collection; follow-up of at least 5 years; attrition less than 20%; standardised or valid measurements of prognostic factors; standardised or valid measurements of outcome measures; appropriate univariate crude estimates of association and appropriate multivariate analysis techniques. The criteria for external validity were: description of source population; description of inclusion and exclusion criteria; information on completers versus non-completers; assessment of relevant prognostic factors; description or standardisation of treatment in cohort; assessment of relevant outcome measures; data presentation of prognostic factors; data presentation of outcome measure. One point was given for each fulfilled criterion. Thus, the assessment resulted in an overall quality score ranging from 0 to 15. Studies with a score of 70% of the maximum obtainable points or higher were rated as high quality studies.

Dependent and independent variables

The dependent variable was disability, defined as experiencing difficulty in activities of daily living (ADL), or instrumental ADL (IADL) or a combination of both. ADL comprises basic activities like bathing, dressing, toileting, transfer and feeding, while IADL includes activities like transportation, shopping, doing housework, and preparing meals. Definitions of impaired functional status, such as dependency on assistive devices or persons, were also included. Independent variables of interest were demographic and socioeconomic factors, lifestyle factors and medical conditions.

Strength of Evidence

As only prospective cohorts of older people with baseline disability were included, it was possible to pool the data if terms of homogeneity were met. In the case of heterogeneity, a synthesis of the best evidence was performed.

The strength of evidence was rated as follows: strong evidence if more than two studies of high quality from separate databases reported a significant association ($p<.05$ or 95% confidence interval [CI] for odds ratios [OR] or relative risks [RR] not including the value 1.0) in the same direction; moderate evidence if at least two studies of high quality or four studies of low quality reported significant associations in the same direction; limited evidence if only one study of high quality or at least two studies of low quality reported a significant association; conflicting (inconsistent) evidence if less than 75% of reported significant associations were in the same direction or if more than 50% of studies showed non-significant associations; evidence for no association was provided if more than two studies showed a non-significant association. The existence of only one study, reporting a non-significant association was rated as no evidence for any association.

RESULTS

Identification and selection of studies

through database searches and reference list screenings an initial set of 2830 references was identified. Based on title and abstract information 2442 references were excluded. After assessment and exclusion 19 studies remained, of which 11 presented transitions between disability states only and eight reported on prognostic factors of disability (Figure 1). These groups were analysed and are presented separately.

Data extraction and methodological quality assessment

Transition

Studies reporting transition rates represent cohorts from the US, France, Finland, UK, and Spain. Length of follow-up ranged from 12 to 72 months (Table 1). There was considerable heterogeneity in the way disability has been defined and categorised. The various definitions and presentation of disability comprised Activities of Daily Living (ADL) only [5]; IADL, considered separately [6] or in combination with ADL [7]; mobility disability based on two items [1] and frequency of help being in ADL and/or IADL [8]. Categorisa-

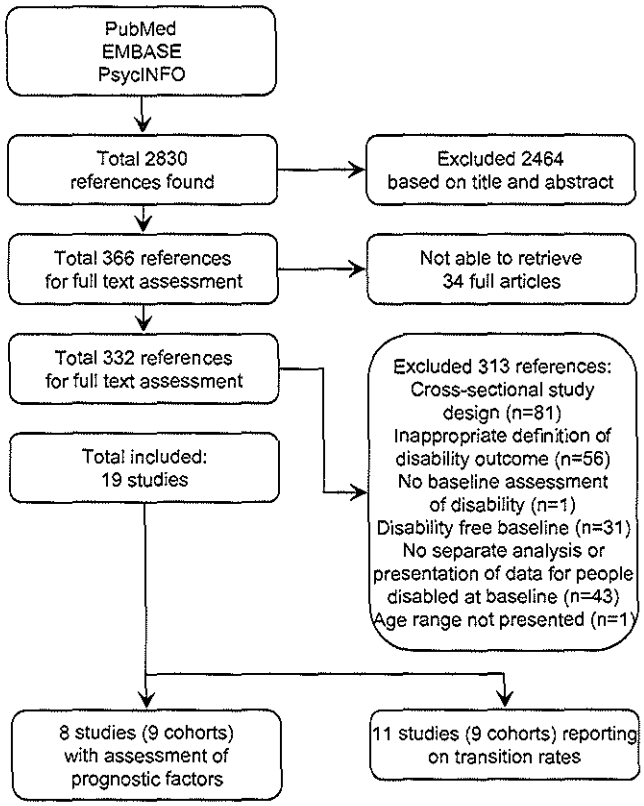

Figure 1. Reference flow prognostic review.

tion of outcome was dichotomous or categorical. In some studies death was considered as an outcome category [6, 7], in others it was not [5, 9, 10].

In general the proportion of elderly progressing to a worse disability state or death was larger than the proportion of those who recovered from disability. However, recovery from moderate and, to a lesser extent, severe disability was common in the cohorts included. Recovery rates from moderate disability in the youngest age category ranged from 3.4 to 9.0% for men and 7.9 to 11.3% for women, while in the oldest age category these rates ranged from 0 to 1.7% and from 0.7 to 2.6% respectively. Transition from severe disability to no disability ranged from 1.3 to 29.2% for men and from 1.1 to 23.5% for women in the lowest age category. In the highest age category these ranges were 0 to 11.6% for men and from 0 to 6.0% for women [1, 2, 6, 9].

Table 1. Studies on transition between disability states

Study descriptors	Author, year	Length of follow-up (months)	Age	Transition rates (%(n)) from severe to no disability			Transition rates (%(n)) from moderate to no disability		
				Men	Women	All	Men	Women	All
LSOA	Mor, 1994 [6]	72	70-79 80 +	6.9 (4) 0.0 (0)	3.5 (4) 0.0 (0)	-	9.0 (16) 1.7 (2)	11.3 (40) 2.6	-
NLTCS	Manton, 1993 [2]	24	65-74 75-84 85 +	1.26 (-) 1.35 (-) 0.0 (-)	1.08 (-) 0.45 (-) 0.0 (-)	-	3.43 (-) 2.62 (-) 0.0 (-)	7.88 (-) 2.66 (-) 0.67 (-)	-
EPESE	Leveille, 2000[a] [1]	12	70 80 90	29.2 (4) 19.8 (7) 11.6 (7)	23.5 (5) 16.1 (7) 5.3 (4)	-	-	-	-
MHCPS	Jette, 1990 [10]	60	65 +	-	-	0.2-1.3 (-)	-	-	0.9-8.8 (-)
PAQUID	Barberger, 2000 [7]	36	65-74 75-84 85 +	0.0 (0) (all ages)	0.0 (0) (all ages)	0.0 (-) 0.0 (-) 0.0 (-)	14.5 (103) (all ages)	10.0 (122) (all ages)	21.7 (167) 6.2 (55) 1.1 (3)
Jyvaskyla, Finland	Laukkanen, 1997[a] [9]		75 80	11.5 (3) 4.5 (1)	16.0 (8) 6.0 (3)	-	-	-	-
Leicestershire, UK	Jagger, 1989 [8]		75 +	-	-	2.9 (3)	-	-	6 (12)
Hackney, London, UK	Bowling, 1997 [5]	24 36	65-84 85 +	-	-	13 (3) 0.0 (0)	-	-	18 (10) 2 (1)
Leganes, Spain	Beland, 1999*	24	65-74 75 +	4.4 (4) (all ages)	2.2 (3) (all ages)	7.0 (3) 0.9 (2)	22.7 (62) (all ages)	12.2 (39) (all ages)	23.5 (52) 8.1 (30)

LSOA, Longitudinal Studies of Aging. NLTCS, National Long Term Care Survey. EPESE, Established Populations for Epidemiologic Studies of the Elderly. MHCPS, Massachusetts Health Care Panel Study. PAQUID, Personnes Agées QUID. [a]Only dichotomous disability state presented; not presented in this paper. *Beland F, Zunzunegui MV. Predictors of functional status in older people living at home. Age Ageing 1999; 28: 153–159.

Prognostic factors

Seven studies were included examining prognostic factors (Table 2). Cohorts from the US, Netherlands, Israel, Taiwan, Japan, and China were represented in this sample of studies. The methodological quality ranged from 73 to 87% indicating that all studies were of high quality. Outcome was defined differently from a single category of improvement [11] to multiple outcome categories such as improved, deteriorated-alive and deteriorated-dead [12].

Length of follow-up ranged from 3 to 120 months [13-15]. The sample size ranged from 206 to 5727 [12, 16]. Associations between outcome and determinants were presented as RRs, ORs, or standardised coefficients. The magnitude of the associations between

Table 2. Summary of studies on prognostic factors

Study descriptors	Author, year	Outcome definitions	Independent variables	Length of follow-up (months)	Sample size	Baseline age (years)	Women (%)	Methodological quality score	Measure of association
EPESE (NH, NC)	Mendes de Leon, 1997 [15]	Recovery Death	Age, sex, education, income, BMI, cognitive function, no. of chronic illnesses, race	120	?	65+	63.4	11	OR
EPESE (NH, EB, I)	Salive, 1994 [11]	Impovement (mobility, ADL)	Visual function	12	1083 340	70+	66	10	RR
NLTCS	Boaz, 1994 [12]	Improved Deteriorated-alive Deteriorated-dead	Age, sex, insurance, hospitalization, chronic condition, mortality rate, cognitive function	24	5722	65+	?	11	Coefficient, probability
PAQUID	Sauvel, 1994 [14]	Independent Dependent	Age, sex, residence, education, visual impairment, hearing impairment, joint pain, dyspnoea, cognitive function, depression	12	1850	65+	58.5	12	OR
NH, CT	Hardy, 2005 [13]	Time to recovery	Age, sex, race, education, living conditions, comorbidity, medications, BMI, cognitive function, depression, psychological factors, social factors, physical activity, smoking, alcohol, physical tests, prior disability status	3 (7.2±8.5)[a]	420	70	64.8	13	OR
Israel	Walk, 1999 [18]	Improvement (bathing, eating, continence, mobility)	Age, sex, functional factors, institutional factors (length of stay, quality of care)	36 (?)	2527	65+	73.6	10	OR
Taiwan	Zimmer, 1998 [17]	Independent Dead	Age, sex, education, marital status, residence, social network, activity level, smoking, alcohol, self-rated health	48	947	60+	56	13	Standardised coefficient
Japan	Liu, 1995 [16]	Not disabled Disabled Dead Non response	Age, sex, education, marital status, residence, social network, chronic disease, activity level, smoking, alcohol, self-rated health, loneliness	36	206	60+	54.6	12	Coefficient, probability

EPESE= Established Populations for Epidemiologic Studies of the Elderly. NH = New Haven. NC = North Carolina. EB = East Boston. I = Iowa. NLTCS = National Long Term Care Survey. PAQUID = Personnes Agées QUID. CT = Connecticut. BMI = body mass index. ? unclear presentation. [a]mean ± standard deviation (proportional hazards regression). OR = odds ratio, RR = relative risk, HR = hazard ratio.

determinants of recovery from disability and worsening of disability are presented with their statistical significance (Table 3).

Table 3. Prognostic factors and their association with disability outcome

Prognostic factors	Cohort	Association with recovery (rec) or deterioration (det)
Age	Me97 (E-NH)	OR (rec) = 0.94 (0.91-0.96)
	Me97 (E-NC)	OR (rec) = 0.96 (0.93-0.98)
	Bo94	β (det) = 0.618 ($p < 0.01$)
	Su94	($p < 0.01$)
	Wa99	NS
	Zi98	β (rec) = -0.054 ($p < 0.01$)
	Lu95	β (rec) = -0.100 ($p < 0.01$)
Gender	Me97 (E-NH)	NS
	Me97 (E-NC)	NS
	Bo94	NS
	Su94	NS
	Wa99	OR (rec) = 1.66 ($p < 0.05$) (male to female; bathing)
	Zi98	NS
	Lu95	NS
Race/ ethnicity	Me97 (E-NH)	OR(rec) = 0.62 (0.42-0.93); (black to white)
	Me97 (E-NC)	NS (black to white)
	Zi98	NS (mainlander)
Education	Me97 (E-NH)	OR (rec) = 0.95 (0.92-0.98) (lower to higher level)
	Me97 (E-NC)	NS
	Su94	NS
	Zi98	NS
	Lu95	NS
Income	Me97 (E-NH)	OR(rec) = 0.56 (0.36-0.86) (low to high)
	Me97 (E-NC)	NS
Marital status	Zi98	β (rec) = 0.298 ($p < 0.05$) (married to unmarried)
	Lu95	NS
Insurance	Bo94	NS
Residence	Su94	MD (rec) ($p < 0.01$) (non-urban)
Social network	Zi98	NS (socializing, organisational membership)
	Lu95	NS (social contacts)
	Lu95	β (rec) = 1.219 ($p < 0.01$) (social participation)
	Lu95	β (rec) = 0.331 ($p < 0.01$) (social support)
Loneliness	Lu95	NS
Emotional support	Zi98	NS

Prognostic factors	Cohort	Association with recovery (rec) or deterioration (det)
Institutional factors	Wa99	OR (rec) = 0.52 ($p < 0.01$) (length of stay; mobility)
	Wa99	OR (rec) = 1.72 ($p < 0.05$) (quality of care; bathing)
Hospitalisation	Bo94	β (det) = 1.126 ($p < 0.01$) (for a longer period)
Functional factors	Wa99	OR (rec) = ? (no. of activities with improvement/decline)
Physical activity level	Zi98	NS
	Ha05	HR (rec) = 1.04 ($p<0.001$) (time to recovery)
Self-rated health	Zi98	β (rec) = 0.443 ($p < 0.01$)
	Lu95	β (rec) = 0.596 ($p < 0.01$) (better)
Cognitive function	Me97 (E-NH)	OR (rec) = 0.70 (0.50-0.97) (poor)
	Me97 (E-NC)	OR (rec) = 0.49 (0.36-0.65) (poor)
	Bo94	β (det) = 0.502 ($p < 0.01$) (impaired)
	Su94	OR (no rec) = 2.6 ($p < 0.01$) (impaired)
Depression	Su94	NS
Visual impairment	Sa94	OR (rec) = 0.5 (0.3-0.9) (mobility)
	Su94	OR (rec) = 0.52 ($p < 0.05$) (IADL)
Hearing impairment	Su94	NS
Joint pain	Su94	NS
Dyspnoea	Su94	NS
Smoking	Zi98	NS for recovery
	Lu95	NS
Alcohol	Zi98	NS
	Lu95	NS
Body Mass Index	Me97 (E-NH)	NS for recovery
	Me97 (E-NC)	OR (rec) = 0.65 (0.48-0.96) (> 27 kg/m2)
	Me97 (E-NC)	OR (rec) = 0.59 (0.43-0.81) (< 23 kg/m2)
Chronic diseases	Me97 (E-NH)	NS for recovery
	Me97 (E-NC)	OR (rec) = 0.87 (0.77-0.98) (presence)
	Bo94	NS for recovery
	Lu95	NS
Population mortality rate	Bz94	NS

OR = odds ratio, β = regression coefficient, NS = statistically not significant. Me97, Mendes de Leon et al, 1997 [15]: E-NH, EPESE – New Haven; E-NC, EPESE – North Carolina (EPESE = Established Populations for Epidemiologic Studies of the Elderly); Bo94, Boaz 1994 [12]; Su94, Sauvel et al 1994 [14]; Wa99, Walk et al 199918; Zi98, Zimmer et al, 1998 [17]; Lu95, Liu et al, 1995 [16]; Ha05, Hardy and Gill, 2005 [13]; Sa94, Salive et al 1994 [11].

