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Healthy ageing

Tackling the burden of disease and disability in an ageing population

Bart Klijs

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BART KLIJS

Healthy Ageing: tackling the burden of disease and disability in an ageing population

Gezond ouder worden:
een aanpak van de last van ziekten en beperkingen
in een verouderende samenleving

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Overige leden:	Prof.dr. P.J.E. Bindels
	Prof.dr. W.B.F. Brouwer
	Prof.dr. P.A. Dykstra
Copromotor:	Dr. W.J. Nusselder

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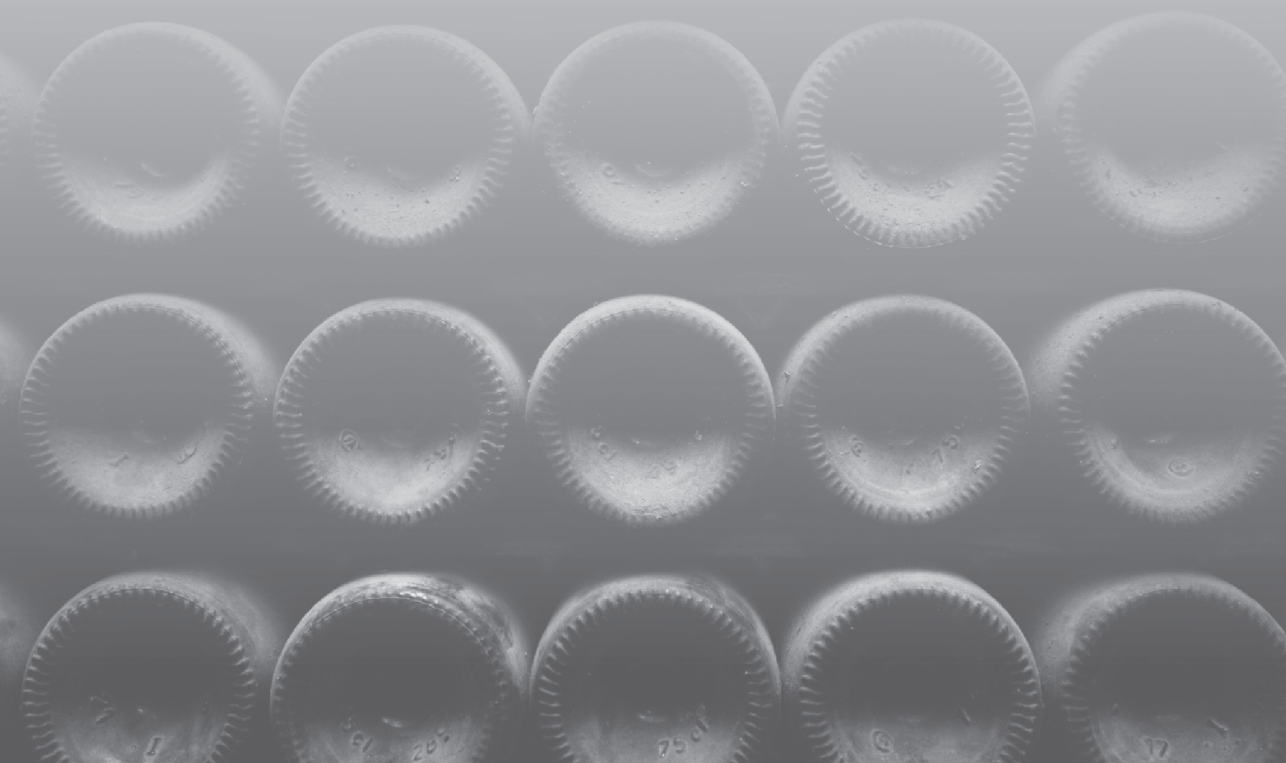

POPULATION AGEING

Population ageing is the shift in the distribution of a country's population towards older ages and is caused by declined fertility rates and increased longevity. This phenomenon is currently occurring in nearly all countries in the world, is unprecedented in human history, and has major implications for all aspect of life (1). Worldwide, declines in fertility and increases in longevity have resulted in a steady rise in the proportion of older persons aged 60 and over, passing from 8 percent in 1950, to 11 percent in 2009, to 22 percent expected in 2050 (1). In the developed world, the very old (age 80+) is the fastest growing population group and, according to Statistics Netherlands, the pace at which population ageing is occurring is currently increasing (2-3). That is, between 2006-2010, the Dutch population aged 65 and over increased by 250.000 persons, whereas between 2011-2015, the increase is expected to double and be 500.000 (3).

Further greying of the population will inevitably occur the next decades. Nevertheless, the extent to which it will occur is uncertain and will particularly depend on future trends in mortality. Regarding the extent past declines in old age mortality will continue into the future, there is ongoing debate, which has its focus on the issue if there is a limit to human life span and whether or not we are approaching this limit. Essentially, two main perspectives are distinguished in the debate. Proponents of the limited-lifespan paradigm put forward that ageing is a natural phenomenon that can be influenced only limitedly (4-9). They claim that from an evolutionary perspective, the human body is not designed for extended survival but for reproduction. Therefore, biological and practical constraints will slow down future gains in life expectancy and the limit to human life expectancy will soon be reached. Adherents of the mortality-reduction paradigm argue that there is no reason to believe that past mortality declines will soon come to an end and that, most likely, the long and favourable trends for life expectancy will continue in the future (10-13). Their prognosis is based on best practice, that is, the highest life expectancy observed somewhere in the world in a given year. Their arguments are further substantiated by referring to trends in sub populations with extreme good health, to rapid mortality declines including in countries with already low levels of old age mortality, and to foreseen biomedical progress.

SOCIETAL CHALLENGES OF POPULATION AGEING

The shift of a country's population towards older ages poses great financial and social challenges (14). Among the main financial challenges are how to keep the current health care system affordable and how to secure the sustainability of the public pension system (15). With respect to the first, a substantial increase in health care expenditures is expected the

next decades, not only as a result of an increasing number of elderly people, who have higher disease risks than younger people, but also as a result of increasing costs per person, among others due to new and more expensive medical technology. According to projections of the National Institute of Health and the Environment, the expenditures will annually increase by 3.4% until 2030 (16). Consequently, health care expenditures are expected to put an increasing claim on the national budget (17). In 2010, healthcare accounted for 7.4% of the Gross Domestic Product, whereas in 2015 this is expected to have increased to 10.9% (17). Major reforms such as budget restraints are already being implemented with the aim to keep health care affordable (18).

The second challenge, the sustainability of the pension system, is importantly related to the structure of the system. In the current system, pension premiums paid by the Dutch working population are at the same time used to pay pensions of others. When the age distribution of a population shifts upward this implies that the number of pension receivers increase while the number of those who pay premiums decrease. Currently, there are four employees to every single elderly person, but, until 2040, this is expected to decline to only two employees (19). Furthermore, ongoing increases in the life expectancy have resulted in a steady rise of the average number of pension years. That is, since the current pension system was initiated in 1957, the pension age in the Netherlands has remained 65, while the life expectancy at age 65 has increased with 3.5 years for males and 5.5 years for females (20). Currently, there is intense debate how to secure the sustainability of the pension system. Discussion points include the linkage of the pensionable age to trends in the life expectancy, linkage of the height of pensions to future economic developments and how to achieve an equitable distribution of risks and benefits between older and younger generations (21).

In addition to the financial issues, population ageing poses major social challenges, such as how to keep the growing population of elderly healthy and how to prevent strong declines in the quality of life. Currently, about half of the Dutch (non-institutionalized) population of 65 years and older has at least one chronic condition and around 20% of the elderly have multiple chronic conditions (22). One third of this population is disabled in hearing, seeing, mobility or ADL and, among persons aged 80 years and older, there are more individuals with disability than without (22). As the risk of the onset of disease and disability increase with age, greying of the population is expected to lead an eminent increase in the number of persons that are diseased or disabled (22). Substantial inequalities exist in the occurrence of disease and disability. Among persons with an elementary education only, the prevalence of mobility disabilities is two times higher and of ADL disabilities almost five times higher than among persons with a tertiary education (22). Therefore, the negative health effects of population ageing may be much stronger among low socioeconomic groups than among high socioeconomic groups. In addition to the health consequences in terms of disease and

disability, population ageing may result in a strong increase in the number of individuals who have mental health problems, such as memory problems and dementia, or have feelings of depression or helplessness (22-23). Increasing trends in physical and mental functioning may lead to an increased demand for formal and informal care, while at the same time sources of support decline.

A keyword in solutions proposed to tackle the challenges of population ageing is 'participation' (22,24-25). Among others, it has been suggested that healthy elderly could participate to provide the (professional) care and support that is needed to take care of the dependent elderly. A raise in the legal pension age and longer working could result in higher lifetime pension premiums and lower pension payments and could contribute to a solution to the pension problem. Although there is no clear consensus about the health effects of working longer, some studies show that labour participation is protective for mental and physical health declines, suggesting that it might also help to prevent or delay the onset of disease among the elderly (26-31). Elderly persons often have knowledge and competencies that younger persons are lacking. Society could benefit from the capacities that are specific to old age by increased participation of elderly in social, cultural and political aspects of society as well as in family and community life (25, 32-33). For persons to participate until older age, however, a certain level of physical and mental functioning is essential. Being unhealthy has been shown to lead to job loss and work disablement as well as to fewer contacts with persons within organisations, friends, and acquaintances (34-37). Therefore, improving health and reducing disability among the elderly are of paramount importance for healthy ageing. Moreover, it has been argued that investing in the health of future generations may help to preserve 'human capital' and can stimulate economic growth (38). In short, successful ageing, defined as ageing free of diseases and risk factors for disease, while maintaining an adequate level of physical and cognitive functioning and being actively engaged with life is a major challenge for coming generations (39-40).