Level of evidence

Because of the heterogeneity in length of follow-up, definition of outcome and presentation of the association the data were not pooled. A best-evidence synthesis was performed instead. Death as an outcome was not taken into consideration since only

four of the seven studies included this outcome in multinomial analysis. Furthermore, death cannot be regarded as the end of a spectrum of disability.

Based on these seven studies (eight cohorts) there was strong evidence that age and cognitive functioning are prognostic factors of disability. Higher age and cognitive impairment reduced the chances of recovery from disability or increased the risk of deterioration. There was moderate evidence that better self-rated health was associated with a more favourable disability outcome, and that visual impairment decreased the chances of recovery from disability. Evidence for income, marital status, residence, social network characteristics, institutional factors, hospitalisation, body mass index and physical activity level as prognostic factors for disability was limited. For several factors some evidence for no association was found: sex, education, ethnicity or race, smoking, alcohol use and presence of chronic diseases. No evidence for any association was found for insurance, loneliness, emotional support, depression, hearing impairment, joint pain, dyspnoea, and population mortality rate with the outcome of disability. No conflicting evidence was found (Table 4).

Table 4: Prognostic factors and their level of evidence

Level of evidence	Prognostic factor
Strong evidence for association	Age (older) Cognitive function
Moderate evidence for association	Self-rated health Visual impairment
Limited evidence for association	Income Marital status Residence (non-urban) Social network characteristics Institutional factors Hospitalisation Body mass index Physical activity level
Some evidence for no association	Sex Race/ ethnicity Education Smoking Alcohol Chronic diseases
No evidence	Insurance Loneliness Emotional support Depression Hearing impairment Joint pain Dyspnoea Population mortality rate

DISCUSSION

This article describes the first systematic review on potential prognostic factors of disability. Strong evidence was found that age and cognitive functioning are important prognostic factors. Self-rated health and visual impairment are prognostic for disability outcome as well, though to a lesser degree. Higher age increases the chances of becoming disabled or, once disabled, of deteriorating. High age also decreases the likelihood of recovering from disability. Although age and cognitive functioning are not modifiable prognostic factors, they must be taken into account in targeting care as they indicate high-risk for increasing disability. Visual impairment is modifiable to some extent; in some cases it may be relieved by surgery, use of ophthalmological devices, or even by good lighting conditions in the home. The reported effect of self-rated health on incidence and prognosis of disability is somewhat unclear. On the one hand, perception of health itself might have a contribution to health outcome, becoming a self-fulfilling prophecy. On the other hand it might indicate unrecognised conditions or a combination of conditions that lead to a certain health outcome.

For other sociodemographic, environmental, lifestyle, and health variables there is, as yet limited or no evidence for their association with disability outcome. This may well be due to the small number of studies that assessed these variables, hence these results should be interpreted with caution. This caution might especially apply to physical activity levels as they are plausibly of importance for musculoskeletal impairment and hence for disability.

Some evidence was found for no association at different levels for sex, ethnicity, education, smoking, alcohol use and the presence of chronic diseases. Although, in general, relatively more women become disabled than men and relatively more men die than women it seems that once disabled, an individual's sex is of no importance for the course of the disability, when adjusted for other factors. Chronic diseases play a role in the incidence of disability. Once prevalent, the course of disability is not much altered by their presence at baseline.

Methodological quality

Most studies in this review, representing large cohorts, proved to be of a high methodological quality in general. This was also the case with respect to internal validity items. An explanation for this relatively uniform high quality may lie in the choice of inclusion criteria for this review, making it only possible for longitudinal, prospective studies to be included. As these are mostly larger cohorts where great effort is put into their investigation, this may influence their methodological quality in a positive manner.

Strengths and limitations of this Review

An important strength of this review is that prognostic factors are now systematically summarised, showing evidence available and the areas in which research is still lacking. Although the initial search was relatively sensitive and produced over 2000 titles on disability, the possibility exists that relevant publications or unpublished studies that would have added to the evidence were missed.

Although different countries are represented in the sample, studies published in languages other than English, Dutch, German, Turkish, French, Danish, Norwegian, and Swedish were excluded, which may have caused loss of evidence.

Although disability was defined mostly in terms of ADL or IADL, there still was considerable heterogeneity in the way disability and age were categorised, affecting transition rates. Besides the fact that recovery rates were lower in higher age categories and occurred more often in people with moderate disability than in those with severe disability, findings, especially with respect to sex differences, were not very consistent.

Implications for future research

Although there are other studies with disability-free or mixed baseline status, as yet there are not many studies on factors that influence the prognosis of disability once it is present. In this review of descriptive longitudinal studies some prognostic factors, such as age and cognitive functioning, were identified with strong-to-moderate evidence based on sufficient numbers of studies on the association. The finding that there is, as yet, limited evidence for the contribution of other plausible and modifiable factors, like body mass index and physical activity, may have more implications for future research, as these factors should be studied more frequently in older people with disabilities. If the number of studies were increased, strong evidence justifying interventional strategies in people with disabilities may be found. If the available evidence however would remain absent or limited this would rather justify preventive strategies in non-disabled older people. Besides tracking this evidence, the next level of research would be to summarise the evidence for existing preventive and interventional treatment programmes and randomised controlled trials, as this was beyond the scope of the review. Finally, although extensively used concepts like ADL and IADL give a common basis for many investigators, heterogeneity in the way they are implemented in research still exists. Further standardisation of assessment and analysis of disability and its prognostic factors in future research is still needed.

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CHAPTER 5

Course and prognostic factors of disability in community-dwelling elderly people with mild disability: the Rotterdam Study

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Submitted

ABSTRACT

Objective: To study the prognosis of community-dwelling elderly with mild disability and its determinants in a general population of older people.

Methods: For this community-based prospective longitudinal study, we used data from the Rotterdam Study that comprised a cohort of 7983 community-dwelling elderly. The study sample of people with mild disability and complete data at baseline and at follow-up, six years later, consisted of 1166 subjects. The determinants evaluated were sociodemographic factors, lifestyle variables, health conditions and disability status assessed at baseline and follow-up. Mild disability was defined as a score on the Health Assessment Questionnaire resulting in a Disability Index (DI) between 0.50 and 1.00. The DI ranges from 0 – 3, with 0 meaning no disability and 3 meaning severely disabled.

Results: Nearly 18% of the study population recovered from mild disability, while 20% stayed mildly disabled. The kind of disabilities varied between people. Another 31% shifted into a severe disability state, while 32% deceased. Relatively more men died while a larger proportion of women had a worsened disability outcome. Multivariate analyses revealed that age, gender, income, self-rated health and alcohol use were predictors of disability prognosis.

Conclusions: Out of over 30 determinants just a few prognostic factors appeared to be related to disability six years later. Only one determinant, age, was related to disability recovery.

INTRODUCTION

Due to demographic changes and improved socioeconomic and medical achievements, many populations, especially those in the West, are aging. As people tend to get older, disability becomes more prevalent. To prevent disability or disability decline in the elderly is one of the major challenges to society and the health care system.

Prevalence of disability ranges from 18.8% for women and 13.3% for men aged 65 to 69 years to 83% and 63.4% for women and men respectively in the highest age category (90 to 95 years) [1, 2]. The point prevalence of disability in the Dutch Rotterdam Study was 31.8% in a population of 55 years and over [3]. Prevalence estimates differ depending on the definition of disability used. The definitions that were most often used are: ADL disability, Instrumental ADL (IADL) disability and mobility disability. ADL comprises basic activities like bathing, dressing, toileting, transfer and feeding while IADL includes activities like transportation, shopping, doing housework and preparing meals. Impaired walking ability, lower extremity disability and homeboundness were all considered as mobility disability [4]. As the prevalence of disability in the older population is relatively high prevention of disability and of disability decline will remain a challenge to society.

Although the general idea about disability is unidirectional in the sense that disability is irreversible, there are studies that have shown recovery from disability in prospective cohorts, though for an overall small percentage and short lasting [1, 5-7]. Recovery percentages found range from 14.5% to 60%, depending on gender (women have higher chance of recovery) and age [6, 7]. Generally there is a need for insight in factors related to (non)recovery which might lead to efforts that warrant long lasting independence.

Studying risk factors for disability has already resulted in development and implementation of preventive interventions [8-10]. Prospective studies of baseline variables that determine the course of disability are necessary for targeting intervention strategies. Population-based longitudinal studies on prognostic factors of disability, however, are scarce [4]. A recent systematic review on prognostic factors for disability found strong evidence that age and cognitive functioning were related to functional decline, but limited to no evidence (limited or no studies evaluated these factors) was found for sociodemographic, lifestyle and health variables such as the influence of physical activity levels, depression and joint pain [4]. Because factors of incident disability seem to differ from those that drive transitions [3, 4] more primary studies are necessary evaluating factors that are related to disability recovery or decline. The notion that recovery from disability is possible enables development of further curative strategies.

With the present study we aim to get more insight in the worsening of disability to help clinicians, mainly general practitioners, to assist their patients in preventing severe disability. Therefore the present study presents transition rates from disability to various prognostic endpoints, such as recovery or severe disability, and analyses specifically the contribution of sociodemographic, lifestyle and health variables to the course of disability.

METHODS

Population

Data were obtained from the Rotterdam Study, carried out in the Netherlands. The study population is comprised of the participants to the Rotterdam Study from April 1990 to July 1993 [11]. The Rotterdam Study is a prospective cohort study among the inhabitants aged 55 years and older living in the Ommoord district, of Rotterdam, the Netherlands. All 10,275 inhabitants were invited to participate and 7983 subjects (77.8%) agreed to participate, of whom 4878 (62%) were women. For this study we excluded people because of missing data on disability at baseline, resulting in a cohort of 7368 subjects.

At baseline, from 1990 to 1993, comprehensive interviews were conducted during home visits by trained researchers (first wave). They were repeated at the first follow-up between 1994 and 1996 (second wave) and at the second follow-up between 1997 and 1999 (third wave). The interviews covered, among others, the following fields that were relevant to this study: sociodemographic information, activities of daily living, the Rose questionnaire (dealing with cardiovascular disease) [12], joint complaints, medical history, medical consumption and life events, smoking, socioeconomic status, medication, family history and hypertension. Anthropometrical, ophthalmology and biochemical variables were measured during visits at the research centre.

The present study is carried out with the data of the first and third wave of the Rotterdam Study, because disability was not evaluated in the second wave. This means we have a follow-up period of six years. In a previous study we evaluated factors related to the occurrence of disability [3]. In the present study we are interested in factors related to the recovery or decline of disability, therefore the study sample consists of people who were at least mildly disabled at baseline, defined on the basis of a disability index.

OUTCOME MEASURES AND INSTRUMENTS

Outcome

Disability

For the assessment of disability the Stanford Health Assessment Questionnaire (HAQ) was used [13]. The HAQ, introduced in 1980, is designed to represent a model of patient-oriented outcome assessment [14]. The HAQ measures disability in eight fields (dressing and grooming, rising, reach, hygiene, eating, walking, grip and activity). Each field comprises two to four items. Per item the status of the respondent is scored as able to do without difficulty (0), with some (1) or much (2) difficulty or unable to do with or without assistance (3). The highest item score determines the final field score. The mean score of all fields constitutes the Disability Index (DI) ranging from 0.00 to 3.00. A person, for example, who experiences only some difficulty in dressing and rising without needing assistance, would be given 2 points. Dividing this by the number of fields with complete information, usually all eight, would give a HAQ-DI of 0.25. If someone would be unable to perform one item in six fields that person would have a HAQ-DI of (3*6)/8=2.25.

Overall, the estimated population mean HAQ-DI was 0.25 (95% confidence interval 0.22-0.28) [14]. There is little consensus on what the cutoff points are for designating a significant level of disability. Some authors suggest for the general population a cutoff value for defining disability (yes/no) of an HAQ-DI > 0 [15] or an HAQ-DI >1.0 [16]. We defined cutoffs in concordance with other publications from the Rotterdam Study, meaning that respondents with a HAQ-DI lower than 0.50 were considered not disabled; with a HAQ-DI from 0.50 to 1.00 as mildly disabled while a DI of 1.00 or higher was regarded as severe disability [17].

Outcome was defined as the disability status at follow-up six years later. This outcome was categorised as: 1) recovery from disability, 2) transition to severe disability and 3) death, which represent mutually exclusive or competitive states.

Determinants

The selection of determinants was based on findings of a systematic review of the literature and on the availability of data in our sample [4, 11].

Sociodemographic variables

Age and gender were assessed. Education was based on the highest level attained while income was assessed as net income per year. Marital status was based on self-report of having a life companion at baseline.

Lifestyle factors
Smoking status was assessed and dichotomised as current smoker. Alcohol intake was assessed and the number of medications was based on the database of the local pharmacists.

Biometric variables
Weight and height were measured. Body mass index (BMI) was defined as weight/height^2 (kg/m^2). Serum levels of total cholesterol and HDL-cholesterol (mmol/l) were measured. Diastolic and systolic blood pressures were measured by hand using a 'random zero' sphygmomanometer.

Medical conditions
Cognitive status was assessed using the Folstein Mini-Mental State Examination (MMSE) [18]. Stroke was assessed as part of the Rose questionnaire. Assessment of myocardial infarction, Parkinson's disease, osteoarthritis, diabetes mellitus, depression, morning stiffness and joint complaints was based on self-reports (yes/no) to questions on these conditions formulated as "Do you have...?" or "Did you ever experience...?". Hypertension was defined as a systolic blood pressure equal to or higher than 160 mmHg and/or a diastolic blood pressure equal to or higher than 100 mmHg. Receiving an anti-hypertensive treatment was also considered as having hypertension. Self-rated health was defined as self-report of the perception of one's own health compared to contemporaries and rated as same, better or worse.

Analysis

All variables were assessed at baseline and at 6-year follow-up. The analyses were performed with SPSS 11.0 for Windows. We calculated frequencies of disability and death and transition from mild disability to recovery, severe disability or death.

The dependent variable was change in disability status (three levels), and the independent variables were sociodemographic variables (5 variables), lifestyle factors (3 variables), biometric variables (6 variables) and medical conditions (10 variables).

In the analyses we entered age as a continuous variable (in years) and self-rated health as conceived level of health compared to contemporaries (same, better or worse). All other variables were dichotomised, with cut-off points: gender (male/female), education (primary/higher), income (€ 955/month), marital status (life companion/ no life companion), BMI (28.4 kg/m^2, highest quartile), total cholesterol (7.4 mmol/l, highest quartile), HDL (1.1 mmol/l, highest quartile), cognitive functioning (MMSE = 27, highest

quartile), individual chronic conditions (present/not present), presence of more than one condition (yes/no), smoking (yes/no), any alcohol intake (yes/no) and number of medications (two). Preferably the choice of cut-offs was based on the literature, either using the mean/median, or the highest quartile as a cut-off and consistent with other publications of the Rotterdam Study.

The influence of the independent variables on disability was assessed using univariate and multivariate regression models. The continuous variable age was checked for linearity. Next, multinomial regression models were run to examine the contribution of each independent variable to change in level of disability. In the regression models, remaining mildly disabled was defined as the reference category. Only independent variables that were univariately associated at $p<0.10$ with one of the outcome states were entered in the final model. The discriminative ability of the logistic regression model and score chart was determined with the area under the receiver operating characteristics curve (AUC). An AUC < 0.6 is considered as moderate discrimination and an AUC ≥ 0.7 as good discrimination.

RESULTS

Population

Of the initial sample of 7368 participants 5024 (68.1%) were considered disability free at baseline, 1166 (15.8%) were considered as mildly disabled and 1178 (16.0%) suffering from severe disability. Of the 1166 subjects with mild disability, 652 participated, but follow-up disability status was assessed in 645 (55.3%). Between baseline and follow-up there were 305 (30.0%) deaths, 181 (15.5%) refused to participate with follow-up measurements, and 28 (2.4%) were not able to complete the follow-up because of physical or mental impairment. These figures differ slightly from the total cohort where 25% deceased and 16.4% was lost to follow-up (refuse or unable). As death was included in the analysis, follow-up data were available for 950 people. In table 1 baseline prevalence of all independent variables are presented for the total study sample and by states at follow-up. In this cohort study less than 5% of the participants were of non-Caucasian origin.

Loss to follow-up appears to be selective as slightly more men participated compared to women and more people of 75 years or older and a lower education were unable to participate at the follow-up measurements. Also more people with low income, hypertension, myocardial infarctions and stroke died. Of people with joint complaints a

Table 1. Prevalence of independent variables at baseline and by follow-up participation status

Independent Variable	Total sample (n=1166)	Follow-up status (n=652)	Refused (n=181)	Unable (n=28)	Deceased (n=305)
Gender					
Female	68.2	72.7	79.0	82.1	50.8
Male	31.8	27.3	21.0	17.9	49.2
Age					
55-64	22.0	33.1	11.6	10.7	5.2
65-74	37.9	43.1	38.7	17.9	28.2
75 and higher	40.1	23.1	49.7	71.4	66.6
Life companion (yes)	56.8	62.0	52.3	44.4	48.8
Education (primary only)	30.4	25.0	35.9	42.9	37.4
Income (< € 955.-)	50.8	42.8	57.7	55.0	66.4
Overweight (BMI ≥ 28.4)	33.8	35.6	38.2	50.0	24.2
Current smoking (yes)	21.9	20.2	21.0	17.9	26.4
Alcohol use (yes)	75.4	78.5	73.7	66.7	66.9
Cognitive impairment (MMSE < 27)	28.5	22.5	31.5	50.0	37.4
Depression (yes)	38.9	39.7	43.9	33.0	34.2
Parkinson's disease (yes)	1.1	0.8	1.7	3.6	1.3
Diabetes mellitus (yes)	7.4	6.3	8.9	3.6	9.3
Hypertension (yes)	40.5	35.5	45.6	42.9	49.6
Myocardial infarction (yes)	10.7	8.5	8.3	14.3	16.4
Stroke (yes)	4.2	2.8	4.4	3.6	6.9
Respiratory disease (yes)	11.5	9.2	8.8	0.0	19.0
Osteoarthritis (yes)	36.3	41.2	36.6	42.3	24.1
Joint complaints	67.4	74.6	67.0	64.3	52.1
Morning stiffness	46.6	54.9	37.6	39.3	34.8
Self-rated health					
Better than contemporaries	39.1	35.6	38.2	60.7	45.1
Same as contemporaries	44.3	46.9	47.6	32.1	37.8
Worse than contemporaries	16.6	17.5	14.1	7.1	17.1
Hearing impairment	6.6	4.9	8.0	7.4	9.3
Vision impairment	3.1	2.2	4.6	3.7	4.1
Dizziness (> once per month)	18.0	17.4	18.3	17.9	19.2
Falling	20.9	19.2	27.1	32.1	19.7
Manual skill impairment	1.1	0.8	0.6	0.0	2.2
Comorbidity (>1)	31.0	30.9	31.7	30.8	30.9
Number of medications (>2)	45.6	43.9	42.5	28.6	52.5
Serum HDL (≤ 1.1 mmol/l)	22.3	21.6	13.4	20.8	30.7
Serum cholesterol (≥ 7.4 mmol/l)	25.0	25.2	30.1	33.3	20.3

higher percentage participated (see table 1). Differences between completers and non-completers were not statistically significant.

Transitions of disability

Data on transitions of disability were presented in table 2. Because other studies showed gender differences concerning transition from disability we decided to present the data for men and women separately [2].

Relatively more men with mild disability at baseline died while a larger proportion of women shifted into severe disability.

Prognostic factors of disability outcome

In table 1 all independent variables are presented. Of these variables seven appeared to be univariately related ($p<0.10$) to change in disability and were entered into the multivariate regression analysis. In table 3 the results of the multivariate multinomial regression are presented.

Table 2 Incidence of transition from mild disability at baseline to outcome status at follow-up

	Men	Women	Total
N	327	623	950
Transition	%	%	%
No disability	19.0	16.7	17.5
Severe disability	17.1	37.6	30.5
Death	45.9	24.9	32.1

The only factor significantly related to recovery is age; older people were significantly less likely to recover from disability. Factors significantly related to develop severe disability are age and income, but most factors (n=5) were significantly related to death. Older people and the ones with a lower income had a higher probability of moving to a worse disability state or dying. Compared to men, women were less likely to die. Alcohol use proved to be significantly protective against death. People who rated their health as worse than their contemporaries were more likely to die. The areas under the curve for the different models are presented in table 3, and are all moderate to good.

Table 3. Prognostic factors of disability: regression analysis with odds ratios (95% confidence intervals)

Independent variable	No disability	Severe disability	Death
Age	0.93 (0.89-0.96)**	1.05 (1.02-1.09)**	1.17 (1.12-1.22)**
Gender	0.74 (0.43-1.28)	1.49 (0.87-2.57)	0.34 (0.19-0.62)**
Income	1.19 (0.68-2.08)	2.03 (1.25-3.28)**	3.31 (1.85-5.92)**
Smoking	0.97 (0.52-1.80)	1.26 (0.70-2.28)	1.99 (0.99-4.01)
Alcohol use	1.80 (0.85-3.80)	0.59 (0.34-1.02)	0.42 (0.22-0.80)**
Cognition	1.07 (0.55-2.09)	1.21 (0.68-2.15)	1.64 (0.87-3.10)
Self-rated health†			
Same	Reference	Reference	Reference
Worse	0.75 (0.37-1.53)	1.51 (0.79-2.86)	2.43 (1.10-5.33)*
Better	1.39 (0.80-2.40)	0.70 (0.42-1.18)	0.76 (0.41-1.40)
AUC (95% CI)	0.775 (0.733-0.817)	0.671 (0.626-0.716)	0.828 (0.790-0.866)

* $p < 0.05$, ** $p < 0.01$; † health compared to contemporaries; AUC = area under the curve.

DISCUSSION

We found that older people were significantly less likely to recover from disability and that older people and the ones with a lower income had a higher probability of moving to a worse disability state or dying. On the other hand any alcohol use seemed to be significantly protective against death.
The way in which death is dealt with in the prognostic analysis of disability differs between studies. While some exclude those that died others consider death as a separate endpoint [19]. We too included it as a separate prognostic outcome category.

Although to a lesser extent than worsening of disability or dying, recovery from disability was possible as seen in approximately one fifth of the respondents. Our results confirm other studies on disability recovery; our proportion of recovery is within the range found [1, 5-7]. Contrary to other studies that also found that women were more likely to recover, we could only identify lower age as a predictor of recovery [6, 7]. Relatively more men died than women and relatively more women became more disabled than men although this attribution of gender was not totally corroborated by multivariate analysis yielding borderline non-significance for the latter association. This difference in transition implies that at higher ages women will be more likely to need assistance in activities of daily living than men. Beside quantitative aspects of allocation of care there may be qualitative aspects to consider as in the older population gender specific roles and patterns may still have consequential influence.

Contrary to the systematic review, we identified income as a prognostic factor of disability at six years [4]. The odds of entering a severe disability state or dying were higher for those with low income. Although poverty in the elderly is not as evident and common in western societies as in developing countries and although health care is better equipped and organised, it is interesting to see that poverty, once present, has its impact on functioning. Though it is not clear whether lower income is an indicator of an unfavourable lifestyle with respect to functioning or an indicator of impeded access to health care in general or of some other undetected variable, it should be taken into account in assessing disability prognosis in the elderly.

Strengths and weaknesses

This is one of the few studies evaluating sociodemographic, life-style and health related factors on disability [4]. We found smoking and self-rated health significantly related to disability decline and those who used alcohol were less likely to die than those who did not use alcohol at all. It has to be mentioned that the proportion of excessive users or abusers was very low in our population. In others studies no significant association was found [20, 21]. Self-rated health was only associated significantly with the outcome of death in our study while others report on a significant association of health rated as better with recovery from disability [20,21].

A limitation of this study is that disability status was assessed only twice in a period of six years. Multiple episodes of recovery and incidence may have been missed, as short term transitions were not observed. The rate at which transitions occurred, indicating underlying acute or chronic mechanisms, could not be discerned [22]. Furthermore, because we used a summarising index, necessary for the analyses, this would have hidden changes in opposing directions in components making up the overall score.

At follow-up 15.5% of the participants refused and another 2.4% were unable to participate. It seems that overall the non-completers were mainly people with poorer outcome. This might have affected our results. Older people and people with low income were more likely to be lost to follow-up. As these factors were also the most important factors related to disability decline or death, the association we found might have been an underestimation of the real association because of possible selective loss to follow-up.

We could not reckon with ethnic background as a prognostic factor as others did [19]. Generalisability of our findings to non-indigenous elderly is limited as the proportion of elderly migrants living in the Ommoord district was negligible. As migrants grow older

it is expected that their contribution to the population, especially in the larger cities in Europe, will increase. Future research should take this into account.

As we did not have data on baseline physical activity level to our disposal we could not include this factor in our analysis. To our knowledge not many studies [19] report on physical activity. This still remains a plausible prognostic factor that should be studied further.

Another limitation of this study is the lack of validation in other cohorts although the size of the derivation cohort may compensate for this.

Compared to risk factors of incident disability we found less prognostic factors of disability [3]. This could imply that once present the course of disability is little altered by modifiable factors. For caregivers this would mean that prevention of disability is more plausible than changing its course. Our observational study did not address the contribution of interventions. Although additional exercise for example has been shown to have a positive effect in preserving strength, ability and function, the long term effect on disability is not yet evident [23]. Future studies should address this question.

CONCLUSIONS

In this study we found, out of over 30 determinants, only a few prognostic factors for disability recovery and decline. We identified people of higher age, low income and to some extent those who rate their health as worse than contemporaries, as being more likely to suffer an adverse prognosis of their disability, while lower age is related to recovery. Our findings indicate that strategies might be aimed at recognising and treating complications of disability in an early stage in order to preserve quality of life as much as possible. Future prospective research should explore the effect of other less studied factors like exercise in order to pave the way for targeting care and interventive strategies.

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CHAPTER 6

Trends in morbidity and disability in the elderly: the Rotterdam study

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Submitted

ABSTRACT

Objective: Populations are aging and many elderly experience disability in daily life. We aim to compare and evaluate changes in health status in the elderly.

Methods: Cross-sectional comparison of baseline data of two separate prospective cohorts of the Rotterdam Study. Both cohorts comprised persons of 55 years and older. The initial cohort (started in 1990) consisted of 7368 persons, and the extension cohort (started in 2000) of 2973 persons. We collected data from both cohorts concerning sociodemographic factors, lifestyle, general health and disability in daily life, and compared data at baseline.

Results: The elderly of the first extension cohort were on average younger, had a higher level of education and were more often living with their spouse. Overall there was less disability in the extended cohort compared with the initial cohort for both men (16% versus 21% respectively) and women (respectively 34% versus 39%). The prevalence of stroke and myocardial infarction was lower while the prevalence of morning stiffness, joint complaints, hypertension and diabetes mellitus was higher in the extension cohort. The prevalence of overweight and obesity increased compared with the initial cohort. More falls were reported in the extension cohort.

Conclusion: Compared with ten years earlier we found lower prevalences of disability. Differences between the cohorts regarding age, education level and general health might explain the possible improvement in disability in daily life.

INTRODUCTION

In many populations, if not in all, the proportion of elderly people is increasing. In the Netherlands for instance the proportion of people of age 65 and older is projected to increase from the present 13% to 23% by the year 2040 [1]. As old age is associated with disability this may entail troubling medical and economical consequences for the individual and society [2]. In order to understand the impact of disability in the long term it is important to gain insight in its development over different periods of time. As yet there are not many studies investigating trends in time of health and disability based on different cohorts reporting different results. Some report a decrease in disability in later cohorts while others report no consistent changes over time [3-5]. A recent review concluded that a compression of disability (disability occurring at older age) might be accompanied by an increase of other health problems [6].

In order to investigate the determinants of chronic diseases and disability the Rotterdam Study started in 1990 including a cohort of people aged 55 years and older [7,8]. A second cohort of the same age group, called the First Extended Cohort of the Rotterdam Study, started in 2000, making the study of differences between the two cohorts possible [9].

By comparing baseline prevalences of chronic diseases and disability as well as their determinants between the original Rotterdam Study cohort and its first extended cohort, this study aims to investigate whether the health status, including disability, in the elderly has changed over a decade.

METHODS

Study population

Data for this study were obtained from the initial Rotterdam Study and the First Extension of the Rotterdam Study, both being population based prospective cohorts that contain mutually exclusive groups of individuals. For both cohorts the sampling frame and recruitment methods were identical. The Rotterdam Study is designed for the study of neurological, cardiovascular, locomotor and ophthalmological diseases in the elderly aged 55 and older living in the Ommoord district, a district of Rotterdam, the Netherlands. In the initial Rotterdam Study of the 10,275 inhabitants invited for the initial cohort 7983 (78%) agreed to participate. After exclusion of 482 respondents with

dementia at baseline and of another 133 persons because of missing data on disability, 7368 remained for analysis.