POPULATION AGEING AND HEALTH

The extent to which future generations will be able to participate actively in society and to work until older ages will not merely depend on the extent persons will live longer in the future, but, more importantly, on the extent people will live longer in good health. With regard to future morbidity developments, two main scenarios have been suggested (4,41). The pessimistic scenario, which was proposed by Gruenberg in 1977, is known as the expansion of morbidity hypothesis (41). According to this hypothesis, further increase in the life expectancy will mainly be due to improvements in life saving treatment of persons who are ill. Furthermore, when persons live longer, a larger proportion will be exposed to nonfatal

disabling diseases of old age. Therefore, according to the expansion hypothesis, population ageing will inevitably increase the years lived in ill health. The optimistic scenario is known as the compression of morbidity hypothesis and encompasses a reduction in the years spent in ill health (4). In its original form, the theory stated that there is a genetically endowed limit to the life of human species and that the average life expectancy is rapidly approaching its limit. Due to further lifestyle improvements, the age at first morbidity onset would be postponed, which, in combination with a fixed length of life, would lead to a shorter time spent in ill health. In its more evolved form, the theory comprises that an absolute compression of morbidity will be achieved when the average age at first morbidity onset will increase more than the average age at death. A third, intermediate hypothesis is that of dynamic equilibrium (42). This hypothesis proposes that increased survival will produce an increase in the years lived with illness, but that the period spent with severe levels of illness will remain constant, because the progression of chronic diseases will be reduced.

To assess possible trends in morbidity, 'disability' has been conceptualised, which is a generic measure of consequences of chronic diseases and ageing on the functioning of a person. This measure is particularly relevant for populations of elderly for whom good physical functioning and maintaining independence in daily life is not guaranteed. Successful ageing includes a reduction in the burden of disability in a situation of increasing life expectancy. For investigating developments in the burden of disability, it is not sufficient to merely look at the age specific prevalence of disability. That is, in a situation of increasing life expectancy, a decreasing age specific prevalence of disability does not always mean a reduction in the years lived with disability because part of the extra years lived may be years with disability. Therefore, in addition to prevalence measures, it is recommended to use summary measures of population health that at the same time reflect survival and physical functioning (43). Such measures include life expectancy with disability (LED) and disability free life expectancy (DFLE) which represent the years lived with and without disability.

Since the various theories on morbidity developments were conceived in the 1970s/1980s, researchers have aimed to investigate according to which of the hypotheses morbidity was developing and whether a compression of morbidity was occurring. Research showing that good health habits can lead to greatly increased functional ability showed that, in theory, a compression of morbidity is feasible (5, 44). Whether a compression indeed occurred was investigated in trend studies. Most of the trend studies in the US showed declines in physical and sensory functional limitations during the 1980s, 1990s and the early twentieth century (45-50). A few studies found no significant change in physical limitations for ages 40-59 for 1997-2006 and no change in hearing problems for 1997-2004 (48, 50). Similar to the declines in functional limitations, most studies showed declines in the prevalence of iADL and ADL disabilities (48, 51-54). Data from the important National Long-Term Care Survey showed that for

the period 1982-2004, mortality declined about 1% a year and that declines in disability averaged 1.27% (51). Although the quality of some studies was less than desirable and differences exist in period, definition of disability, treatment of the institutionalized population, and age standardizing of results, the general impression from the several studies performed in the US is that compression of morbidity has occurred (55). For (Western) Europe, the evidence is less consistent. For Austria, the UK and Spain, there is evidence for a compression (56-58). A recent meta-analysis in the Netherlands showed no evidence for declines in the prevalence of 10 out of twelve activity limitations and suggested expansion (59). For France, an analysis using various national datasets showed patterns diverging according to the underlying disability measure, which connects most closely to dynamic equilibrium (60). Some years ago, a synthesis of evidence was conducted within the REVES network on health expectancy (61). It was suggested that part of the cross-national differences in disability trends is related to severity of disability (61). Severe disability would develop more favourably than mild disability, which gave the overall impression of a dynamic equilibrium in Europe (61). However, the evidence was not very strong and it is unclear whether the conclusions also hold for more recent years.

For the coming decades, a compression of mild and severe disability would obviously be advantageous given the positive effects on the quality of life and the positive influence that can be expected for care expenditures. An increase in the years lived free of disabilities would allow individuals to work longer in good health and to participate until older ages. However, it is currently unclear whether a compression or an expansion is to be expected.

RESEARCH QUESTIONS

Important suggestions how to investigate future developments of morbidity when a further increase in the life expectancy is expected come from health economics research. Studies in this field of research investigated how strong health care costs are related with age (time since birth) and time to death and it was shown that a substantial part of costs for health care is reserved to the end of life. Given this relationship of costs with the end of life, a further increase in the life expectancy is expected to combine with a shift of health care costs towards older ages and an increase in the life time costs that is only moderate (62-65). A similar relationship with approaching death could also exist for the occurrence disability. Describing current associations of disability with age (time since birth) and time to death could shed important new light on potential future developments of disability.

Quantification of disease burden using generic measures such as disability is important to obtain an overall impression of a populations (future) health status. In addition, for health policy decisions and future health care planning it is important to know frequencies of occur-

rence for specific diseases. Underlying cause of death statistics are often used to quantify the burden of a specific disease and are a frequent basis for policy decisions. However, as these statistics are intended to represent primary causes of death, the burden of diseases that are no direct cause of death but contribute as a secondary cause may be underestimated. Combined use of individually linked data sources may yield a more complete overview of (co-) occurrences of diseases at the end of life.

Insight in the causes of disability is essential. The expected increase in the number of elderly persons may lead to an inevitable increase of disability in the population, but interventions effectively targeting the determinants of disability could potentially prevent part of the expected increase. A variety of diseases and risk factors have been shown associated with disability onset and years lived with disability (5, 66-71). However, it is not fully understood which diseases and risk factors contribute most to disability and among which groups the largest reductions could be achieved.

As groups with a low socioeconomic position have a substantially higher burden of disability than groups with a high socioeconomic position, these groups also have substantial potential for reductions in the burden of disability (68-72). Disability reductions among low socioeconomic groups could contribute to reducing health inequalities. Currently, it is insufficiently known which diseases contribute most to socioeconomic inequalities in the burden of disability. To effectively target inequalities in the burden of disability, knowing which diseases contribute most to the inequalities is crucial, as well as elucidating whether diseases contribute most by differences in their prevalence or by differences in the extent they lead to disability (disabling impact).

The research questions assessed in this thesis are:

1. What is the current burden of disease and disability?
2. Which determinants explain the current burden of disability?

For research question 1 a specific focus will be on the occurrence of disease and disability in relationship with the end of life. The focus for research question 2 will be on diseases and life style factors as determinants of (inequalities in) the burden of disability. The following sub questions will be addressed:

1. What is the prevalence of diseases and co-occurrences in the last two years of life?
2. To what extent is the occurrence of disability associated with age (time since birth) and time to death?
3. Which diseases contribute most to the burden of disability?

4. Which diseases contribute most to educational inequalities in the burden of disability?
5. Which lifestyle factor is most important for spending many years with disability: obesity, smoking or heavy drinking?

OUTLINE OF THE THESIS

This thesis is divided into two main parts that correspond with the two research questions.

Part I Disease and disability occurrence

In chapter 2, the prevalence of diseases most common at the end of life is assessed as well as the prevalence of their most common co-occurring conditions. Nation-wide individually linked information is used regarding underlying and secondary cause of death and diagnosis of hospital discharge within two years prior to death. It is assessed whether multiple causes of death (underlying + secondary) provide complete information on end of life disease occurrence or whether substantial additional information is contained in hospital discharge records.

Chapter 3 consists of two parts. In part 3.1, the prevalence, incidence and severity of ADL and OECD disabilities (functional limitations) are described in relationship with age (time since birth) and time to death. This is done for various age groups and for groups in presence of various chronic conditions. Aiming to test the key assumption of the theory of a dynamic equilibrium, which is that mild disability is related most strongly with age and severe disability most strongly with time to death, part 3.2 describes relationships of ADL disabilities with age and time to death for three severity levels of disability. The agreement of our findings with observed disability trends is discussed as well as the implications for future disability developments. Data from six annual waves of the Dutch GLOBE longitudinal study and a subsequent 12-year mortality follow-up are used.

Part II Explaining the burden of disability

The contribution of chronic diseases to the burden of ADL disability is investigated in chapter 4 using data from the Dutch POLS survey 2001-2007. Using an additive regression model and accounting for co-morbidity, the disabling impact of selected chronic diseases is calculated. The disabling impact and information on diseases present in individuals are used to partition the prevalence of disability and years lived with disabilities into contributions of specific diseases.

In chapter 5 it is assessed to what extent diseases contribute to educational inequalities in the prevalence of OECD disabilities. Pooled data of seven subsequent years (2001-2007) from the Dutch POLS survey and a methodology similar to that in chapter 4 is used. However, in this analysis disease contributions to the prevalence of disability are estimated for groups differing according to their highest level of education obtained. Furthermore, it is investigated to what extent disease contributions to inequalities are due to differences in the disabling impact.