For the extended cohort out of 4472 invited 3011 elderly (67.3%) agreed to participate and after exclusion of respondents with missing data on disability 2973 remained for the analysis.

For both cohorts comprehensive interviews were conducted covering among others the following fields that were relevant to our study: general information, activities of daily living, Rose questionnaire of cardiovascular disease, joint complaints, ophthalmology, medical history, medical consumption and life events, smoking, socioeconomic status, medication, family history and hypertension [10]. Anthropometrical and biochemical variables were measured at the research centre.

Detailed information on the Rotterdam Study has been published previously [7, 9]. Informed consent was obtained from the participants of both cohorts and the Medical Ethics Committee of the Erasmus Medical Center approved the overall study.

Variables

Demographic variables
Age and gender were assessed. Education was based on the highest level attained. Income was assessed as net income per year and household income. Marital status at baseline was based on whether or not having a life companion.

Lifestyle variables
Smoking status was assessed as never, former and current smoker. Self-report of alcohol intake was approximated in grams per day.

Anthropometric and biochemical variables
Weight and height were measured. Body mass index (BMI) was defined as weight/height^2 (kg/m^2). Serum levels of total cholesterol and HDL-cholesterol (mmol/l) were measured. Diastolic and systolic blood pressures were measured by hand using a 'random zero' sphygmomanometer.

Psychological variables and comorbidities
Self-rated health was defined as self-report of the perception of one's own health compared to contemporaries. Stroke was assessed as part of the Rose questionnaire [10]. Assessment of depression, Parkinson's disease, myocardial infarction, diabetes mel-

litus, osteoarthritis, joint complaints, morning stiffness, falls and dizziness was based on self-report (yes/no) to questions on these conditions formulated as "Do you have...?" or "Did you ever experience...?". Hypertension was defined as a systolic blood pressure equal to or higher than 160 mmHg and/or a diastolic blood pressure equal to or higher than 95 mmHg [11]. Receiving an anti-hypertensive treatment was also considered as having hypertension. Data on vision and hearing were based on observations during the interview.

Disability

For the assessment of disability the Stanford Health Assessment Questionnaire (HAQ) was used [12]. The Health Assessment Questionnaire has proven to be reliable, valid and sensitive to change in both general populations and populations with a specific disease [13-15]. The HAQ measures disability in eight fields (dressing and grooming, rising, reach, hygiene, eating, walking, grip and activity). Each field comprises two to four items. Per item the status of the respondent is scored as able to do without difficulty (0), with some (1) or much (2) difficulty or unable to do with or without assistance (3). The highest item score determines the final field score. The mean score of all fields constitutes the Disability Index (DI) ranging from 0.00 to 3.00. A person, for example, who experiences only some difficulty in dressing and rising without needing assistance, would be given 2 points. Dividing this by the number of fields with complete information, usually all eight, would give a HAQ-DI of 0.25. If someone would be unable to perform one item in six fields that person would have a HAQ-DI of (3*6)/8=2.25. In the present study respondents with a HAQ-DI lower than 0.50 were considered not disabled. A DI from 0.50 to 1.00 was considered as mild disability while a DI of 1.00 or higher was regarded as severe disability [16].

Data analysis

Cross-sectional comparison of baseline data was performed using SPSS15. Frequencies of variables were estimated for both cohorts and for men and women separately. In the analyses age, total cholesterol and HDL were entered as a continuous variable. Dichotomised variables (with their cut-off points) were gender, marital status (life companion/no life companion), alcohol consumption (yes/no), comorbidities (presence of two or more conditions out of seven: depression, Parkinson's disease, diabetes mellitus, hypertension, myocardial infarction, stroke and osteoarthritis), hearing and vision (impaired/not impaired). Variables with three or more categories were education (primary, secondary, higher), smoking (never, former, current), BMI (< 25, 25-30, >30) and self-rated health (same, better, worse).

In order to explore associations between relevant determinants and trends in health and disability we also stratified for relevant determinant exposure status (e.g. age, education etc). Baseline prevalences were compared using Student's t-test for continuous variables, Pearson's χ^2 for categorical variables and Mann-Whitney U test for not normally distributed continuous variables.

RESULTS

Initial cohort of the Rotterdam Study

Baseline prevalences of both cohorts are presented in table 1. In the initial cohort women were on average older than men. Men on the other hand had a better socioeconomic status. Women suffered twice as much from locomotor complaints like morning stiffness, joint complaints, osteoarthritis and disability. Women were also more often obese than men. More men smoked and consumed alcohol than women.

First extended cohort of the Rotterdam Study

Average age did not differ significantly between men and women in the extended cohort of the Rotterdam Study. At older age men more often lived with their spouse than women and in comparison they were more educated. Although proportionally more men had overweight (54% versus 44% with BMI between 25 and 30), the prevalence of obesity (BMI > 30) was higher in women than in men as were the mean HDL and total cholesterol levels. Current smokers were evenly distributed between both genders in this cohort although there were still more women who had never smoked than men (41% versus 19%). Men on the other hand had stopped smoking relatively more often. Some medical conditions like stroke, myocardial infarction and diabetes mellitus occurred more often in men than in women whereas women experienced more adversities of the locomotor tract like morning stiffness, osteoartritis and mild disability.

Comparison between the original cohort and the first extended cohort

Social and demographic factors

The participants of the extended cohort were on average younger and more often lived with their spouse than those of the original cohort. The proportion of men who had a higher education in the extended cohort (26.1%) was twice that of those in the original cohort (14.6%) while the proportion of men who had an intermediate level education

Table 1. Prevalences of determinants by sex for the two populations of the Rotterdam Study

	Men			Women		
	Original cohort (n=2957)	**Extended cohort (n=1309)**	**p- value**	**Original cohort (n=4411)**	**Extended cohort + (n=1664)**	**p-value**
Age (years)	68.4 (±8.3)	64.7 (±7.8)	< 0.001	70.3 (±9.5)	65.7 (±8.9)	< 0.001
Life companion (%)	81.3	84.8	0.005	50.7	61.2	< 0.001
Education (%)			< 0.001			< 0.001
· lower	16.8	6.6		30.0	11.2	
· intermediate	68.6	67.3		65.9	79.4	
· higher	14.6	26.1		4.1	9.4	
Disability (%)			< 0.001			< 0.001
· no	78.8	84.3		61.1	65.9	
· mild	11.9	10.2		17.3	20.9	
· severe	9.3	5.6		21.6	13.3	
Self-rated health compared to contemporaries (%)			< 0.001			< 0.001
· same	36.0	38.8		39.7	44.2	
· better	54.3	53.0		49.5	45.2	
· worse	9.7	8.2		10.8	10.6	
Depression (%)	2.8	8.3	< 0.001	4.9	14.8	< 0.001
Stroke (%)	4.6	4.4	0.741	3.7	2.7	0.040
Hypertension (%)	31.3	37.9	< 0.001	39.3	39.0	0.838
Myocardial infarction (%)	14.5	9.2	< 0.001	5.8	3.6	0.001
Osteo-arthritis (%)	16.5	5.0	< 0.001	30.0	10.0	< 0.001
Morning stiffness (%)	25.2	26.9	0.235	37.9	44.7	< 0.001
Joint complaints (%)	40.5	64.5	< 0.001	58.8	81.4	< 0.001
Falls (%)	10.1	15.6	< 0.001	21.3	27.5	< 0.001
Hearing impairment (%)	6.5	1.4	< 0.001	6.0	1.7	< 0.001
Visual impairment (%)	2.2	1.3	0.062	3.5	1.1	< 0.001
Diabetes mellitus (%)	6.1	8.1	0.016	6.7	6.9	0.748
Body mass index (kg/m2)			< 0.001			< 0.001
· < 25	41.9	29.5		35.7	31.7	
· 25-30	50.9	54.0		44.2	43.7	
· > 30	7.2	16.5		20.1	24.6	
HDL (mmol/L)	1.22 (±0.33)	1.22 (±0.30)	0.530	1.44 (±0.37)	1.50 (±0.39)	< 0.001
Total cholesterol (mmol/l)	6.32 (±1.18)	5.54 (±0.98)	< 0.001	6.84 (±1.21)	5.95 (±0.95)	< 0.001
Smoking (%)			< 0.001			< 0.001
· never	8.1	18.7		54.5	40.9	
· former	61.5	60.9		27.5	38.7	
· current	30.4	20.4		18.0	20.4	
Alcohol use (%)	87.4	82.3	< 0.001	73.6	82.8	<0.001

was almost the same. Women of the extended cohort more often had a higher education (9.4%) than those ten years earlier (4.1%) although proportionally still less than men.

General health

There were differences between the cohorts regarding self-rated health. In the extended cohort more men and women reported depression, while in both cohorts more women than men reported depression. Prevalences of depression range from 2.8% for men in the original cohort to 14.8% for women in the extended cohort. The prevalence of stroke was more or less the same for men in both cohorts whereas it had decreased for women. The prevalence of diabetes mellitus had remained the same for women while it had increased in men ranging from 6.1% to 8.1%. Compared to the original cohort more men and women reported morning stiffness and joint complaints in the extended cohort but

Table 2: Prevalences of disability by sex and age for the two populations of the Rotterdam Study

Age (years)	Disability	Men		Women	
		Original cohort (n=2957); n (%)	Extended cohort (n=1309); n (%)	Original cohort (n=4411); n (%)	Extended cohort (n=1664); n (%)
55-59	No	466 (91.4)	420 (93.1)	597 (84.3)	431 (79.4)
	Mild	32 (6.3)	21 (4.7)	83 (11.7)	87 (16.0)
	Severe	12 (2.4)	10 (2.2)	28 (4.0)	25 (4.6)
60-64	No	574 (89.7)	358 (90.6)	682 (82.5)	406 (79.3)
	Mild	41 (6.4)	27 (6.8)	98 (11.9)	76 (14.8)
	Severe	25 (3.9)	10 (2.5)	47 (5.7)	30 (5.9)
65-69	No	540 (83.9)	140 (84.3)	540 (72.0)	95 (62.9)
	Mild	70 (10.9)	17 (10.2)	133 (17.7)	42 (27.8)
	Severe	34 (5.3)	9 (5.4)	77 (10.3)	14 (9.3)
70-74	No	386 (76.4)	100 (80.0)	465 (62.5)	84 (58.3)
	Mild	76 (15.0)	17 (13.6)	153 (20.6)	32 (22.2)
	Severe	43 (8.5)	8 (6.4)	126 (16.9)	28 (19.4)
75-79	No	240 (66.7)	59 (62.1)	269 (45.3)	52 (36.4)
	Mild	69 (19.2)	22 (23.2)	143 (24.1)	54 (37.8)
	Severe	51 (14.2)	14 (14.7)	182(30.6)	37 (25.9)
80-84	No	92 (46.9)	21 (41.2)	115 (28.1)	22 (21.4)
	Mild	43 (21.9)	14 27.5()	100 (24.4)	39 (37.9)
	Severe	61 (31.1)	16 (31.4)	194 (47.4)	42 (40.8)
90+	No	6 (26.1)	1 (16.7)	2 (1.7)	1 (7.1)
	Mild	4 (17.4)	2 (33.3)	10 (8.4)	0 (0.0)
	Severe	13 (56.5)	3 (50.0)	107 (89.9)	13 (92.9)

osteoarthritis was reported less. Stratifying for age, next to an increase in falls with age we found that more participants of the extended cohort reported falls regardless of age. Overall there was less disability in the extended cohort compared with the initial cohort for both men (16% versus 21% respectively) and women (respectively 34% versus 39%). Both men and women reported less often severe disability. More men and women were disability free in the extended cohort. When stratified for age this gain was lost for women (see table 2).

Stratifying for education level and age we found different trends. In the extended cohort women with higher education had less disability and those with lower education had more disability. Probably due to the small numbers this difference was statistically non-significant. Especially among older women proportionally there was less severe disability and more mild disability in the extended cohort compared with the initial cohort (table 2). This difference was not seen as clearly in men.

Cardiovascular risk profile

Compared to the initial cohort the proportion of men with overweight or obesity was larger in the extended cohort (7.2% versus 16.5%). Although to a lesser degree, this was also the case for women (20.1% versus 24.6%). Further analysis showed that the body mass index was not significantly related to educational level. In the extended cohort participants had lower cholesterol levels, and more men had hypertension. Fewer men used alcohol and smoked while more women used alcohol and smoked. Finally, less people suffered a myocardial infarction.

DISCUSSION

Compared to ten years earlier the elderly in Ommoord were in general less severely disabled. We found that the prevalences of depression, joint complaints, overweight and obesity increased in ten years while prevalences of osteoarthritis, cholesterol levels, myocardial infarctions and hearing impairment decreased. Participants of the extended cohort were on average younger and had a higher education when compared to the initial cohort, which may have affected other determinants in this study, but in the analysis we stratified for this.

Methods

The response rate was lower in the extended cohort compared to the initial cohort with over 10%. This could be expected because of the widespread decline in survey

participation. No information is available about the difference between responders and non-responders, but we do not think this 10% difference in response rate influences the results because overall the response rate was rather high (over 60%).

The percentage exclusions was lower in the extended cohort compared to the initial cohort (1.3% and 7.7% respectively). The difference in percentage is small and we therefore do not think this has any effect on our findings.

Disability

We found differences in the proportion of disability between cohorts and between men and women. Overall there was less (severe) disability in the extended cohort. Men also had less mild disability while women, especially those with a low educational level, had more mild disability in the extended cohort.

To our knowledge there is no other European study on trends in disability in older people. In the Framingham Heart Study (FHS), the authors, comparing two cohorts of 1974 and 1994 respectively, conclude that participants of the latter experienced fewer disabilities and had a better health status [17]. Although the sampling time frame between the FHS study and the Rotterdam study are different, the results are comparable, indicating a more generalizing trend of decrease in disability prevalence.

We also found that participants of the extended cohort, although younger on average, reported more falls. When stratified this proved to be consistent for all age categories. Higher activity and mobility levels that may increase risk of falling among the later generation of elderly may explain this finding.

The differences in the prevalence of osteoarthritis between the cohorts may partly be due to a slight change in related questions. While in the original cohort this was based on self-report to a specific question, in the extended cohort there were more response options including several diagnoses of locomotor conditions (confirmed by a physician).

The increase in the prevalence of diabetes mellitus among men may be explained by the increase of overweight and obesity. Our findings that in the extended cohort both men and women experienced less myocardial infarction, stroke and osteoarthritis corroborate similar findings in the FHS. The same accounts for our findings that the relatively more educated participants of the extended cohort had a higher BMI.

Other studies have shown that it is possible to have a decrease in disability over time [6, 18-23]. Many studies however focus on people of age 65 and older whereas the pathway to chronic conditions and disability starts earlier in life. More research is therefore needed in the age group 55-70 years.

The differences in phrasing questions and defining cut-offs remain an obstacle in comparing studies. The use of more standard questionnaires internationally would be welcome.

CONCLUSION

Our findings indicate that disability among the elderly decreased over a period of ten years. Some factors of general health improved, such as osteoarthritis, cholesterol levels, myocardial infarctions and hearing impairment. Nevertheless prevalences of depression, joint complaints, overweight and obesity increased in ten years.

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CHAPTER 7

Age, gender and disability predict future disability in the elderly: the Rotterdam Study

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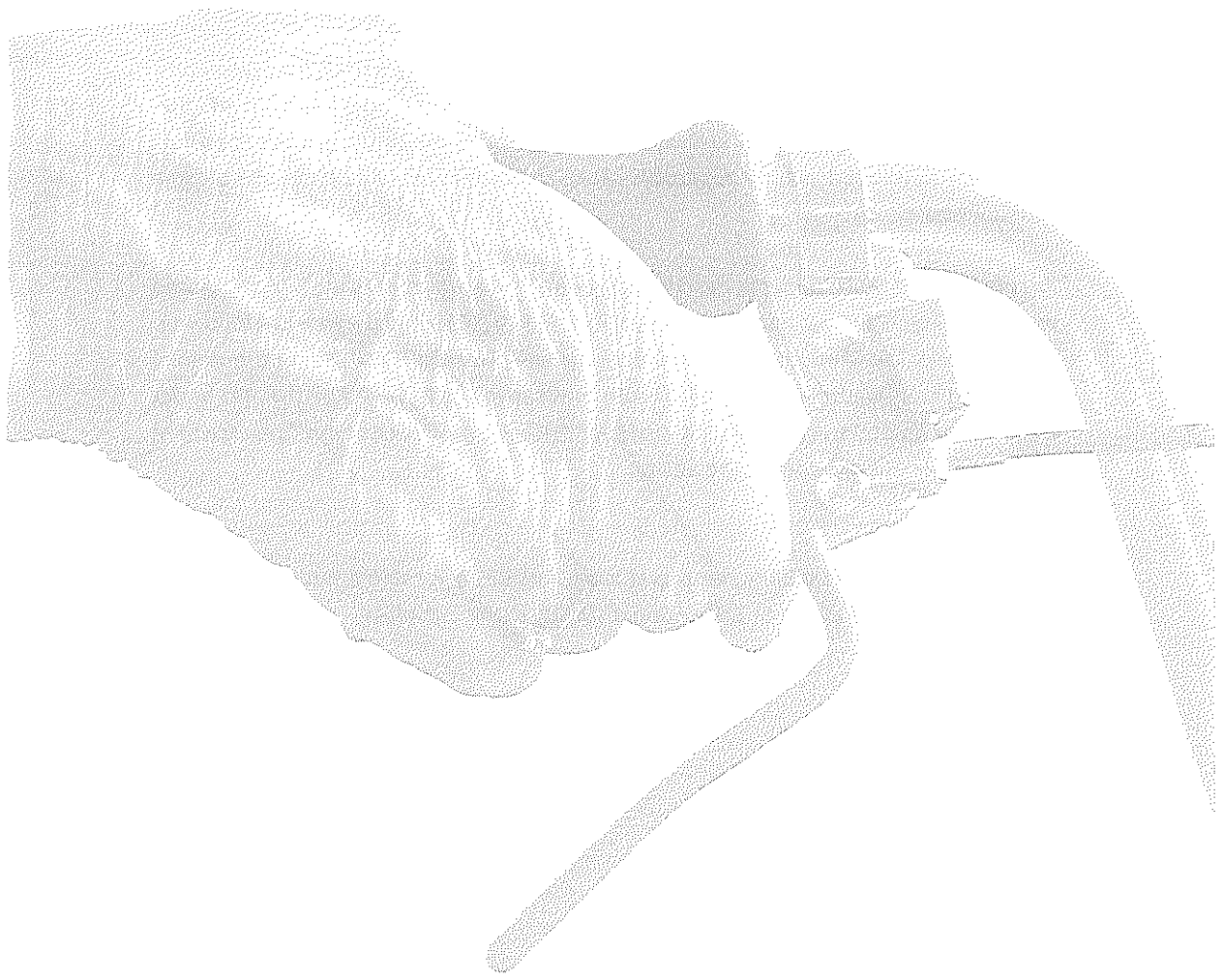
Submitted



ABSTRACT

Background: Disability in the elderly is a common and chronic condition producing individual and societal burden. Insight in the predictors of disability is needed to target preventive strategies for people at increased risk.

Objectives: To develop a model that predicts disability in community-dwelling older people.

Methods: Data were obtained from the Rotterdam Study, including subjects of 55 years and over. Subjects who had complete data for sociodemographic factors, life style variables, health conditions, disability status at baseline and complete data for disability at follow-up were included in the analysis (n=5027). Disability was expressed as a Disability Index (DI) measured with the Health Assessment Questionnaire.

We used a multivariable polytomous logistic regression to derive a basic model comprising age, gender and prior disability status and an extended model which in addition comprised body mass index, self-rated health, joint complaints and hypertension. Finally we developed readily applicable score charts for the calculation of outcome probabilities.

Results: Of the 5027 subjects included, 2449 (49%) had no disability, 878 (18%) had mild disability, 781 (16%) had severe disability and 919 (18%) had deceased at follow-up after six years. The strongest predictors were age and prior disability. The contribution of other predictors was relatively small. The discriminative ability, based on the area under the receiver operating characteristic curve, of the basic model was high. The extended model did not enhance predictive ability.

Conclusion: As prior disability status predicts future disability status, interventive strategies should be aimed at preventing disability in the first place.

INTRODUCTION

Disability, especially in the elderly, is a common problem and in most cases a chronic condition. Prevalence rates range from 30% for people aged 75 or older to 40% for those aged 85 and older [1].

Elderly with disability may become dependent on assistive devices or other people. This may have a negative impact on the quality of their lives. At the end, the level of disability will determine whether elderly will be able to live in their own house, with or without modifications, or whether they have to live in a home for the elderly or nursing home. For the future the expected increase in disability produces economical and logistical challenges for society. There will be a an increasing demand of professional caregivers as most children of elderly people will not be in the position, either by choice or (economical) necessity, to take care of their own parent(s).

For targeting preventive, curative or palliative strategies it is important that disability can be predicted in order to identify high-risk groups. Prediction of high-risk groups is only helpful when effective preventive strategies can be provided to these groups. Several systematic reviews report on treatment strategies with favourable outcome on disability like the use of memantine in dementia, centre based physical activity programs for older adults with cardiovascular disease, chronic obstructive airway disease or osteoarthritis and vitamin D supplementation to reduce hip fractures [2, 3, 4]. There are several other studies on possible preventive strategies like resistance or endurance training, preventive home visits or multidimensional geriatric assessment [5, 6, 7, 8].

There is a clear need for predicting disability. This may also help the individual, the care giving relatives and the related institutions to anticipate to future dependency and improve their policy. There are however, as yet no (comprehensive) prediction rules for disability in a general population of elderly. Though many individual predictors have already been identified, studies on absolute risk are sparse [9]. Also baseline disability is not always taken into account. Therefore we developed a prediction rule for long-term disability in elderly people based on a number of easily obtainable predictors including baseline disability status.

METHODS

Study population

The Rotterdam Study is a population-based prospective cohort study of the incidence and determinants of chronic diseases and disability in the elderly [10]. The Medical Ethics Committee of the Erasmus Medical Centre approved the study. All 10,275 inhabitants of a district of Rotterdam aged 55 years or older were invited to participate. A total of 7,983 (78%) men and women consented and entered the study.

At baseline, between July 1989 and June 1993, comprehensive interviews were conducted during home visits by trained researchers followed by further assessments of the participants at the research centre. The interview and assessments were repeated at the first follow-up between 1994 and 1996 and at the second follow-up between 1997 and 1999. The interviews comprised questions on demographic factors, socioeconomic status, activities of daily living, cardiovascular diseases, joint complaints, medical history, medical consumption, life events, smoking, medication and family history. Assessments at the research centre included anthropometrical, ophthalmological and biochemical factors.

The present study is carried out with data of the baseline and the second follow-up of the Rotterdam Study, as activities of daily living were not assessed at the first follow-up. The follow-up period therefore comprises about six years.

Outcome: disability status

For the assessment of disability the Stanford Health Assessment Questionnaire (HAQ) was used [11]. The Health Assessment Questionnaire has proven to be reliable, valid and sensitive to change in both general populations and populations with a specific disease [12]. The HAQ measures disability in eight fields (dressing and grooming, rising, reach, hygiene, eating, walking, grip and activity). Each field comprises two to four items. Per item the status of the respondent is scored as able to do without difficulty (0), with some (1) or much (2) difficulty or unable to do with or without assistance (3). The highest item score determines the final field score. The mean score of all fields constitutes the Disability Index (DI) ranging from 0.0 to 3.0. A person, for example, who experiences only some difficulty in dressing and rising without needing assistance, would be given 2 points. Dividing this by the number of fields with complete information, usually all eight, would give a DI of 0.25. If someone would be unable to perform one item in six out of eight fields that person would have a DI of (3*6)/8=2.25. We defined the outcome categories

as follows: no disability (DI < 0.50), mild disability (DI 0.50 to 1.00) and severe disability (DI > 1.00) [13]. We included death as a separate outcome category.

Predictors

Based on previous analyses and the literature we selected candidate predictors [9]. These candidate predictors, as shown in table 1, comprised age and gender beside other demographical, socioeconomical, anthropometrical and biochemical variables.

Analysis

After univariable analyses of the individual predictors and disability the significant predictors (p value < 0.05) were entered in multivariate analyses. We used polytomous logistic regression analysis with disability status at follow-up as the dependent variable comprising four categories. With the 'no disability' category being the reference category, regression coefficients were estimated for the other categories of mild disability, severe disability and death.

Based on the predictor variables with the highest χ^2 in multivariate analyses we finally fitted two multinomial logistic models: one basic model with the three strongest predictors ($\chi^2 > 100$): age, gender and baseline disability, and an extended model including the predictors, which in earlier regression models have proven to be significantly associated: joint complaints, self-rated health, cognitive functioning, BMI and hypertension. Interaction terms were included in the models.

The ability of the models to discriminate between different outcomes was studied by estimating the area under the receiver operating characteristics curve (AUC). Based on the regression coefficients of the prediction model we developed a score chart with which outcome probabilities can easily be calculated. The regression coefficients were multiplied by five and rounded to the nearest integer. Probabilities of outcome were calculated with the formulas presented in the appendix.

RESULTS

Study population

Subjects who had complete data for sociodemographic factors, lifestyle variables, health conditions and disability status at baseline and complete data for disability at

Table 1. Baseline characteristics by outcome status after six years

	No disability (n=2449)	Mild Disability (n=878)	Severe disability (n=781)	Death (n=919)
Age*	63.9 (5.9)	67.5 (6.8)	72.1 (7.7)	75.5 (8.7)
Women*	50.8	62.9	77.5	48.9
Life companion*	74.6	69.6	54.7	53.5
Educational level*				
Low	13.1	18.1	31.3	33.6
Intermediate	74.8	72.9	64.3	60.3
High	12.1	9.0	4.4	6.1
Income level*				
Low	16.1	20.6	32.2	31.8
Intermediate	49.2	53.4	54.1	52.2
High	34.7	26.0	13.8	16.0
Insurance (public)*	46.0	51.5	61.7	61.1
Smoking*				
Never	28.9	35.9	44.9	32.0
Formerly	48.0	42.6	36.1	40.8
Currently	23.1	21.5	19.0	27.2
Disability Index*	0.11 (0.2)	0.28 (0.1)	0.71 (0.6)	0.71 (0.8)
MMSE*	28.2 (1.4)	27.9 (1.5)	27.5 (1.8)	27.0 (2.0)
Self-rated health*				
Better	59.0	49.7	40.1	48.1
Same	36.9	41.3	43.3	37.2
Worse	4.0	9.0	16.6	14.7
BMI*	25.9 (3.3)	26.7 (3.7)	27.5 (4.0)	26.0 (3.9)
Hypertension*	24.9	35.5	39.7	46.4
Depression*	29.3	35.5	43.3	34.9
Parkinson's disease*	0.0	0.1	1.8	1.1
Diabetes mellitus*	3.0	5.1	9.3	11.1
Myocardial infarction*	5.6	8.5	8.6	15.9
Stroke*	1.2	2.1	5.5	7.8
Respiratory disease*	3.1	5.5	6.0	8.9
Osteoarthritis*	18.2	30.2	37.0	23.3
Joint complaints*	42.6	58.8	71.7	49.0
Morning stiffness*	24.8	36.7	51.3	33.7
Falls*	9.7	14.7	23.0	22.2
Hearing impairment*	2.1	2.9	6.0	11.4
Vision impairment*	0.5	1.4	4.3	5.3
Dizziness	6.0	10.1	20.4	14.4
Comorbidities (>1)*	11.6	21.9	30.9	28.1
Medication (>2)*	16.8	30.4	49.4	48.6
Total cholesterol (mmol/l)	6.7 (1.2)	6.7 (1.1)	6.7 (1.2)	6.4 (1.3)
HDL (mmol/l)	1.4 (0.4)	1.3 (0.3)	1.4 (0.4)	1.3 (0.4)

Data are means with standard deviations for continuous variables and percentages for categorical variables; * $p<0.001$; p values are for differences between completers and non-completers: † Mann-Whitney U test, ‡ Student's t-test, all other p values are based on χ^2 for categorical variables.

follow-up were included in the analysis (n=5,027). Of the subjects included, 2,449 (49%) had no disability, 878 (18%) had mild disability, 781 (16%) had severe disability and 919 (18%) had deceased at follow-up after six years. Baseline characteristics of the study sample are presented to outcome status in table 1. In this cohort study less than 5% of the participants were of non-Caucasian origin.

Predictors

Of the 19 candidate variables that were univariately significantly associated with the outcome, eight remained significant (p value < 0.05) at multivariate analysis: age, gender, DI at baseline, cognitive functioning, joint complaints, hypertension, BMI and self-rated health. Odds ratios with 95% confidence intervals are presented for both the basic and extended model in table 2.

The AUC's of the basic model for the outcomes no disability, mild disability, severe disability and death were 0.83, 0.67, 0.81 and 0.81 respectively. The AUC's for the extended model were slightly higher: 0.85, 0.69, 0.82 and 0.83 respectively.