Chapter 6 addresses which lifestyle factor (obesity, smoking or heavy drinking) is associated most with living many years with ADL disability using a Sullivan life table approach. Furthermore, it is assessed whether Sullivan life table estimates are improved by stratification according to age at death. Data from the Dutch POLS Survey 1997-1999 with mortality follow-up until 2006 are used

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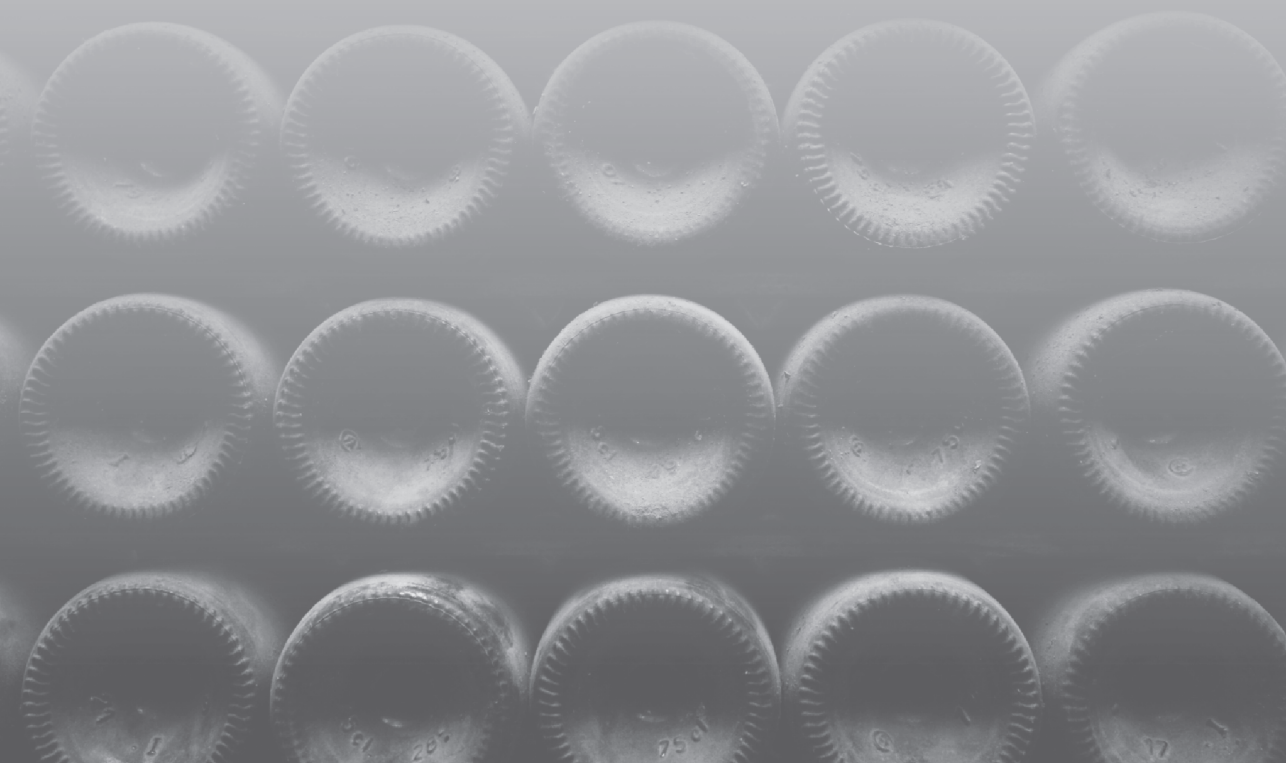
Part I

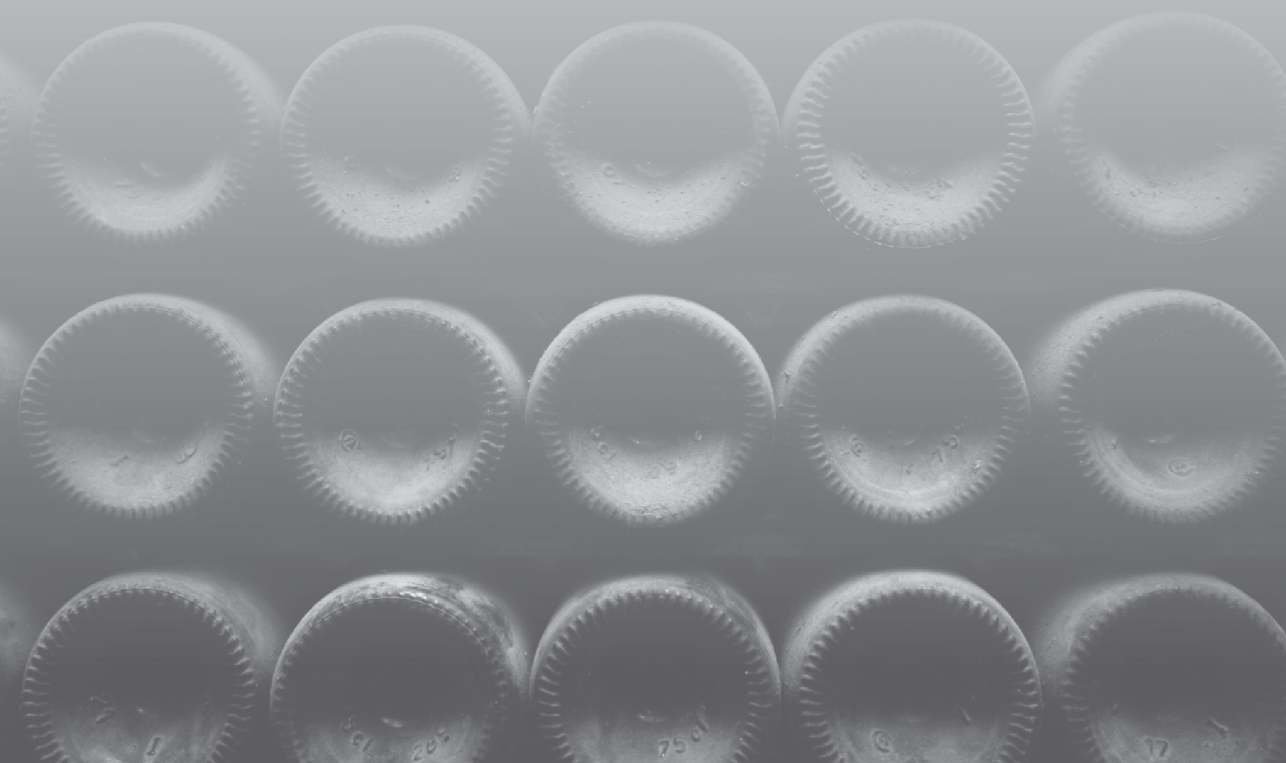
Disease and disability occurrence



2

Disease prevalence in the last two years of life

Klijs B, Nusselder WJ, Mackenbach JP. Disease presence among decedents: a nationwide study using combined information from death certificates and hospital discharge records. Manuscript



Introduction The end phase of life is characterized by substantial health declines and complex multi-morbid disease patterns. The primary aim of this paper is to investigate whether multiple causes of death provide a complete overview of disease occurrence at the end of life, or whether individual linkage with hospital discharge records provides substantial additional information. A secondary aim is to provide the prevalence for the diseases most common at the end of life as well as for their co-occurrences, using the individually linked data.

Methods Nationwide multiple causes of death information was individually linked with diagnoses of discharge within two years prior to death available through the National Medical (hospital) Registration for all Dutch inhabitants aged 50-84, who died in 2005 (n=86,987). The change in disease prevalence and ranking with and without using hospital discharge information was assessed. The two year period prevalence was provided for the diseases most common at the end of life, as well as for their three most prevalent co-occurrences, using all information combined.

Results For some diseases, especially for neoplasms, information from hospital discharge records added only little to the information provided in multiple causes of death. Other conditions, such as cataract and anaemia were hardly mentioned as a cause of death, but had a high prevalence (4.7 and 3.8 in males and 5.1 and 4.3 in females) when including hospital diagnoses. Although the order of the ranking of the 5 most common diseases changed, the content of the top 5 remained unaffected, with the exception of heart failure in women (from rank 12 to 5). In males, diseases most prevalent at the end of life were pneumonia (14%), cancer of trachea, bronchus and lung (13%), acute myocardial infarction (12%), COPD and bronchiectasis (12%) and cerebrovascular disease (11%). In females, these were cerebrovascular disease (13%), pneumonia (12%), dementia (11%), diabetes (11%) and heart failure (9%). 70-80% of all deaths had one or more concurrent conditions and 20-30% even had three or more co-occurring conditions.

Conclusion Multiple causes of death do not provide complete information regarding disease occurrence prior to death. Using individual information from hospital records in addition results in higher estimates of disease prevalence and co-occurrences. Although this affects the order of ranking of the most common conditions, it does not lead to substantially different conclusions regarding which diseases are most important.

INTRODUCTION

Cause of death statistics are of major importance for quantifying burden of disease and are often relied on for policy decisions. Cause of death statistics originated in the era of infectious diseases, in which most persons died due to one major cause and at a relatively young age. It was therefore that burden of disease could validly be quantified according to frequencies of the underlying cause of death, which was conceptualized as "the disease or injury that initiated the train of morbid events leading directly to death" (1). Now, after completion of the epidemiologic transition, persons tend to die at older ages and, in most instances, in presence of multiple co-occurring conditions (2-6). To illustrate, it has been estimated that 55-98% of the elderly who have a chronic condition have at least one other disease (3). Consequently, it is increasingly recognized that analysis of underlying causes of death alone might not be sufficient to represent the complex burden of multi morbidity at the end of life (7-8).

To enable analyses of multi disease patterns, "secondary causes of death" were conceptualized, which represent "consequences or complications of the underlying cause of death, or another disease present at the moment of death that may have contributed to death" (1). Recent multiple causes of death analysis for the US among others revealed that diseases such as anaemia, pneumonia, diabetes and chronic lower respiratory diseases frequently occur at the end of life, but are poorly represented as underlying cause of death (9-10). Using multiple instead of underlying causes of death resulted in altered conclusions regarding the relative importance of specific diseases (10). Similar results were found also for other countries (11-12).

Although multiple causes of death analyses are expected to yield more accurate information regarding end of life disease burden, they may still not provide a complete overview of disease presence during the last years of life. Because causes of death statistics encompass diseases that contribute to death, the burden of non-lethal conditions may be underestimated or disregarded. Furthermore, some studies show a decline in the number of co-occurrences reported for ages of 80 years and older, which may indicate less accurate report of secondary causes of death among the oldest old (12). Demographic characteristics and non-medical factors such as place of death have been shown related with fewer co-occurrences, which also suggests variation in the accuracy of secondary causes of death (13). Moreover, a study of Johansson et al. showed that for one third of the persons who resided in hospital within one year prior to death, the main diagnosis of discharge was not mentioned on the death certificate, either as an underlying or contributing cause of death (14).