Table 2. Predictors of disability outcome; basic and extended model

Independent variable	Mild disability		Severe disability		Death	
	Basic model	Extended model	Basic model	Extended model	Basic model	Extended model
Age (per 10 years)	2.2 (2.0-2.5)**	2.2 (2.0-2.5)**	3.9 (3.4-4.5)**	4.2 (3.6-4.9)**	7.2 (6.3-8.4)**	7.0 (6.0-8.1)**
Gender (female)	1.5 (1.3-1.8)**	1.4 (1.2-1.6)**	2.3 (1.8-2.8)**	2.1 (1.7-2.6)**	0.6 (0.5-0.7)**	0.6 (0.5-0.7)**
Disability Index	8.7- (6.4-11.8)**	11.6 (6.3-21.3**)	36.3 (26.6-49.5)**	37.0 (19.9-68.6)**	34.7 (25.4-47.5)**	42.7 (23.5-77.7)**
MMSE		0.9 (0.9-1.0)**		0.9 (0.9-1.0)**		0.8 (0.8-0.9)**
Self-rated health†						
Same		1.0		1.0		1.0
Better		0.9 (0.7-1.0)		0.7 (0.6-0.9)**		0.8 (0.6-1.0)*
Worse		1.7 (1.2-2.3)		2.2 (1.6-3.2)**		2.7 (1.9-4.0)**
Body mass index						
Lower than 25		1.0		1.0		1.0
25 to 30		1.1 (1.0-1.4)		1.3 (1.0-1.6)*		0.8 (0.7-1.0)
30 or higher		1.5 (1.2-2.0)		1.9 (1.4-2.6)**		0.9 (0.7-1.2)
Hypertension		1.4 (1.1-1.6)**		1.3 (1.0-1.6)*		1.9 (1.5-2.3)**
Joint complaints		1.7 (1.4-2.1)**		1.9 (1.4-2.5)**		0.9 (0.7-1.2)
AUC (95% CI)	0.67 (0.66-0.69)	0.69 (0.67-0.71)	0.81 (0.79-0.82)	0.82 (0.80-0.83)	0.81 (0.79-0.82)	0.83 (0.81-0.84)

Numbers are odds ratios (95% confidence intervals); * p < .05, ** p < 0.01.

Score charts for the basic and extended models are presented in tables 3 and 4 respectively. Age and prior disability are the strongest contributors to both models Maximum scores on the MMSE, implying good cognitive functioning, yield a lower probability of disability and death. The contribution of other variables in the extended model was small compared to age and prior disability status.

In figure 1 the probabilities of different outcomes based on the basic prediction model are given for different baseline profiles: profile one is of a man who is 60 years old and has no baseline disability; profile 2 is of a man who is 75 years old and has mild disability; profile 3 is of a woman who is 70 years and has severe disability at baseline.

DISCUSSION

This study shows that prior disability and age are the strongest predictors for future disability in the elderly. Female gender, cognitive functioning, self-rated health as worse than peers, obesity, hypertension and joint complaints contribute to the increase

Table 3. Score chart basic model

Predictors	Mild disability	Severe disability	Death
Age			
60	24	42	60
70	28	49	70
80	32	56	80
90	36	63	90
Gender			
Male	0	0	0
Female	2	4	-3
Disability Index			
0.0	0	0	0
0.5	5	9	9
1.0	10	18	18
1.5	15	27	27
2.0	20	36	36
2.5	25	45	45
3.0	30	54	54
Constant	-34	-59 +	-76
	Sumscore*	Sumscore*	Sumscore*

*The prognostic score for a given subject can be obtained by adding the scores for each applicable characteristic resulting in a sumscore. The sumscores correlate with the predicted probability of the outcome category it relates to through the formula presented in the appendix.

Table 4. Score chart extended model

Predictors	Mild disability	Severe disability	Death
Age			
60	24	42	60
70	28	49	70
80	32	56	80
90	36	63	90
Gender			
Male	0	0	0
Female	2	4	-3
Disability Index			
0.0	0	0	0
0.5	5	9	9
1.0	10	18	18
1.5	15	27	27
2.0	20	36	36
2.5	25	45	45
3.0	30	54	54
MMSE			
20	0	0	0
22	-1	-1	-2
24	-2	-2	-4
26	-3	-3	-6
28	-4	-4	-8
30	-5	-5	-10
Self-rated health			
Same	0	0	0
Better	-1	-2	-1
Worse	3	4	5
BMI			
< 25	0	0	0
25-30	1	1	1
> 30	2	2	3
Hypertension	2	2	3
Joint complaints	3	3	0
Constant	-26	-49	-45
	Sumscore*	Sumscore*	Sumscore*

*The prognostic score for a given subject can be obtained by adding the scores for each applicable characteristic resulting in a sumscore. The sumscores correlate with the predicted probability of the outcome category it relates to through the formula presented in the appendix.

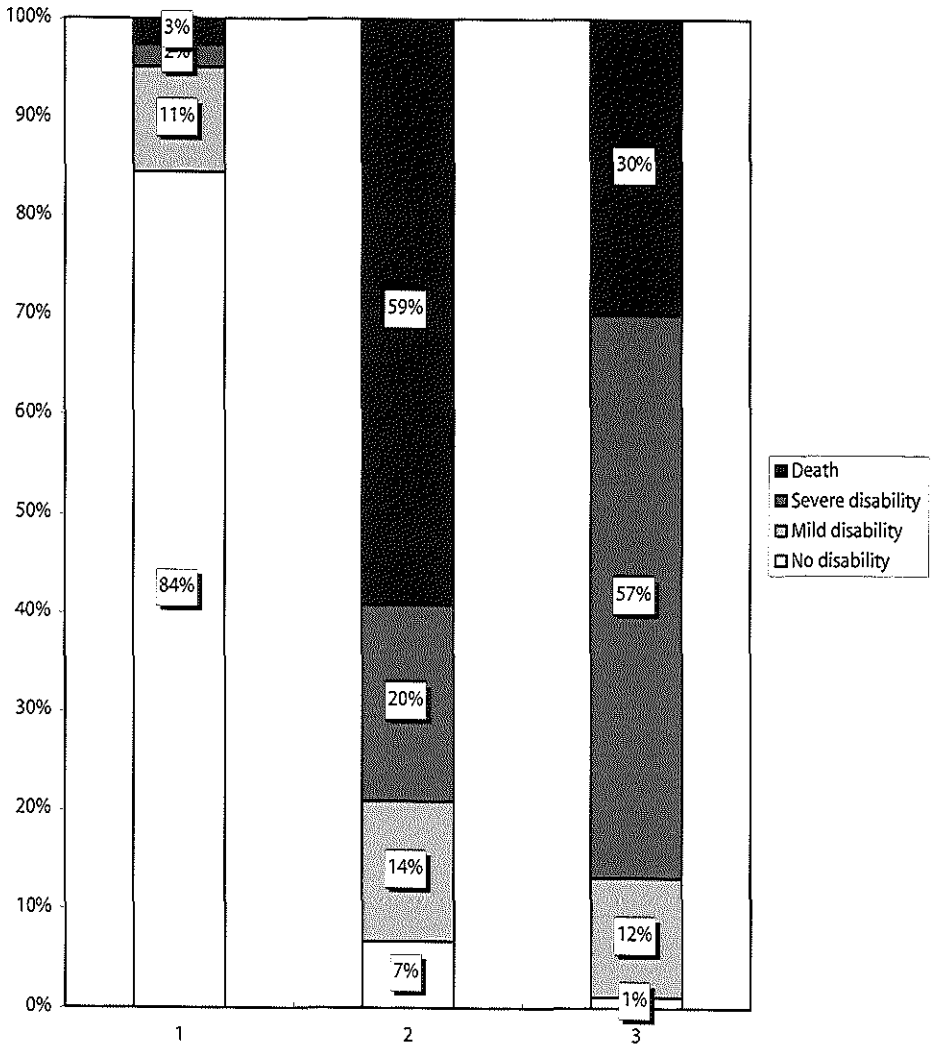


Figure 1. Probabilities of outcome at six years for three elderly with different risk profiles.

of disability but yield relatively low scores on the chart. In the oldest age groups with prior disability for example, their relevance in predicting future disability status would be negligible. The finding that one can predict future disability with a relatively small set of variables is rather unique. In a recent study a compact frailty index with three components performed as well as a more complex frailty index with five components in predicting falls, disability and mortality [14].

Strengths and weaknesses

Although prediction models have been developed for functional decline or disability in elderly who were hospitalised because of specific medical conditions, to our knowledge, this is not the case for community-dwelling elderly [15]. In this study we developed a model and a score chart to predict disability in the elderly. This method has been used in other areas of research [16, 17].

The large cohort from which the prediction rule was derived and the ease with which health care providers may obtain the predictive factors contribute to the strength of this study. The easily obtainability of variables may contribute to a higher implementability of preventive assessment of the elderly. Another merit of this study is the large ROC areas implicating a good ability of the models to discriminate between different outcomes.

A limitation of this study is the lack of validation of the prediction rule in other cohorts although the size of the derivation cohort may compensate for this. In the year 2000 however the first extension cohort of the Rotterdam Study has started comprising over 3000 elderly. As longitudinal outcomes are gathered at the moment, external validation can be done in this cohort in the near future.

As prior disability is the most important predictor and as disability status may be changed for the better by interventive strategies this would imply that there is an opportunity for preventing and treating future disability. A previous study showed that factors related to incident disability (age, gender, self-rated health, BMI, joint complaints, depression and medication) are comparable to the factors found in the current extended model on prognosis [18]. This means that interventive strategies can be implemented for preventing as well as treating disability. Although the general idea about disability is that it is irreversible, there are studies that have shown recovery from disability [19, 20]. There are several studies on possible strategies including medication or vitamin supplementation, training, home visits and geriatric assessment [2-8]. The care for the elderly with disability yields high costs. Choosing optimal preventive and therapeutic intervention remains a challenge. To guide these choices more studies on cost-effectiveness are needed as, at present, they are sparse and their results not conclusive [21].

CONCLUSION

In this study we were able to predict disability with only a few easily obtainable variables: gender, age and prior disability level. Targeting care and interventive strategies on these predictors would yield the greatest benefits.

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APPENDIX

For the three outcome categories the submodels that constitute the multinomial model can be formulated as follows:

$$Log\ (P\ 'mild\ disability'/P\ 'no\ disability') = \alpha_1 + \beta_{11}X_1 + \beta_{12}X_2 + \ldots \beta_{18}X_8 = lp_m$$
$$Log\ (P\ 'severe\ disability'/P\ 'no\ disability') = \alpha_2 + \beta_{21}X_1 + \beta_{22}X_2 + \ldots \beta_{28}X_8 = lp_s$$
$$Log\ (P\ 'death'/P\ 'no\ disability') = \alpha_3 + \beta_{31}X_1 + \beta_{32}X_2 + \ldots \beta_{38}X_8 = lp_d$$

Based on these coefficients found, probabilities for the outcomes can be calculated:

$$Probability\ (mild\ disability) = exp(lp_m) / [1 + exp(lp_m) + exp(lp_s) + exp(lp_d)] = P_m$$
$$Probability\ (severe\ disability) = exp(lp_s) / [1 + exp(lp_m) + exp(lp_s) + exp(lp_d)] = P_s$$
$$Probability\ (death) = exp(lp_d) / [1 + exp(lp_m) + exp(lp_s) + exp(lp_d)] = P_d$$
$$Probability\ (no\ disability) = 1 - P_m - P_s - P_d$$

CHAPTER 8

General discussion

GENERAL DISCUSSION

The increase of life expectancy due to socioeconomic and medical progress in the 20th century has yielded a population of elderly people that is growing in size and proportion. In the Netherlands, people of age 65 and older constitute 14% of the total population. As by 2010 the generation of the 'post-war baby boom'–referring to the increased birth-rate after the end of the Second World War– will pass the age of 65, this proportion will increase further reaching 24% by the year 2050 [1].

Aged people, especially those with chronic conditions, are predisposed to the onset of impairments and disability. Impairment is the loss or abnormality in a physiologic or anatomic structure or function of an organ. Disability indicates any restriction or inability (resulting from an impairment) to perform an activity in the manner considered normal for that individual. Disability often makes the elderly lose control over their lives and as a consequence reduces quality of life and participation in daily activities.

The development of disability through medical disorders and functional impairments is a complex phenomenon. The determinants are heterogeneous and may comprise socioeconomical, biological, psychological, lifestyle and medical factors. Often however, studies on disability focus on specific determinants in specific populations like the incidence of disability in hospitalised patients with a specific medical condition. This thesis aims to study the incidence and prognosis of disability and their determinants at different levels in a population of community-dwelling elderly.

In this chapter we briefly discuss our findings and their relevance and implications in a broader context. In separate sections, issues concerning determinants of new disability, determinants of the prognosis of prevalent disability and methodological issues are addressed and suggestions are made for future research.

Differentiation between risk factors and prognostic factors

Strategies for primary prevention, which is prevention of the occurrence of disability, may differ from strategies for secondary and tertiary prevention, which are respectively prevention of worsening of disability and prevention of complications due to existing disability. It may therefore be useful to differentiate between risk factors that contribute to the onset of new disability and prognostic factors that determine the course of disability once it is present. In our approach we have chosen to do so.

The Rotterdam Study

Besides two systematic reviews, this thesis was based on analyses from the Rotterdam Study. The Rotterdam Study is a large prospective cohort study on determinants of cardiovascular, neurological, psychiatrical, ophthalmological and locomotor diseases in the elderly [2, 3].

Initially the study comprised 7983 people of 55 years of age or over living in the Ommoord district of the city of Rotterdam in the Netherlands who were recruited from 1990 onwards. An extended cohort of 3011 participants of the same age category started in 1999.

For our research questions on risk and prognostic factors and prediction of disability we used data of the baseline and the second follow-up (six years after baseline) of the initial cohort. For our study on secular trends of disability we used data from the baselines of the initial cohort of 1990 and the extension cohort of 1999. Due to the size of the cohorts the analyses in this thesis had sufficient power to reveal statistically significant associations between determinants and outcome.

Risk factors: determinants of new disability

Our findings of the systematic review, indicate that higher age, female sex, obesity, cognitive impairment, self-rated health, depression, smoking, decreased social contacts, low income or educational level, visual impairment, diabetes mellitus, osteoarthritis, stroke, presence of co-morbidity are risk factors for the onset of disability. Higher exercise or activity levels and moderate alcohol use on the other hand seem to protect against disability. In the Rotterdam Study we detected statistically significant associations with disability for all risk factors resulting from the review, except for visual impairment, alcohol use and smoking. Furthermore we found that cognitive impairment and osteoarthritis were associated with disability in women while stroke and the presence of comorbidities were associated with disability in men. We also found that use of more than two medications was a risk factor for disability with a stronger association than the presence of comorbidities, in both men and women.

There is indistinctness in gender differences concerning the occurrence and risk factors of disability. Many studies have found there is more disability among women while some indicate that this is only the case for the oldest elderly [4]. In the Rotterdam Study we found that cardiovascular disorders such as myocardial infarction and stroke were more prevalent among men and osteoarthritis more common in women. We also found

statistically significant associations between stroke and incident disability in men and osteoarthritis and incident disability in women. This may indicate that the risk profile for disability in men has a cardiovascular accent, also contributing to an earlier death while in women it has a locomotor origin.

The nature of the relation between self-rated health and disability is unclear. Does self-rated health constitute a proxy variable for adverse health determinants, which we could not account for adequately in our multivariate analyses? Does it represent a negative psychological and behavioral state of the individual at risk? Could for example psychotherapy affect self-rated health and therefore disability outcome positively? Further research on modifiability of self-rated health and its effect on disability is needed to answer these questions.

Our review showed that in comparison with abstinence, moderate alcohol intake has a protective effect against incidence of disability. In the Rotterdam Study there was a protective trend against disability, and a significant inverse association with death. This favourable effect of moderate alcohol consumption may be due to the reduction of other risk factors or unfavourable variables like coronary heart disease, ischemic stroke and low bone mineral density [5, 6]. Moderate alcohol consumption may on the other hand represent a better risk factor profile, including higher socioecenomic status, than alcohol abstinence [7]. Before advising moderate alcohol consumption as a preventive measure to non-drinkers this relation should be further investigated.

Especially in western societies obesity has been acknowledged as a major determinant for adverse health outcomes and widespread campaigns have been initiated to raise public awareness. The relation of obesity with disability may be twofold. On the one hand obesity may influence functional status through biological and mechanical pathways, through medical conditions like diabetes mellitus or osteoarthritis or otherwise, resulting in disability. On the other hand it may itself be a result of lifestyle factors such as sedentariness and adverse dietary habits that concurrently result in disability. Addressing obesity remains necessary in order to improve health.

Medication use as a risk factor may also implicate different mechanisms. On the one hand it may represent the presence of chronic diseases, not accounted for, that lead to disability. On the other hand it may produce disability by itself through impairment of body functions like sensory impairment, orthostatic hypotension or renal failure.

Cognitive impairment, often measured with the Mini Mental State Examination (MMSE) is known to be a risk factor [8]. The MMSE however measures different aspects of cognitive

functioning like memory or executive control function [9]. For interventional purposes in a high-risk group it may be obligatory to know which aspects of cognitive function loss contribute most to incident disability. This shows that the pathways through which specific determinants exert their influence on disability seem complex. Knowledge of these pathways may be essential in better targeting preventive strategies.

Prognostic factors: determinants of the course of prevalent disability

Recovery from disability is possible. Findings from our review indicate strongly that factors like younger age, better cognitive performance and better self-rated health may facilitate recovery and that their opposites contribute to worsening of disability. For many other variables like gender, income, marital status, social contacts, body mass index and physical activity the evidence for association with prognosis of disability was limited. In the Rotterdam Study almost a fifth of those with mild disability at baseline were disability free at follow-up after six years. As there were only two measurements of disability over six years it was not possible for us to discern whether there were more episodes of disability and recovery during this period. We could only detect age and income as prognostic factors increasing the likelihood of deterioration of disability or death. When the results of our study were included in the systematic review the level of evidence for income would increase from limited to moderate.

Though it is not clear whether lower income is an indicator of an unfavourable lifestyle with respect to functioning or an indicator of impeded access to health care in general or of some other undetected variable, it should be taken into account in assessing prognosis of disability in the elderly. Especially in the light of the recent global economic recession this finding may concern a larger population of elderly.

The evidence for the influence of gender on the course of disability was not consistent as was also indicated by our findings in the Rotterdam Study. Of the people with prior mild disability relatively more men died and more women developed severe disability although this association did not seem to hold after correcting for other variables in multivariate analysis. The crude transition rates however imply that older women will be more likely to need assistance in activities of daily living than men at higher ages.

Compared to risk factors we found fewer prognostic factors for disability. The evidence for many possible determinants that were studied was limited. This may implicate that once disability is present it becomes the strongest determinant of future disability status overshadowing other variables. The limited number of studies may on the other hand,

also explain the limited evidence on the prognosis of disability in community-dwelling elderly.

Secular trends

Existing literature is not conclusive on cohort differences regarding disability. Whereas some studies indicate that there is a decrease of disability others state that the prevalence is fluctuating. Compared with the original cohort, participants of the extended cohort were on average younger and more often cohabitating. There were favourable changes between the two cohorts in time. Participants suffered less myocardial infarction, osteoarthritis and disability and rated their health more positively. Fewer women had experienced stroke. Among men there was a decrease of alcohol use and smoking. Unfavourable changes were the higher prevalence of depression, especially among women, joint complaints, obesity and the higher incidence of falls. Men had a higher prevalence of diabetes. Alcohol use and smoking had increased among women.

Factors like improved treatment of diseases, better living and working conditions and improved socioeconomic status, especially the educational level of women, may have contributed to the decline of disability. Results of a third cohort will show whether this decrease will continue. If it does, more elderly will have in prospect a life with prolonged independence. A longer follow-up with more frequent assessments will also enable us to study compression of disability towards older age.

As for now however despite decreasing prevalence rates the proportion of elderly with disability remains substantial. The search for effective intervention and development of well-adapted and accessible assistive devices for the individual elderly will remain important in order to regain or maintain a certain level of quality of life.

Prediction model for disability

Prediction models comprising information regarding patient characteristics, test results and other disease characteristics are often used to estimate the probability of occurrence of a certain outcome in an individual. They may be useful in informing patients and making clinical decisions. In order to be implemented a prediction model has to be sensible, easily applicable and above all validated in other populations than it was derived from to test its accuracy. In the longer run performing an impact analysis may be essential in order to assess the actual use and effect of the prediction model on practice and patient outcomes [10].

We developed a prediction model aiming at predicting the risk of becoming disabled and the risk of a decrease of disability in one model. Age, prior disability, female sex, cognitive impairment, poorly rated health, obesity, hypertension and joint complaints are the strongest predictors of disability. A compact multivariate model comprising only age and prior disability predicted as well as a comprehensive model comprising all mentioned variables.

For assessing risk or prognosis of disability by often busy general practitioners or their assistants, a limited number of variables to retrieve would be convenient. Although this model seems robust given the large population it was derived from it should of course be validated externally before implementation. This could be done using data of the first extension cohort of the Rotterdam Study.

Additionally we developed a user-friendly spreadsheet with which health care workers may calculate the individuals' absolute risk for different outcome categories including disability. Strategies of primary or secondary prevention could be targeted more effectively.

Methodological aspects

Research on disability is complicated. There are methodological issues regarding outcome, determinants and study design. In this section we will briefly discuss these points. To start with the outcome: disability. What is disability? Should it be measured by a questionnaire or by physical assessment? Which questionnaire out of the numerous versions should we use?

We defined disability as experiencing some difficulty in tasks concerning daily living like washing oneself or grooming. We used the Stanford Health Assessment Questionnaire (HAQ), which is a sensitive tool to detect changes in functional status compared to the widely used but less sensitive Activities of Daily Living formulated by Katz [11, 12]. The HAQ is very useful in comparing disability within consecutive cohorts of the same study but less so in comparing between different studies because of the limited number of general population cohorts in which it has been used worldwide.

The HAQ produces a disability index ranging from 0 (no disability) to 3 (maximum disability). In general someone with a disability index less than 0.50 is regarded as completely self-sufficient. That is why in the Rotterdam Study we chose this cut-off point defining disability [13]. Other cut-off points have been suggested [14]. Using a disability index is convenient for statistical purposes as it makes multivariate analyses easier to handle but

may be troublesome regarding interpretation of disability. Because the index comprises different components of function, individuals with the same disability index may differ from each other concerning the nature and impact of their disability. This makes the interpretation of study figures difficult. Using a summarising disability index may also hide changes in opposite directions in components making up the overall score.

As in our study disability status was only assessed twice in a period of six years we may have missed multiple episodes of recovery and incidence because short-term transitions were not observed. The mechanisms that lead to disability may have an acute or chronic nature resulting in more or less dynamic disability. Preferably there should be three or more moments of assessment with shorter intervals in order to better study the determinants of incidence and course of disability.

Heterogeneity in defining and assessing determinants remains a methodological problem within and between studies. In the Rotterdam Study some questions were phrased differently in the consecutive interviews, as was the case for osteoarthritis. As we found in the systematic reviews the definition criteria and ways of assessment of disability and its determinants differ between cohorts. While in some studies data are based on self-report, in others they are based on measurement. Even if determinants are measured in the same manner the cut-off value for a certain determinant may vary between different studies. This obviously impairs interpretation and comparison of the findings. Despite the overall acceptable quality of the studies we were not able to pool the data in a meta-analysis because of the heterogeneity in assessment of outcome and determinants and analysis of the associations. This may delay the development of strategies for prevention and treatment.

Research that is based on a large prospective cohort has its obvious strengths regarding the associations found between determinant and outcome and statistical (analytical) power. A drawback one can hardly escape from however is the difficulty of adjusting the often complex data collection to later understanding. In this study for example we missed information on baseline exercise or physical activity levels of the participants. At the time of the cohort design this variable generally was not regarded as relevant or reckoned with. Today however regular exercise has been acknowledged as a determinant of vibrant health and is often recommended by general practitioners to tackle different health problems ranging from depression to diabetes mellitus. Nevertheless we were able to answer most of our research questions adequately with the available data.

Our study data were largely based on self-report. We know from literature that the agreement between self-report and other methods of assessment of disability and chronic diseases may vary. Determinants of this variability in agreement are patient characteristics and the nature of the condition itself as some conditions may be subject to overreporting. In our study this may have been the case for osteoarthritis. In case of disability, self-report may however still be the proper way of assessment, as the way a person experiences his or her functioning may have more impact on the quality of life than more objective measurements by others.

The methodological quality of the studies, which we included in the corresponding systematic reviews was quite high contributing to a higher level evidence. On the one hand this may be due to the effort that is often put in such large cohorts resulting in high methodological quality. On the other hand it may be due to an existing overlap between items regarding study population and design, outcome and determinants in our selection criteria list and our list of methodological assessment criteria. Included studies would then be more likely to be of high methodological quality.

Suggestions for future research

External validation of our prediction model is necessary before it can be recommended for use as a tool in daily medical practice. This can be done with longitudinal data of the first extension cohort of the Rotterdam Study.

We recommend that multiple assessments of disability with shorter intervals are realised in order to reveal the complex pathways between determinants and disability and gain more insight in transition of disability.

As our study was of a descriptive nature we cannot give any recommendations on intervention strategies concerning disability. Randomised controlled trials are needed in order to make these suggestions. Interventional studies on disability will have to reckon with gender, prior disability, self-rated health, body mass index and cognitive functioning as well as with detection and treatment of medical conditions like osteoarthritis. As yet there is no conclusive evidence on effective and efficient prevention strategies on disability. There is evidence that multidimensional geriatric assessment including clinical examination and regular follow-up may delay the onset of disability. Given the intensiveness of such a program this may not be easily implemented in the general population of elderly [15]. The search for effective prevention requiring less effort will continue.

Existing intervention studies on exercise effects in the elderly with disability have not shown a significant reduction in disability consistently, although there was some improvement of body functions like strength, endurance and balance. This may indicate that non-physical factors like the individual's perceptions on health and disability and coping strategies are as important as the individuals' physical condition [15]. Methodological limitations regarding population selection, type of intervention and duration of follow-up may also have contributed to the inconsistent findings. Future research should therefore comprise a multidimensional intervention comprising physical and non-physical aspects in a general population of elderly with a sufficiently long follow-up period.

For future studies on disability we recommend the HAQ as it is a sensitive tool for measuring change of disability status. As there is no consensus on a universal tool for the measurement of disability we also recommend that in addition to specific instruments ADLs are used for purposes of comparison between studies internationally. Further standardisation of assessment, design and presentation is required internationally in order to be able to pool the often painstakingly produced study results.

The Rotterdam Study comprised mainly white Dutch elderly therefore we cannot generalise our findings to elderly with other ethnic backgrounds. As a growing proportion of the immigrants of the 60's and 70's in the Netherlands, like those from Surinamese, Turkish and Moroccan origin, reach old age they too become eligible and should be considered for inclusion in future prospective disability research. Already cross-sectional validity studies in this field have started [17].

Implications for daily practice

As prior disability status is the major predictor of future disability status, professionals, especially general practitioners and others working in primary care, should assess disability in their elderly patients on a regular basis in order to give them proper care or advise timely. As cognitive functioning also predicts disability this should be assessed in the elderly as well using for example the Mini-Mental State Examination (MMSE). It would probably take half an hour per elderly to assess disability and cognition with the HAQ, ADL and MMSE, which seems workable and could be done by the doctor's assistant. Feasibility studies however are needed to find out whether such a screening really would be viable. Another issue is the availability of a feasible intervention program without which it would be difficult to convince primary care professionals to monitor disability in the elderly. As disability is a common problem in the elderly there should

be more attention for it during the training of medical professionals, especially general practitioners.

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Summary

SUMMARY

The risk of disability increases with age. Therefore disability, in most cases being a chronic condition, constitutes a common health problem among the elderly and yields economical and logistical challenges for society. The main objective of this thesis is to identify risk factors and prognostic factors of disability and to study possible secular changes of disability in community-dwelling elderly. The factors that were considered comprise mainly determinants that can be easily obtained in a primary care setting by history taking, physical examination or basic laboratory studies.

Chapter 2 presents a systematic review of the evidence on the impact of sociodemographic and (bio)medical variables on incident disability. Articles up to June 2009 presenting prospective studies comprising elderly who were disability free at baseline were reviewed. Due to heterogeneity of the studies a meta-analysis could not be performed and a synthesis of the available evidence was made. High age, depression and comorbidity, especially arthritis were identified as moderate to strong predictors of disability. These factors should be taken into account in developing preventive policies while further standardisation of methodology is required to obtain higher levels of evidence with meta-analysis.

Chapter 3 reports our study on the incidence of disability in the elderly and its risk factors using original data from the Rotterdam Study. The study sample comprised people who were 55 years of age and over and disability free at baseline. The follow-up period was 6 years. Disability was defined as a Disability Index (DI) ≥0.50 according to the Health Assessment Questionnaire. Multivariate analyses revealed that age, self-rated health, overweight, depression, joint complaints and medication use were predictors of disability for both men and women. Stroke, falling and presence of comorbidities predicted disability in men only while having a life companion, poor cognitive functioning, osteoarthritis and morning stiffness only predicted disability in women.

Chapter 4 describes our systematic review of the evidence on the influence of sociodemographic, lifestyle and (bio)medical variables on the course of prevalent disability and transition rates to different outcome categories in community-dwelling elderly people. Prospective population studies that assessed disability at baseline and reported on associations between potential prognostic variables and disability were included. After synthesis of the available evidence we found moderate to strong evidence that higher age, cognitive impairment, vision impairment and poor self-rated health are prognostic factors of disability.