Although the latter study shows that a substantial part of the diseases present at the end of life is not represented in cause of death statistics, it also shows that improved estimates can expectedly be obtained by employing information from hospital discharge records in addi-

tion. The primary aim of this study is to investigate whether multiple causes of death provide complete information regarding disease occurrence at the end of life, or whether individual record linkage with the Dutch hospital information system provides relevant additional information. A secondary aim is to provide the prevalence for the diseases most common at the end of life as well as for their co-occurrences, using the full linked data.

Our study population consists of all Dutch inhabitants who died in 2005 at age 50-84. For each individual, multiple causes of death data are linked with data from the National Medical Registration, which provide information on the presence of diseases clinically diagnosed within two years prior to death. In the Netherlands, causes of death are manually coded without use of an automated coding system, and the number of secondary causes is restricted to a maximum of three.

METHODS

Study population

For our analyses, we used nation wide individually linked data from the National Medical Registration and the Cause of Death Registration. As we intended to use data as recent as possible, but the coverage of the National Medical Registration strongly declined in the years after 2005, we chose all persons who resided in the Netherlands and died in 2005 (n=136 385) as our base population. From this base population, persons aged 50 and older were selected (n=128 049, 78%). Whereas the number of co-occurrences is generally expected to steadily increase with age, in our data, the number showed a decline at age 85 and above (Figure 2.1) (12,15). As this decline was expected to reflect limitations of our data rather than an actual decline, the analysis was restricted to age 50-84. The study population consisted of 48 671 males and 38 316 females who on average died at age 72.0 and 73.6.

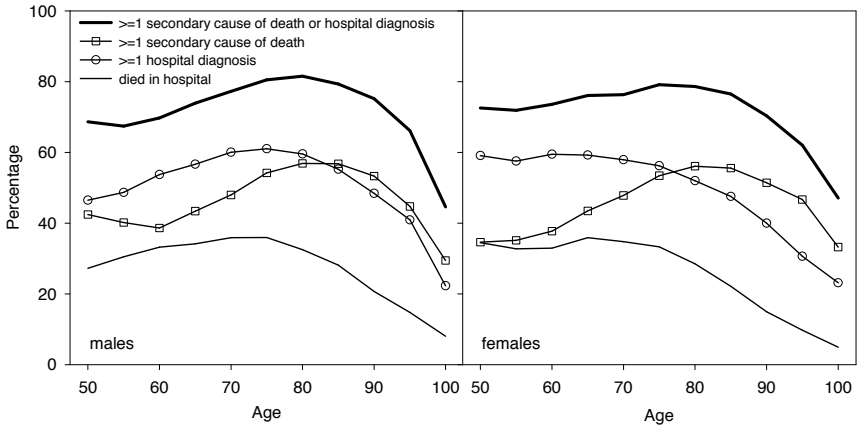


Figure 2.1 Percentage of decedents with at least one additional diagnosis as compared to their underlying cause of death and numbers died in hospital, by age and gender, the Netherlands, 2005.

Data sources

Data from the Dutch Cause of Death registration and the National Medical Registration were individually linked on the basis of personal identification numbers contained in both sources (16-17). The Cause of Death registration is governed by Statistics Netherlands. Data are collected through a legislative system in which a physician or autopsist provides one underlying and up to three secondary causes of death on a death certificate for every decedent. Coding of causes of death is done by Statistics Netherlands according to WHO coding rules given in the 10th revision of the International Classification of diseases (1). In our analysis, multiple causes of death data consisted of the underlying and secondary causes of death reported for each individual.

Data on the diagnosis of discharge for, in principal, every person who resided in a Dutch hospital within two years prior to death were available through the National Medical Registration. This registration is governed by Dutch Hospital Data and contains information on the main reason for admission as recognized at the end of hospitalization or responsibility period for both clinical and one-day admissions. Coding of the diagnoses is according to the Clinical Modification of the 9th International Classification of Diseases (ICD-9-CM).

Disease groups were defined on the basis of ICD-9-CM and ICD-10 codings using a classification according to the International Shortlist for Hospital Morbidity Tabulation (ISHMT), version 2008-11-10 (18). This list was developed in the Hospital Data Project (HDP) of the European Union Health Monitoring Programme and is an international agreed standard (18). The disease groups 'other malignant neoplasms', 'other ischemic heart diseases' and 'other diseases of the circulatory system' were rest groups but nevertheless had a high prevalence. Therefore,

these groups were further split into more specific diseases. Diseases classified as 'unknown and unspecified causes of morbidity (including those without a diagnosis)', 'other symptoms, signs and abnormal clinical and laboratory findings', 'complications of surgical and medical care, not elsewhere classified', 'medical observation and evaluation for suspected diseases and conditions', 'other medical care (including radiotherapy and chemotherapy sessions)' and 'other factors influencing health status and contact with health services' were excluded from the analysis. Following this approach, individual information regarding end of life disease occurrence for 147 diseases was available as underlying cause of death, secondary cause of death and hospital diagnosis within 2 years prior to death. The prevalence of diseases and their co-occurrences is presented for the 20 diseases most common according to information from underlying and secondary cause of death and hospital diagnosis combined.

Statistical analysis

To assess whether hospital records provide information regarding end of life morbidity that is additional to information from multiple causes of death, disease occurrence was studied according to the number of mentions as underlying or secondary cause of death combined. Subsequently, it was assessed to what extent disease prevalence and rankings changed when individual hospital discharge information was also included. Correlations between cause of death rankings and rankings according to the full linked data were calculated using the Spearman's rank correlation coefficient (r_s). Two year period prevalences were estimated as the number of persons who had a specific disease according to the full linked data, divided by the total number of individuals in the study population. Double mentions of diseases in the various data sources were accounted for. To investigate whether differences according to age exist in the extent hospital records provide information additional to multiple causes of death, the analysis was also performed among subgroups aged 50-74 and 75-85.

Using the full linked information, the prevalence of 'more than one' to 'more than four' morbidities was presented by 5 year age categories. Furthermore, for each of the 20 diseases most common, the prevalence of their three most frequent co-occurrences was provided conditional on the presence of the index disease. That is, each disease that, in addition to the index disease, at any moment had occurred in the last two years of life was considered a co-occurrence.

RESULTS

In males, including information from hospital discharge records resulted in higher prevalence estimates as compared to estimates based on multiple causes of death, for each of the twenty diseases most common at the end of life (Table 2.1a). For some diseases, the discharge records added to a limited extent only (less than 10% increase of prevalence), as was the case for malignant neoplasms of the lung and prostate, diabetes, dementia and hypertension. For other diseases, the increase was stronger. For heart failure and conduction disorders, for instance, the increase was from 3.8% to 9.0% and from 4.5% to 8.8%. Anaemia and cataract were common conditions with a prevalence of 3.8% and 4.7% according to the full linked data, but were hardly or not at all represented as a cause of death.

Table 2.1a Estimated disease prevalence during last 2 years of life, based on individually linked information regarding underlying cause of death, secondary cause of death and hospital diagnosis, males aged 50-84, 2005, the Netherlands.

	Prevalence (ranking) based on isolated data sources			Prevalence (ranking) based on individually linked data sources	
	Underlying cause of death	Secondary cause of death	Hospital diagnosis	Underlying or secondary cause of death	Underlying/secondary cause of death or hospital diagnosis
Pneumonia	3.0 (9)	7.5 (1)	6.0 (3)	10.6 (3)	14.4 (1)
Malignant neoplasms trachea, bronchus and lung	11.8 (1)	0.5 (35)	7.7 (1)	12.3 (1)	12.9 (2)
Acute myocardial infarction	8.7 (2)	1.7 (12)	3.8 (8)	10.3 (4)	12.3 (3)
COPD and bronchiectasis	5.7 (4)	5.2 (3)	4.4 (7)	10.9 (2)	12.2 (4)
Cerebrovascular disease	5.9 (3)	2.9 (7)	5.9 (4)	8.6 (5)	10.6 (5)
Heart failure	2.8 (10)	1.0 (21)	6.5 (2)	3.8 (15)	9.0 (6)
Conduction disorders, cardiac arrhythmias	3.6 (7)	0.9 (24)	4.9 (5)	4.5 (10)	8.8 (7)
Diabetes	2.6 (12)	5.6 (2)	1.4 (26)	8.2 (6)	8.8 (8)
Other forms of chronic IHD	3.4 (8)	2.8 (8)	2.2 (14)	6.3 (7)	7.9 (9)
Other diseases respiratory system	1.1 (24)	2.7 (9)	3.5 (11)	3.8 (16)	6.6 (10)
Dementia	1.8 (18)	4.4 (4)	0.5 (69)	6.2 (8)	6.4 (11)
Diseases of arteries, arterioles and capillaries‡	2.3 (14)	1.1 (19)	3.6 (9)	3.4 (17)	5.6 (12)
Malignant neoplasms prostate	3.7 (6)	1.1 (16)	2.1 (15)	4.9 (9)	5.2 (13)
Septicaemia	0.7 (33)	3.8 (5)	1.0 (39)	4.4 (11)	5.0 (14)
Malignant neoplasms colon, rectum, anus	3.9 (5)	0.4 (36)	3.1 (12)	4.3 (12)	5.0 (15)
Other heart diseases§	2.5 (13)	1.6 (13)	1.4 (25)	4.0 (13)	5.0 (16)
Cataract	0.0 (-)	0.0 (-)	4.7 (6)	0.0 (-)	4.7 (17)
Other diseases nervous system and senses	1.6 (21)	1.8 (11)	1.7 (23)	3.3 (18)	4.5 (18)
Hypertensive diseases	0.6 (35)	3.4 (6)	0.2 (91)	4.0 (14)	4.2 (19)
Anaemia	0.1 (53)	0.3 (45)	3.5 (10)	0.4 (57)	3.8 (20)

Note: Prevalence based on underlying and secondary cause of death combined can be lower than the prevalences based on the two data sources in isolation added because of overlap in diagnosis.

‡ excluding atherosclerosis

§ excluding conduction disorders, arrhythmias and heart failure

Using hospital discharge information in addition to multiple causes of death resulted in rank changes of up to nine positions, as was the case for heart failure. The diseases that were among the twenty most common conditions at the end of life, however, remained largely unchanged, except for anaemia and cataract. The correlation (r_s) between the ranking according to multiple causes of death and according to the full linked data was 0.80. Underlying causes of death used in isolation gave a poorer reflection of disease occurrence at the end of life (r_s=0.72). Six of the twenty diseases most common at the end of life according to the full linked data were not among the twenty most common underlying causes of death.

Similar to males, higher prevalence estimates were obtained when using hospital discharge information in addition to multiple causes of death in females (Table 2.1b). For dementia, lung cancer, breast cancer, hypertensive diseases and septicaemia, the estimates increased less than 10%. For heart failure and other endocrine, nutritional and metabolic disorders, the estimates more than doubled, that is from 4.4% to 9.4% and from 2.5% to 5.0%. As represented by a prevalence of 5.1% and 4.1%, cataract and anaemia were common conditions but were poorly reflected as a cause of death.

In females, the ranking of diseases was affected to a limited extent when discharge information was added to multiple causes of death. Heart failure was affected most and increased seven ranks. The diseases that were among the twenty most common conditions at the end of life remained unchanged, except for anaemia and cataract, which were predominantly represented as a hospital diagnosis. The correlation between ranking according to multiple causes of death and according to the full linked data was high (r_s=0.81). Six of the twenty diseases most common according to full linked information were not represented as a common underlying cause of death. This was also represented in a relatively low correlation (r_s=0.71).

An analysis among subgroups of similar size aged 50-74 and 75-84 suggested that the extent hospital diagnoses provide additional information to multiple causes of death is similar across age groups (results not shown). That is, in both age groups three out of twenty diseases most common according to information from cause of death and hospital registrations combined were not represented in the diseases most common according to causes of death only. This was true for both males and females. Furthermore, also the correlation between the ranking according to causes of death and cause of death and hospital registrations was similar for both age groups (males: $r_{s50\text{-}74}$=0.82, $r_{s75\text{-}84}$=0.83; females: $r_{s50\text{-}74}$=0.82, $r_{s75\text{-}84}$=0.84).

Table 2.1b Estimated disease prevalence during last 2 years of life, based on individually linked information regarding underlying cause of death, secondary cause of death and hospital diagnosis, females aged 50-84, 2005, the Netherlands.

	Prevalence (ranking) based on isolated data sources			Prevalence (ranking) based on individually linked data sources	
	Underlying cause of death	Secondary cause of death	Hospital diagnosis	Underlying or secondary cause of death	Underlying/secondary cause of death or hospital diagnosis
Cerebrovascular disease	8.2 (1)	3.3 (7)	6.7 (1)	11.4 (1)	13.0 (1)
Pneumonia	3.0 (11)	6.2 (3)	4.1 (5)	9.3 (4)	11.8 (2)
Dementia	3.7 (7)	7.0 (1)	0.5 (71)	10.7 (2)	11.0 (3)
Diabetes	3.3 (10)	6.9 (2)	1.5 (26)	10.1 (3)	10.8 (4)
Heart failure	3.5 (8)	0.9 (22)	6.2 (2)	4.4 (12)	9.4 (5)
Acute myocardial infarction	6.5 (3)	1.4 (14)	2.8 (11)	7.8 (6)	9.2 (6)
COPD and bronchiectasis	4.7 (5)	3.4 (6)	3.4 (9)	8.1 (5)	9.1 (7)
Malignant neoplasms trachea, bronchus and lung	6.8 (2)	0.2 (54)	4.6 (4)	7.0 (7)	7.3 (8)
Malignant neoplasms breast	6.0 (4)	0.9 (21)	2.4 (13)	6.9 (8)	7.3 (9)
Conduction disorders, cardiac arrhythmias	3.3 (9)	1.0 (18)	3.4 (7)	4.4 (13)	7.3 (10)
Hypertensive diseases	0.7 (35)	4.7 (4)	0.2 (88)	5.4 (9)	5.6 (11)
Malignant neoplasms colon, rectum, anus	4.3 (6)	0.3 (44)	3.3 (10)	4.7 (10)	5.4 (12)
Septicaemia	0.8 (28)	3.8 (5)	1.0 (36)	4.6 (11)	5.1 (13)
Cataract	0.0 (-)	0.0 (-)	5.1 (3)	0.0 (-)	5.1 (14)
Other diseases respiratory system	0.9 (26)	2.2 (8)	2.4 (14)	3.1 (17)	5.0 (15)
Other heart diseases‡	2.7 (12)	1.5 (13)	1.3 (28)	4.2 (14)	5.0 (16)
Other endocrine, nutritional, metabolic diseases	0.5 (42)	2.0 (9)	2.7 (12)	2.5 (20)	5.0 (17)
Other forms of chronic IHD	2.0 (16)	1.6 (11)	1.1 (34)	3.6 (15)	4.4 (18)
Other diseases nervous system and senses	1.7 (18)	1.6 (12)	1.8 (17)	3.2 (16)	4.4 (19)
Anaemia	0.2 (57)	0.5 (33)	3.8 (6)	0.7 (46)	4.3 (20)

Note: Prevalence based on underlying and secondary cause of death combined can be lower than the prevalences based on the two data sources in isolation added because of overlap in diagnosis.

‡excluding conduction disorders, arrhythmias and heart failure

Figure 2.2 represents the prevalence of multi morbidity at the end of life by age. In males, 65-80% of all deaths had one or more co-occurring conditions and 20-30% even had three or more co-occurrences. The prevalence of multi morbidity was higher towards older ages. The prevalence of multi morbidity among females was slightly lower than among males, but the pattern was similar.

Tables 2.2a and 2.2b represent the diseases most common at the end of life, together with the prevalence of their three most common co-occurrences. In males, the diseases most common at the end of life were pneumonia (14.4%), lung cancer (13.9%), acute myocardial infarction (12.3%), COPD and bronchiectasis (12.2%) and cerebrovascular disease (11.6%). Pneumonia was the most common co-occurring condition for nine of twenty conditions and occurred particularly frequently in combination with septicaemia (29%), COPD and bronchiectasis (28%), dementia (26%), other diseases of the nervous system and senses (22%), and other diseases of the respiratory system (21%). Diabetes occurred particularly frequently in combination with acute myocardial infarction (18%) and heart failure (16%) and was a frequent concurrence to hypertensive diseases (24%). Among persons who had cancer, the prevalence of each co-occurrence was relatively low.

In females, cerebrovascular disease (13.0%), pneumonia (11.8%), dementia (11.0%), diabetes (10.8%) and heart failure (9.4%) were the most prevalent conditions at the end of life. Pneumonia as well as diabetes were the most common co-occurring condition for 6 of the 20 diseases. Diabetes occurred particularly frequently in combination with cardiovascular disease. Of all decedents with diabetes, 16% had cerebrovascular disease, 15% heart failure and 15% acute myocardial infarction. In 28% of the persons who had hypertensive diseases, diabetes was a co-occurrence. Among persons with breast and colon cancer, the prevalence of the main co-occurrences was low (<=7%).

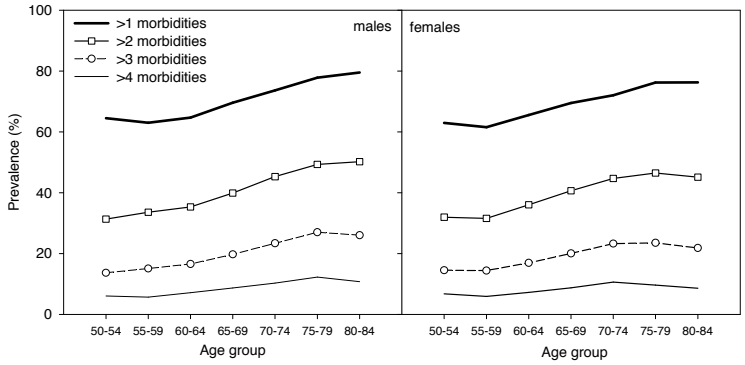


Figure 2.2 Prevalence of more than one, two, three or four morbidities during the last two years of life, by age and gender, the Netherlands, 2005.

Table 2.2a Estimated prevalence of most common diseases and their co-occurrences during the last two years of life, males aged 50-84, 2005, the Netherlands.

Disease	Prevalence (%)	Most common co-occurrences (prevalence)		
Pneumonia	14.4	COPD and bronchiectasis (24%)	Cerebrovascular disease (13%)	Mal neoplasms trachea, bronchus and lung (12%)
Mal neoplasms trachea, bronchus and lung	12.9	Pneumonia 13%)	COPD and bronchiectasis (10%)	Other diseases respiratory system (7%)
Acute myocardial infarction	12.3	Diabetes (13%)	Heart failure (11%)	COPD and bronchiectasis (10%)
COPD and bronchiectasis	12.2	Pneumonia (28%)	Heart failure (13%)	Mal neoplasms trachea, bronchus and lung (11%)
Cerebrovascular disease	10.6	Pneumonia (18%)	Dementia (10%)	Diabetes (10%)
Heart failure	9.0	Other forms of chronic IHD (18%)	COPD and bronchiectasis (17%)	Pneumonia (16%)
Conduction disorders, cardiac arrhythmias	8.8	Heart failure (15%)	Acute myocardial infarction (13%)	COPD and bronchiectasis (12%)
Diabetes	8.8	Acute myocardial infarction (18%)	Heart failure (16%)	Pneumonia (14%)
Other forms of chronic IHD	7.9	Heart failure (20%)	Acute myocardial infarction (15%)	Diabetes (15%)
Other diseases respiratory system	6.6	Pneumonia (21%)	COPD and bronchiectasis (18%)	Mal neoplasms trachea, bronchus and lung (14%)
Dementia	6.4	Pneumonia (26%)	Cerebrovascular disease (16%)	Other diseases nervous system and senses (10%)
Diseases arteries, arterioles and capillaries‡	5.6	Other forms of chronic IHD (12%)	COPD and bronchiectasis (12%)	Diabetes (12%)
Malignant neoplasms prostate	5.2	Pneumonia (11%)	Anaemia (10%)	COPD and bronchiectasis (8%)
Septicaemia	5.0	Pneumonia (29%)	Heart failure (10%)	COPD and bronchiectasis (10%)
Malignant neoplasms colon, rectum, anus	5.0	Paralytic ileus and intestinal obstruction§ (8%)	Anaemia (7%)	Other mal neoplasms digestive organs¶ (7%)
Other heart disease£	5.0	Heart failure (24%)	Other forms of chronic IHD (15%)	COPD and bronchiectasis (14%)
Cataract	4.7	COPD and bronchiectasis (18%)	Pneumonia (17%)	Mal neoplasms trachea, bronchus and lung (13%)
Other diseases nervous system and senses	4.5	Pneumonia (22%)	Dementia (15%)	Cerebrovascular disease (12%)
Hypertensive diseases	4.2	Diabetes (24%)	Acute myocardial infarction (23%)	Cerebrovascular disease (20%)
Anaemia	3.8	Pneumonia (17%)	Mal neoplasms prostate (14%)	Mal neoplasms trachea, bronchus and lung (13%)