In **chapter 5** we describe our study on the prognosis of disability and its determinants in a population of older people based on data from the Rotterdam Study. Of a total of 950 people who had mild disability at baseline and completed the follow-up six years later nearly 18% recovered from disability, 20% stayed mildly disabled, 31% shifted into a severe disability state and 32% deceased. Relatively more men died than women and a larger proportion of women had a worsened disability outcome. Age, gender, income, self-rated health and alcohol use were predictors of disability prognosis. These few prognostic factors that are limitedly or not modifiable provide little space for successful intervention once disability has become present.

In **chapter 6** we compare and evaluate changes over time in health status, including disability, in the elderly using baseline data of two consecutive cohorts of the Rotterdam Study. Of the initial cohort (baseline measurement 1990) 7368 persons of 55 years and over were included while of the first extension cohort (baseline measurement 2000) 2973 persons were included. Compared to the initial cohort the elderly of the extension cohort were on average younger, had a higher level of education and were more often living with their spouse. The prevalence of stroke and myocardial infarction was lower while the prevalence of morning stiffness, joint complaints and diabetes mellitus was higher in the extension cohort. Overall there was less disability in the extension cohort. Mean total cholesterol levels were lower. The prevalence of overweight had increased compared with the initial cohort. More falls were reported in the extension cohort. Aside from some adverse trends, in general the elderly were healthier compared with ten years earlier.

Chapter 7 describes the development of a prediction model for disability in community-dwelling older people based on data from the Rotterdam Study, including 5027 subjects of 55 years and over. We used a multivariate polytomous logistic regression to derive a basic model comprising age, gender and prior disability status and an extended model which in addition comprised body mass index, self-rated health, joint complaints and hypertension. Finally we developed readily applicable score charts for the calculation of outcome probabilities. The strongest predictors were age and prior disability. The contribution of other predictors was relatively small. The discriminative ability, based on the area under the receiver operating characteristic curve, of the basic model was high. The extended model did not enhance predictive ability. As prior disability status predicts future disability status, interventive strategies should be aimed at preventing disability in the first place.

Chapter 8 discusses the main questions and findings addressed in this thesis. The chapter especially deals with the way different factors may exert their influence on the

incidence and prognosis of disability and several methodological aspects of research on disability. Finally implications for further research in this field and daily practice are discussed and some recommendations are made.

Samenvatting

SAMENVATTING

Het risico op het ontstaan van beperkingen in het functioneren neemt toe met de leeftijd. Het hebben van een funtionele beperking is vaak een chronische aangelegenheid die veel ouderen treft en de maatschappij voor economische en logistieke uitdagingen stelt. De belangrijkste doelstelling van deze dissertatie is het identificeren van risico – en prognostische factoren van functionele beperking en mogelijke verschillen in functionele beperking over een langere periode te onderzoeken. De onderzochte variabelen zijn voornamelijk determinanten die eenvoudig te achterhalen zijn via anamnese, lichamelijk onderzoek of basaal bloedonderzoek.

Hoofdstuk 2 geeft een systematische review weer naar het bewijs voor de bijdrage van sociaal-demografische en (bio)medische variabelen op het ontstaan van functionele beperking. Hiervoor werden artikelen tot juni 2009 beoordeeld van prospectieve studies met een populatie van ouderen die op baseline functioneel niet beperkt waren. Wegens heterogeniteit van de sudies kon geen meta-analyse worden verricht. In plaats daarvan werd een 'best evidence'- synthese uitgevoerd. Hoge leeftijd, depressie en comorbiditeit, met name artrose kwamen naar voren als (matig) sterke voorspellers van functionele beperking. Bij het ontwikkelen van preventieve strategieën zou met deze determinanten rekening moeten worden gehouden. Verdere standaardisatie van onderzoek is gewenst teneinde middels meta-analyse een hoger bewijsniveau te verkrijgen.

Hoofstuk 3 beschrijft ons onderzoek naar de incidentie en risicofactoren van functionele beperking bij deelnemers van het ERGO-cohort in Rotterdam. De onderzoekspopulatie bestond uit mensen van 55 jaar of ouder die op baseline geen functionele beperking hadden. De follow-up periode bedroeg 6 jaar. Functionele beperking werd gedefinieerd als een Disability Index (DI) ≥0.50 aan de hand van de Health Assessment Questionnaire. Multivariate analyse wees uit dat leeftijd, ervaren gezondheidsniveau, overgewicht, depressie, gewrichtsklachten en medicijngebruik bij mannen en vrouwen functiebeperking voorspelden. Doorgemaakte beroerte, vallen en de aanwezigheid van comorbiditeit waren alleen bij mannen voorspellers, terwijl het hebben van een life companion, verminderd cognitief functioneren, artrose en ochtendstijfheid alleen bij vrouwen voorspellers waren van functionele beperking.

Hoofdstuk 4 beschrijft onze systematische review van het bewijs voor de bijdrage van sociaal-demografische en (bio)medische variabelen op de prognose van functionele beperking en de overgang naar verschillende categorieën van functionele beperking bij ouderen. Prospectieve studies met baselinegegevens over functionele beperking en analyses van de relatie met prognostische variabelen werden geïncludeerd in de review.

Na synthese vonden wij matig tot sterk bewijs dat hogere leeftijd, cognitieve dysfunctie, gezichtsbeperking en een slechter ervaren gezondheid prognostische determinanten zijn van functionele beperking.

In **hoofdstuk 5** beschrijven wij onze studie naar de prognose van functionele beperking en determinanten daarvan bij de deelnemers van het ERGO-cohort in Rotterdam. Van de 950 personen die op baseline een lichte beperking hadden was tijdens de follow-up zes jaar later bijna 18% vrij van beperking, had 20% een lichte beperking, kreeg 31% een ernstige beperking en overleed 32%. Relatief meer mannen dan vrouwen stierven gedurende de studieperiode en een groter deel van de vrouwen had meer beperkingen bij de vervolgmeting. Leeftijd, geslacht, inkomen, ervaren gezondheidsniveau en alcoholgebruik waren voorspellers van de prognose van functionele beperking. Deze determinanten, die nauwelijks of niet beïnvloedbaar zijn, bieden weinig ruimte voor een succesvolle interventie wanneer functionele beperking eenmaal is ontstaan.

In **hoofdstuk 6** vergelijken en bespreken wij de veranderingen in de gezondheidstoestand van ouderen, inclusief functionele beperking, over een langere periode. Hierbij maken wij gebruik van de data van twee opeenvolgende cohorten van het ERGO-onderzoek in Rotterdam. Van het eerste cohort (baseline-meting 1990) werden 7368 personen van 55 jaar en ouder geïncludeerd, van het vervolgcohort 2973 personen (baseline-meting 2000). Vergeleken met het eerste cohort waren de deelnemers van het vervolgcohort gemiddeld jonger, hadden een hoger opleidingsniveau en leefden vaker samen met hun life companion. De prevalentie van beroerte en hartinfarct in het vervolgcohort was lager terwijl de prevalentie van ochtendstijfheid, gewrichtsklachten en diabetes mellitus hoger was. Over het geheel was er minder functionele beperking in het vervolgcohort. Ook de gemiddelde cholesterolwaarden waren lager. Vergeleken met het eerste cohort was de prevalentie van overgewicht in het vervolgcohort hoger. Meer ouderen rapporteerden een val in dit cohort. Concluderend waren de ouderen van het vervolgcohort, op enkele ongunstige ontwikkelingen na, in het algemeen gezonder dan tien jaar daarvoor.

Hoofdstuk 7 beschrijft de ontwikkeling van een predictiemodel voor functionele beperking bij ouderen gebaseerd op data van 5027 deelnemers van 55 jaar en ouder in het ERGO-onderzoek in Rotterdam. Wij maakten gebruik van multivariate logistische regressie om een basismodel af te leiden met leeftijd, geslacht en prevalente functionele beperking en een uitgebreider model met hieraan toegevoegd body mass index, ervaren gezondheidsniveau, gewrichtsklachten en hypertensie. Tenslotte ontwikkelden wij een gebruiksklare scorekaart voor de berekening van de kansen van de verschillende uitkomsten. De sterkste voorspellers waren leeftijd en prevalente functionele beperking.

De bijdrage van andere voorspellers was relatief klein. Het onderscheidend vermogen van het basismodel was groot. Het uitgebreide model vergrootte het predictief vermogen niet. Aangezien pre-existente functionele beperking toekomstige functionele beperking het best voorspelt zou het beleid in de eerste plaats erop gericht moeten zijn om het ontstaan van functionele beperking te voorkomen.

In **hoofdstuk 8** bespreken we de belangrijkste vragen en uitkomsten van deze dissertatie. Er wordt met name uiteengezet hoe verschillende determinanten mogelijk van invloed zijn op het ontstaan en de prognose van functionele beperking. Enkele methodologische kwesties in het onderzoek naar functionele beperking worden behandeld. Tenslotte worden de implicaties voor toekomstig onderzoek op dit gebied besproken en worden enkele aanbevelingen gedaan.

Dankwoord

DANKWOORD

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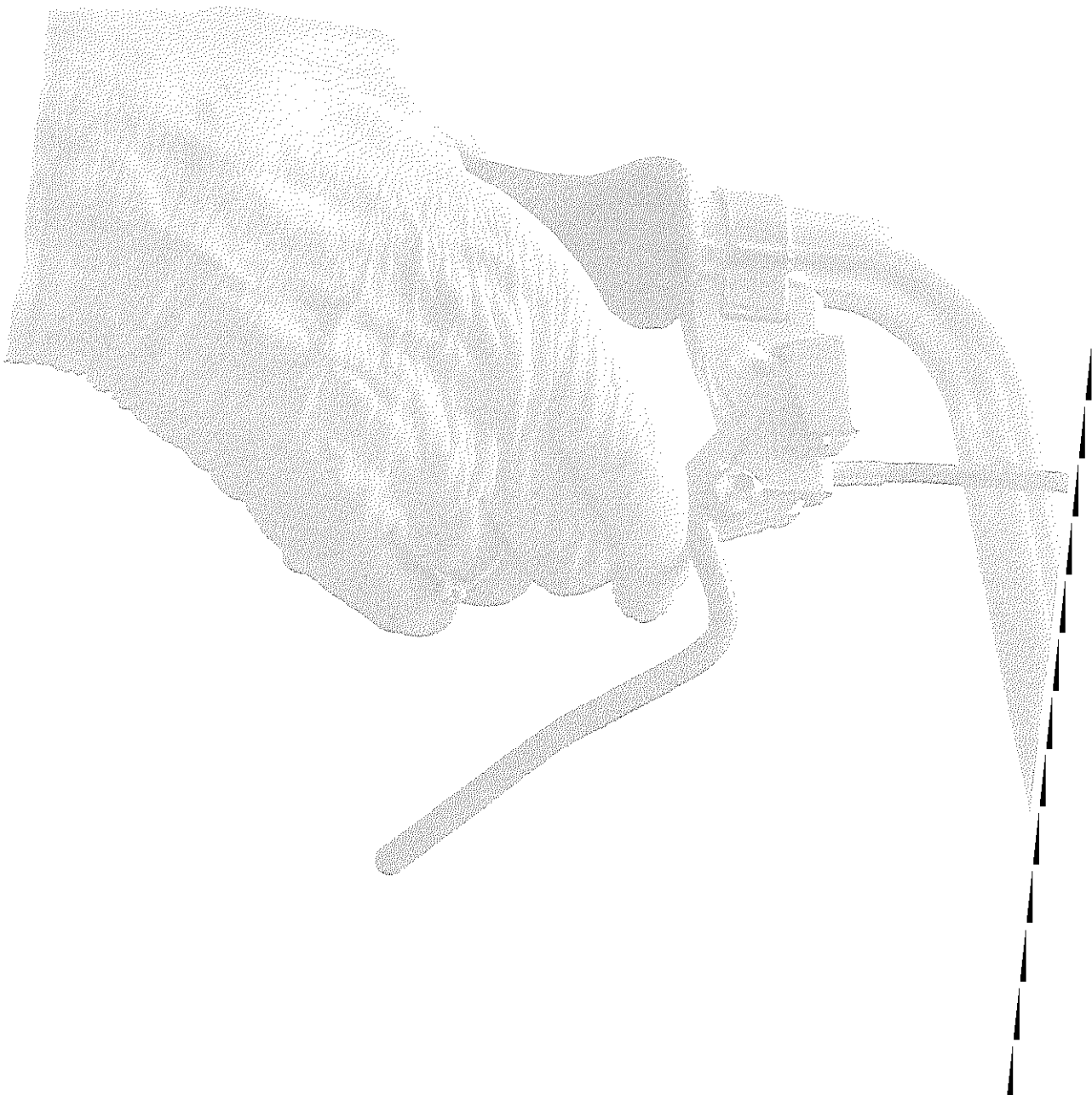
Lieve Marianne, bij jou kan ik aan de gang blijven. Laat ik maar samenvatten: bedankt dat je er bent...

Curriculum Vitae

CURRICULUM VITAE

Ümit Taş werd geboren in Amsterdam op 4 februari 1971. Hij heeft twee zussen en drie broers. Na het behalen van zijn VWO diploma aan het Katholiek College Amsterdam, voorheen het Pius X Lyceum werkte hij een jaar lang in het verzekeringswezen wegens uitloting voor de studie geneeskunde. In 1990 begon hij alsnog aan deze studie aan de Vrije Universiteit te Amsterdam. Tijdens zijn opleiding verzorgde hij werkgroepen voor de vakken 'Filosofie en ethiek van de geneeskunde' en 'Cultuur en gezondheid'. Na het behalen van het artsexamen begon hij in 2002 aan het gecombineerde traject van de opleiding tot huisarts en onderzoeker waarvan deze dissertatie een onderdeel vormt. In deze periode behaalde hij zijn Master of Science in de klinische epidemiologie aan het Netherlands Institute for Health Sciences. Sinds 2007 werkt hij als waarnemend huisarts.

Vanaf de studententijd is hij betrokken geweest bij verschillende organisaties die tot doelstelling hebben de dialoog tussen mensen met verschillende culturele en religieuze achtergronden te bevorderen. Hij is getrouwd met Marianne Vorthoren en woont in Rotterdam.



PHD PORTFOLIO

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1. PHD TRAINING

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MSc in Clinical Epidemiology, NIHES, Rotterdam, 2002-2004 70 EC
GENERO workshop 'geriatric assessment', Erasmus MC, 2009

Professional Education

Vocational training for general practitioner, ErasmusMC, Department of General Practice, 2003 - 2007

Presentations

Annual Science Conference of the Dutch Society of General Practitioners
- Leiden, 2004 (oral presentation)
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Annual Conference of the Society for Academic Primary Care, Keele, United Kingdom, 2006 (poster presentation)

International Congress of Elderly Health of the Geriatrics Society , Istanbul, Turkey, 2006 (oral presentation)

9th Scientific Conference of the International Federation of Orhopaedic Manipulative Therapists, Rotterdam, 2008 (oral presentation)

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Supervising medical students practical, 2007 – 2008

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