Abbreviations: mal = malignant

‡ excluding atherosclerosis

§ without hernia

¶ excluding oesophagus, stomach, pancreas, colon, rectum and anus

£ excluding conduction disorders, arrhythmias and heart failure

Table 2.2b Estimated prevalence of most common diseases and their co-occurrences during the last two years of life, females aged 50-84, 2005, the Netherlands.

Disease	Prevalence (%)	Most common co-occurrences conditions (prevalence)		
Cerebrovascular disease	13.0	Diabetes (13%)	Dementia (13%)	Pneumonia (12%)
Pneumonia	11.8	COPD and bronchiectasis (19%)	Dementia (17%)	Cerebrovascular disease (13%)
Dementia	11.0	Pneumonia (18%)	Cerebrovascular disease (15%)	Diabetes (11%)
Diabetes	10.8	Cerebrovascular disease (16%)	Heart failure (15%)	Acute myocardial infarction (15%)
Heart failure	9.4	Diabetes (18%)	Other heart diseases‡ (15%)	Pneumonia (13%)
Acute myocardial infarction	9.2	Diabetes (17%)	Heart failure (12%)	Hypertensive diseases (11%)
COPD and bronchiectasis	9.1	Pneumonia (25%)	Heart failure (12%)	Diabetes (12%)
Mal neoplasms trachea, bronchus and lung	7.3	Pneumonia (10%)	COPD and bronchiectasis (10%)	Other diseases respiratory system (6%)
Malignant neoplasms breast	7.3	Pneumonia (7%)	Diabetes (6%)	Anaemia (6%)
Conduction disorders, cardiac arrhythmias	7.3	Heart failure (15%)	Cerebrovascular disease (15%)	Diabetes (11%)
Hypertensive diseases	5.6	Diabetes (28%)	Cerebrovascular disease (24%)	Acute myocardial infarction (18%)
Malignant neoplasms colon, rectum, anus	5.4	Anaemia (7%)	Paralytic ileus and intestinal obstruction§ (7%)	Other mal neoplasms digestive organs¶ (7%)
Septicaemia	5.1	Pneumonia (23%)	Diabetes (11%)	Other diseases of urinary system (9%)
Cataract	5.1	Diabetes (15%)	Heart failure (15%)	Cerebrovascular disease (14%)
Other diseases respiratory system	5.0	Cerebrovascular disease (16%)	COPD and bronchiectasis (15%)	Pneumonia (15%)
Other heart diseases‡	5.0	Heart failure (27%)	Diabetes (14%)	Acute myocardial infarction (12%)
Other endocrine, nutritional, metabolic diseases	5.0	Diabetes (22%)	Heart failure (14%)	Hypertensive diseases (14%)
Other forms of chronic IHD	4.4	Heart failure (21%)	Diabetes (21%)	Acute myocardial infarction (16%)
Other diseases nervous system and senses	4.4	Pneumonia (17%)	Dementia (15%)	Cerebrovascular disease (13%)
Anaemia	4.3	Heart failure (17%)	Pneumonia (14%)	Diabetes (13%)

Abbreviations: mal = malignant

‡ excluding conduction disorders, arrhythmias and heart failure

§ without hernia

¶ excluding oesophagus, stomach, pancreas, colon, rectum and anus

DISCUSSION

Summary of results

Multiple causes of death do not provide complete information regarding disease occurrence prior to death, but additional information is contained in hospital discharge records. Employing this information results in higher prevalence estimates and, in some instances, in considerable changes in ranking. The content of the top 5, however, is unaffected, except for heart failure in women. Using the full linked data, pneumonia, lung cancer, acute myocardial infarction, COPD and bronchiectasis and cerebrovascular disease are the most common conditions among male decedents. In females, these conditions are cerebrovascular disease, pneumonia, dementia, diabetes and heart failure. The condition that most frequently occurred as the main co-occurrence to the 20 most common conditions in males was pneumonia and in females these were pneumonia and diabetes.

Methodological considerations

Cause of death registration comprises three steps that each contribute to its validity: the diagnostic process, completion of a death certificate, and coding of the statements on the death certificate (1). Some clues about the validity of the diagnostic process come from autopsy studies (19-20). These studies show that for 25% of the autopsies, a primary cause of death is found that is clinically undetected (19-20). However, as autopsies are probably most often performed among cases for which the clinical diagnosis was difficult, these results are probably not generalizable to our population. Nonetheless, diagnostic constraints may have affected our results to some extent.

The validity of certification and coding of causes of death in the Netherlands was studied by Mackenbach et al., using COPD and cancer case histories to be certified by physicians and coded by the National Statistics office (21). It was shown that on 12% of the certificates COPD had falsely remained unmentioned, either as an underlying or secondary cause of death, but for cancer, this was true for only 2% (21). These results suggest that some diseases, such as cancers, are more adequately certified than others, such as COPD (21). Although the study showed that coding practices of Statistics Netherlands partly adjusted for inaccurate certification, we cannot exclude that the prevalence of COPD was underestimated to a certain extent in the cause of death registration. Our results show that using additional information from hospital discharge records at least partially corrects for such underestimation. The inter coder reliability of underlying causes of death was studied by Harteloh et al. (22). It was found that for major causes of death such as cancers and acute myocardial infarction, the inter coder agreement was high (>= 90%), but for diseases such as diabetes and hypertension, the agreement was substantially lower (53% and 71%) (22). Low inter reliabilities for these conditions imply a considerable random variation in coding decisions. Although it is expected that

a substantial part of the variation is adapted for by mentions as a secondary cause of death, it cannot be excluded that variation in inter reliability has affected our prevalence estimates, particularly those based on underlying cause of death only.

Variation in diagnostic processes may have influenced disease occurrences according to hospital discharge information in a way similar to for cause of death registration (19-20). A study on the reliability of the Dutch National Medical Registration showed that 99% of the diagnoses of discharge was recorded correctly in the register (23).

To categorize ICD codings into a convenient number of chronic conditions that were still specific enough, and to achieve concordance between ICD-10 codings in the cause of death registration and ICD-9-CM in the hospital registration, we chose to use the ISHMT. This categorization was chosen because it represents not only major causes of death but also less lethal conditions. It is good to realize that the choice of disease categorization may have influenced the prevalence and ranking of the conditions, as well as the total number of diseases and therefore the prevalence of co-occurrences (15).

As we used two year period prevalence in our study, all diseases reported present at any moment during the last two years of life were assumed to co-exist. As most conditions at the end of life have a quite long duration, this assumption is expected reasonably valid. However, in some instances, the existence of diseases may have been subsequent instead of concurrent.

In the Netherlands, causes of death are coded manually and the number of secondary causes is restricted to a maximum of three. This may limit the generalizability of our results to countries that have an automated coding system and allow more than three contributing causes, such as the US and a number of European countries (24-15). A recent study investigating discontinuities related with implementation of automated coding in trends of 13 causes of death found no discontinuities for Sweden, France and Germany (25). In England, the only discontinuity relevant to our study was for heart failure (25). In an Australian study, a reasonably good concordance between manual and automated coding was found for most conditions, except for mental disorders such as dementia (26). These studies suggest that automated coding has no large influence on the extent multiple causes of death data represent end of life morbidity, except for a few conditions such as dementia and heart failure. In our data, the maximum of three secondary causes of death was provided for less than 6% of the deaths. If the tendency of certifiers to report multiple causes of death in other countries is similar to that in the Netherlands, this suggests that the possibility of reporting more than three secondary causes in practice may not result in a substantial extra number of diseases reported. Therefore, also the restriction in the number of conditions that can be reported as a cause of death may not largely affect the generalizability of our results.

Comparison with previous studies

Our study was among the first to investigate whether multiple causes of death provide complete information regarding disease presence prior to death. Together with a few earlier studies, our results show that hospital discharge records contain information regarding disease presence prior to death that is not contained in cause of death registrations and that the amount of extra information contained varies according to disease (14,27). Adding to previous studies, we showed that employing the extra information from hospital discharge records results in larger prevalence estimates for each of the twenty conditions most common at the end of life. The ranking of some diseases was substantially affected by including the hospital information, whereas for other diseases, the ranking was hardly or not at all affected.

In a recent Dutch study, incidence rates of coronary heart disease, acute myocardial infarction, unstable angina pectoris and heart failure estimated on the basis of hospital and cause of death record linkage were validated against the cardiovascular registry of the Dutch Maastricht cohort study (28). A high percentage of the cases of cardiovascular disease were only found in the cardiovascular registry and not in the cause of death or hospital data, varying from 14.2% for acute myocardial infarction to 47.5% for heart failure. This suggests that even though hospital registries contain substantial information regarding disease presence additional to information from underlying and secondary causes of death, the individually linked data of these sources combined may still be incomplete. However, in this study, disease information from death certificates was available for a minor part of the population (3.7%) as most participants were survivors. As in our study deaths only were included, cause of death information was available for the whole study population, which probably has resulted in information much more complete. The differences in disease prevalence with and without cause of death information, as well as results from international studies including a larger proportion of deaths, confirm this (29-31).

Interpretation of findings

Cause of death statistics originate from the era before the epidemiologic transition and are among the oldest and most widely applied indicators of population health. After completion of the epidemiologic transition, in the era of chronic diseases, it was recognized that cause of death statistics might less accurately reflect population health, and it was advocated to use measures representing non-fatal disease consequences in addition (32). Comparing disease ranking based on underlying cause of death only with ranking based on the full linked data, our results suggest that, indeed, underlying cause of death statistics do not very accurately reflect burden of disease in the population in terms of disease prevalence. Using multiple causes of death, however, seems to provide a rather accurate reflection. That is, although using hospital discharge information in addition to multiple causes of death data results in some change of the ranking, almost all diseases most common at the end of life are also

represented in the top 5 based on multiple causes of death. Nonetheless, these results should be interpreted with some reservation. Where cause of death statistics importantly focus on lethal conditions, the same might to some extent be true for hospital statistics. It is plausible that persons who have a life-threatening condition have a higher hospitalization rate than persons who have a non-lethal condition. Although using individually linked cause of death and hospital data is expected to reflect end of life disease burden more accurately than cause of death data only, our analysis might still to some extent underestimate the burden of non-lethal conditions.

Previous studies reported a decline in the number of secondary causes of death for ages older than 80, and it was speculated that this is related with physicians not feeling the need to provide an extensive explanation of deaths at very old age (12). Aiming at a more complete overview of end of life morbidity, also among the oldest old, we linked cause of death registrations with hospital discharge records. Unfortunately, it appeared that not only report of secondary causes of death declined at ages older than 85 but also the number of diseases reported in hospital records. It appears that doctors may not only feel less need to provide an expansive explanation on the death certificate, but that also their tendency to opt for extensive diagnostic procedures in the hospital is less strong for persons at older ages. This hypothesis is supported in our data by strong declines towards older ages in the number of persons dying in the hospital and strong increases in the number of deaths in homes for the elderly. That is, the percentage of persons that died in a home for the elderly increased from 15% at age 70-74 to 35% at age 95-100. At age 95-100, almost 75% died in a nursing home or home for the elderly. We found that the extent to which hospital diagnoses provide information additional to multiple causes of death does not differ among groups aged 50-74 and 75-84. This suggests that although cause of death and hospital registrations may provide less complete disease information for persons aged 85 and older, the relative extent multiple causes of death represent end of life morbidity may not decline for these ages.

The occurrence of one disease simultaneously to another can find its origin in etiology, that is, multiple diseases can result from a common risk factor or are different expressions of one pattern of physical decline, but can also refer to age patterns in the occurrence of unrelated diseases (33). It has been shown that common chronic diseases co-occur more frequently in one individual than expected on the basis of chance only (34). The large dataset used in our study offers great opportunities to study patterns in the occurrence of diseases and co-morbidities and requires further analysis. As previous studies found a somewhat higher prevalence of co-morbidity among females than among males, the lower prevalence among females in our study was unexpected (2, 4, 35). The difference with other studies may be related with the number and types of diseases distinguished (15).

Implications; conclusion

It was investigated whether multiple causes of death provide a complete overview of disease occurrence at the end of life. It is concluded that underlying cause of death statistics are not a very accurate representation of end of life morbidity and that statistics based on multiple causes of death are more accurate. Therefore, for health policy decisions, it is recommended to use multiple causes of death. We showed that, for most individuals, the end phase of life is characterized by the occurrence of multiple chronic conditions and that the burden of disease at the end of life is high. The next decades, the number of people in their last phase of life is expected to increase substantially due to ageing of the population. In the Netherlands, for instance, between 2010 and 2050, the annual number of decedents is expected to increase by almost 60% (36). The future health system should be prepared to provide adequate and sufficient care to support a worthy end of life for these elderly individuals.

Acknowledgement

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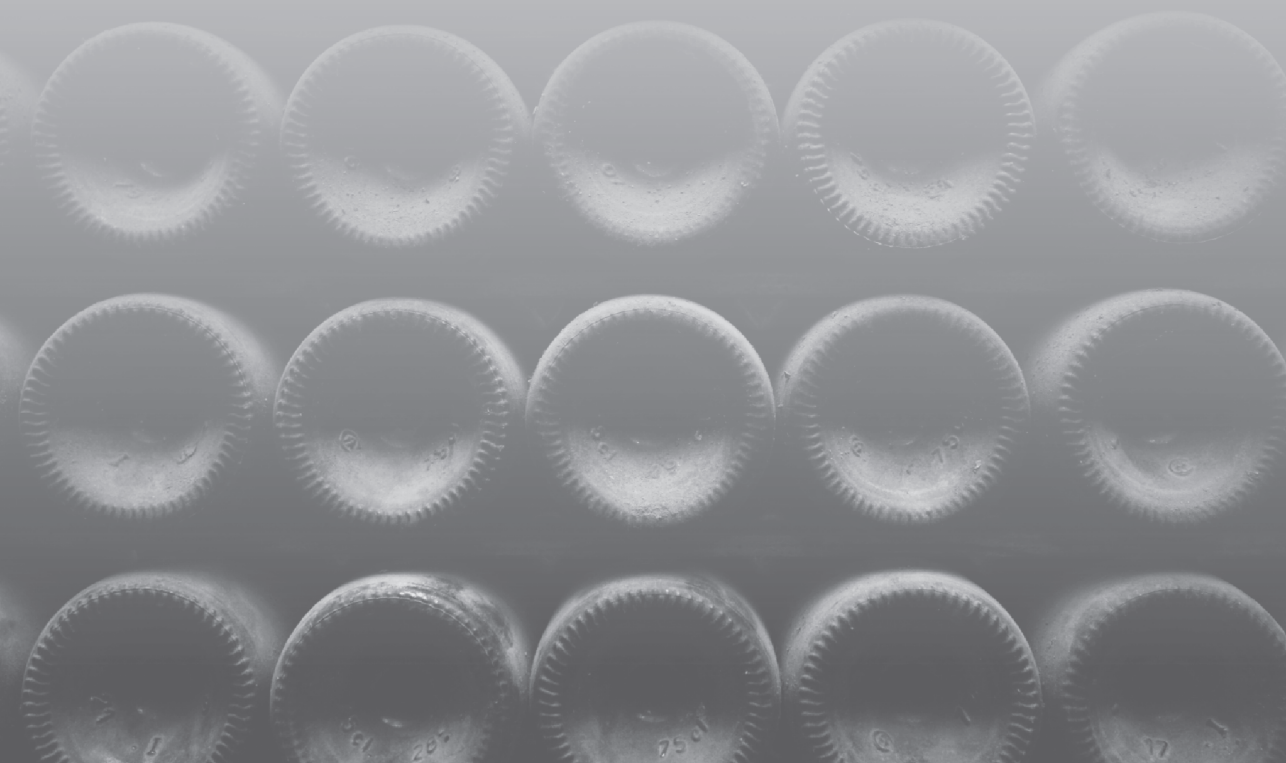
3

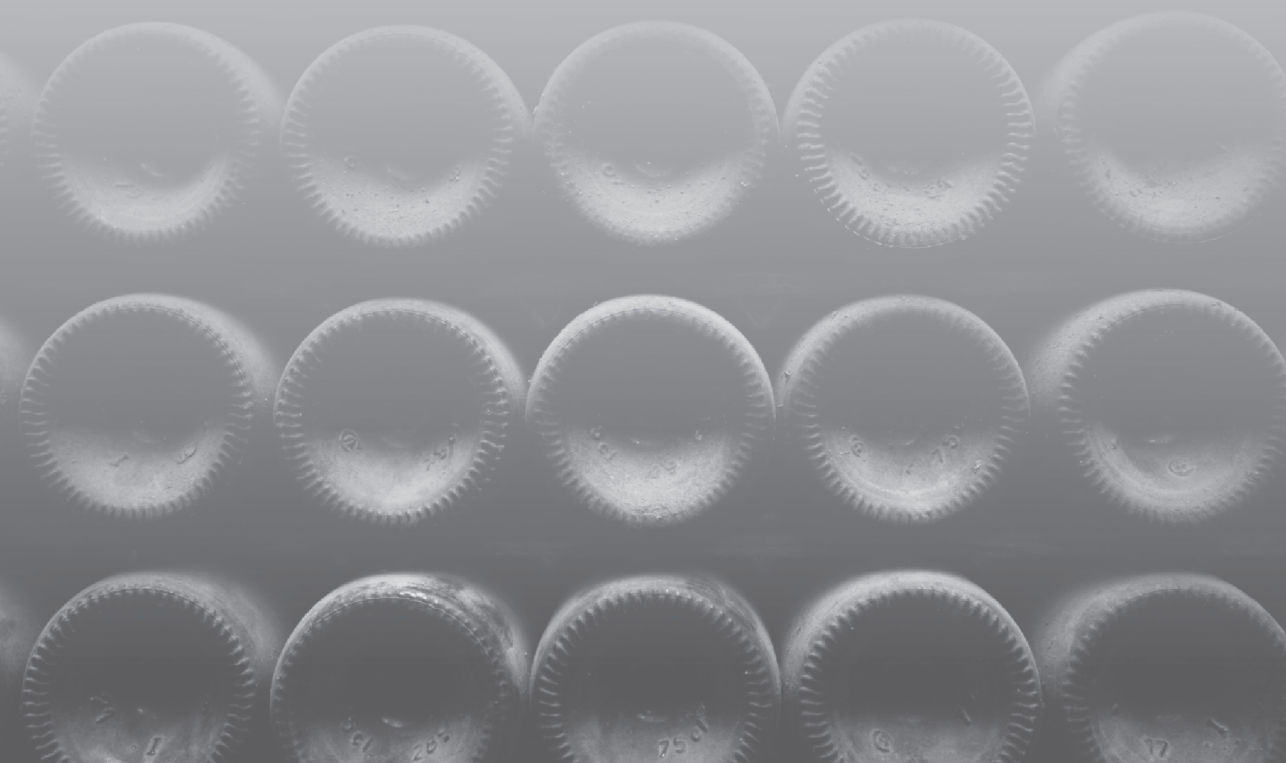
Disability occurrence and proximity to death



3.1

Association between disability occurrence and proximity to death

Klijs B, Mackenbach JP, Kunst AE. Disability occurrence and proximity to death. Disabil Rehabil. 2010, 32(21):1733-41."



Introduction This paper aims to assess whether disability occurrence is related more strongly to proximity to death than to age.

Methods Self reported disability and vital status were available from six annual waves and a subsequent 12-year mortality follow-up of the Dutch GLOBE longitudinal study. Logit and Poisson regression methods were used to study associations of disability occurrence with age and with proximity to death.

Results For disability in activities of daily living (ADL), regression models with proximity to death had better goodness of fit than models with age. With approaching death, the odds for ADL disability prevalence and incidence rates increased 20.0% and 18.9% per year, whereas severity increased 4.1% per year. For the ages younger than 60, 60–69 and older than 70 years, the odds for ADL disability prevalence increased 6.4%, 16.0% and 23.0% per year. Among subjects with asthma/chronic obstructive pulmonary disease, heart disease and diabetes increases were 25.1%, 19.5% and 22.7% per year. Functional impairments were more strongly related to age.

Conclusion The strong association of (ADL) disability occurrence with proximity to death implies that a substantial part of the disability burden may shift to older ages with further increases in life expectancy.

INTRODUCTION

Life expectancy in Western societies has shown substantial increases during the 20th century. In the Netherlands, between 1950 and 2005, life expectancy increased with 6.8 years in males and with 8.9 years in females (1). Worldwide, comparable increases in life expectancies occurred (2,3). This trend is not expected to come to an end in the near future. Instead, the average length of life is expected to further increase with approximately 5 years between 2005 and 2050 (2–5).

One of the key issues in public health is whether these extra life years gained will be years in good health or, otherwise, will be spent in ill health or disability (6-8). The alternative scenarios for future trends in disability occurrence are crucial not only for chances of individual lifelong well-being (9), but will also influence future demands for health care recourses (10-11).

The future burden of disability among elderly populations may expand at a relative low pace if the disability occurrence among the elderly would, along with the increasing length of life, shift towards ever older ages. The possibility of such a concomitant shift is suggested by end-of-life studies showing that trajectories of functional decline may be linked to the end phase of life (12-19). As life expectancy increases, trajectories of disability can be expected to at least partially shift to older ages. It is uncertain, however, to what extent this would happen. For this, it is important to assess to what extent disability occurrence is related to proximity of death (time to death) on the one hand and to age (time since birth) on the other hand. To our knowledge, the two dimensions of age have not been compared with regards to their relationship to disability occurrence. This paper aims to assess whether disability occurrence is related more strongly to proximity to death than to age.

This paper is linked to recent health economics research that assessed the extent to which increase of life expectancy is likely to increase health care spending. Several studies determined the association of health care costs with age and proximity to death respectively (10, 20-22). It was found that health care costs were in part determined by proximity to death and that, hence, population ageing is likely to have a more moderate effect on health care spending than was previously assumed (11,20-22). The outcomes of our analysis may help to assess whether similar effects may be expected for disability occurrence.

METHODS

Study population

We used data from the (GLOBE) study, a prospective cohort study investigating the explanation of inequalities in health in the Netherlands (23). The study comprised a baseline postal survey in 1991, conducted among a stratified random sample of 27,070 inhabitants of the city of Eindhoven (40%) and surrounding municipalities (60%). The age range was set at 15–74 years with overrepresentation of 45 years and older. Institutionalised persons were excluded in Eindhoven but not in the surrounding municipalities. The response to the baseline questionnaire was 70.1% (n=18,973).

A subsample (n=3,968) of the initial cohort was invited for an oral interview and received annual follow-up questionnaires until 1997 (except for 1996). The subsample overrepresented subjects suffering from asthma/chronic obstructive pulmonary disease (COPD), heart disease and diabetes mellitus. The response to the oral interview was 72.2% (n=2,867). All analyses in the current paper were based on data from the subsample.

The mean age of the subsample at baseline was 52.6 years and 8% of the subjects were disabled in their activities of daily living (ADL). At the moment of the last administrative follow-up in 2004, 16% of the sample had died. Among subjects being ADL disabled at baseline, this was 37% compared to 14% among non-disabled subjects (Table 3.1.1).

Table 3.1.1 Baseline characteristics of respondents and deaths during follow-up.

	Respondents			Deaths before end of follow-up		
	Number of subjects (%)	Mean age (sd)	Number ADL disabled (%)	Among all (%)	Among baseline ADL disabled (%)	Among not baseline ADL disabled (%)
All	2867 (100)	52.6 (14.1)	241 (8)	468 (16)	88 (37)	380 (14)
<60 yrs	1888 (66)	45.4 (0.3)	112 (6)	128 (7)	22 (20)	106 (6)
60-69 yrs	748 (26)	64.7 (0.1)	92 (12)	222 (30)	45 (49)	177 (27)
>=70 yrs	231 (8)	72 (0.2)	37 (16)	118 (51)	21 (57)	97 (50)
Asthma/COPD	588 (21)	53.1 (0.7)	75 (13)	147 (25)	33 (44)	114 (22)
Heart disease	446 (16)	61.4 (0.4)	71 (16)	178 (40)	40 (56)	138 (37)
Diabetes	262 (9)	60.2 (0.6)	36 (14)	92 (35)	20 (56)	72 (32)

Attrition and item non response

The maximal number of questionnaires that could have been obtained during follow-up of the GLOBE subsample was six waves time the 2,867 initial respondents = 17,202 questionnaires. However, 3,337 questionnaires were not returned during follow-up, leaving a total of 13,865 questionnaires.

Among questionnaires that were returned, 403 had incomplete data on disability as measured by the Organization for Economic Co-operation and Development (OECD) indicator and 572 had incomplete data on ADL disability. Information was missing for only one item on OECD disability in 192 cases, and in 226 cases for ADL disability. In these cases, we imputed the missing item with the value of the preceding year or (for 1991) the next year. In total 13,654 questionnaires with information on OECD disability were available and 13,519 with ADL disability information. Information on the presence of asthma/COPD, heart disease and diabetes was missing for, respectively, 50, 39 and 62 subjects.

Measures of disability

As the study results may depend on the type of disability used (24,25), we used different disability measures, including a measure based on 10 ADL questions, and a functional limitation measure based on 8 questions of the OECD indicator of long-term disabilities (26). ADL items were 'walking down/up stairs, moving outdoors, leaving/entering house, sitting down/getting up from chair, moving on same floor, getting in/out of bed, eating/drinking, getting (un)dressed, washing face/hands and washing completely'. OECD items were 'able to have conversation with one person, able to have conversation with three persons or more, reading small letters, recognising faces, biting/chewing food, carry 5 kilos for 10 m, bending/take something from ground, and walking 400 m'. In terms of the International Classification of Functioning, Disability and Health (27), the OECD list focuses on impairments of body functions, e.g., hearing, and the ADL list focuses more on activities, i.e., the execution of a task or action by an individual. We preferred using these measures, instead of measures like disease occurrence or general self-assessed health, because of the direct implications that disability and impairment have for the independence of elderly and for their need for formal and informal care. For each ADL and OECD item, subjects were asked whether they were able to perform the actions 'without difficulty', 'with minor difficulty', 'with major difficulty', 'not able to perform/only with help'. Disability was defined as having at least one item answered with 'with major difficulty' or 'not able to perform/only with help'. In sensitivity analyses, we also applied an alternative cut-off point to define prevalence cases, as those who had at least two (instead of one) items with 'with major difficulty' or 'not able to perform/only with help'

Information on age, sex and presence of asthma/COPD, heart disease and diabetes mellitus was obtained from the baseline survey. Table 3.1.1 presents baseline characteristics of all respondents and of those who died during follow-up.

Data analysis

The variables 'prevalence', 'incidence', 'severity' and 'proximity to death' were created for the six waves of data collection separately. 'Prevalence' indicated whether disability was reported at the time the data were collected. An individual was considered 'incident' if disability existed in the year of observation but was absent in the preceding year. For all cases of disability, 'severity' was calculated by counting the case in which respondents reported having 'much difficulty', 'no/just with help'. 'Proximity to death' was calculated as the difference between the moment of death, available from linkage to population registers, and the moment of the survey.

For all statistical analysis, Stata 10.0 was used. Generalised Estimating Equations (GEE) models were used to account for the interdependence of observations from one individual. Prevalence data were analysed using logistic regression analysis, while incidence and severity data were analysed using Poisson regression. Dependent variables were 'prevalence', 'incidence' and 'severity' and independent variables were 'age', 'proximity to death' and 'sex'. A dichotomous variable was added to the models indicating whether or not subjects had died during follow-up, and to capture differences in disability between those who died and those who survived until the end of follow-up. Consequently, the relationship of disability to proximity to death could be estimated only from subjects who died during follow-up.

Stratifications were applied according to age (younger than 60, 60–69 and older than 70 years) and presence of a chronic disease (asthma/COPD, heart disease and diabetes mellitus). To indicate the goodness of fit of the models wald chi2 values were calculated.

RESULTS

Figure 3.1.1 presents ADL prevalence, incidence and severity rates by 5 year age groups and by time to death. Disability prevalence increased from around 0.05 up to 0.35 in the oldest age category of 80–84 years. In relationship to proximity to death, disability prevalence increased from 0.12, 12 years prior to death, to 0.38 in the year prior to death. Increases of disability incidence were more pronounced with approaching death as compared to increasing age. The maximum value of disability incidence was 0.10 at the highest age group as compared to 0.26 within the year prior to death. Increases of severity also were more pronounced with approaching death. Severity was especially high the last 4 years prior to death.

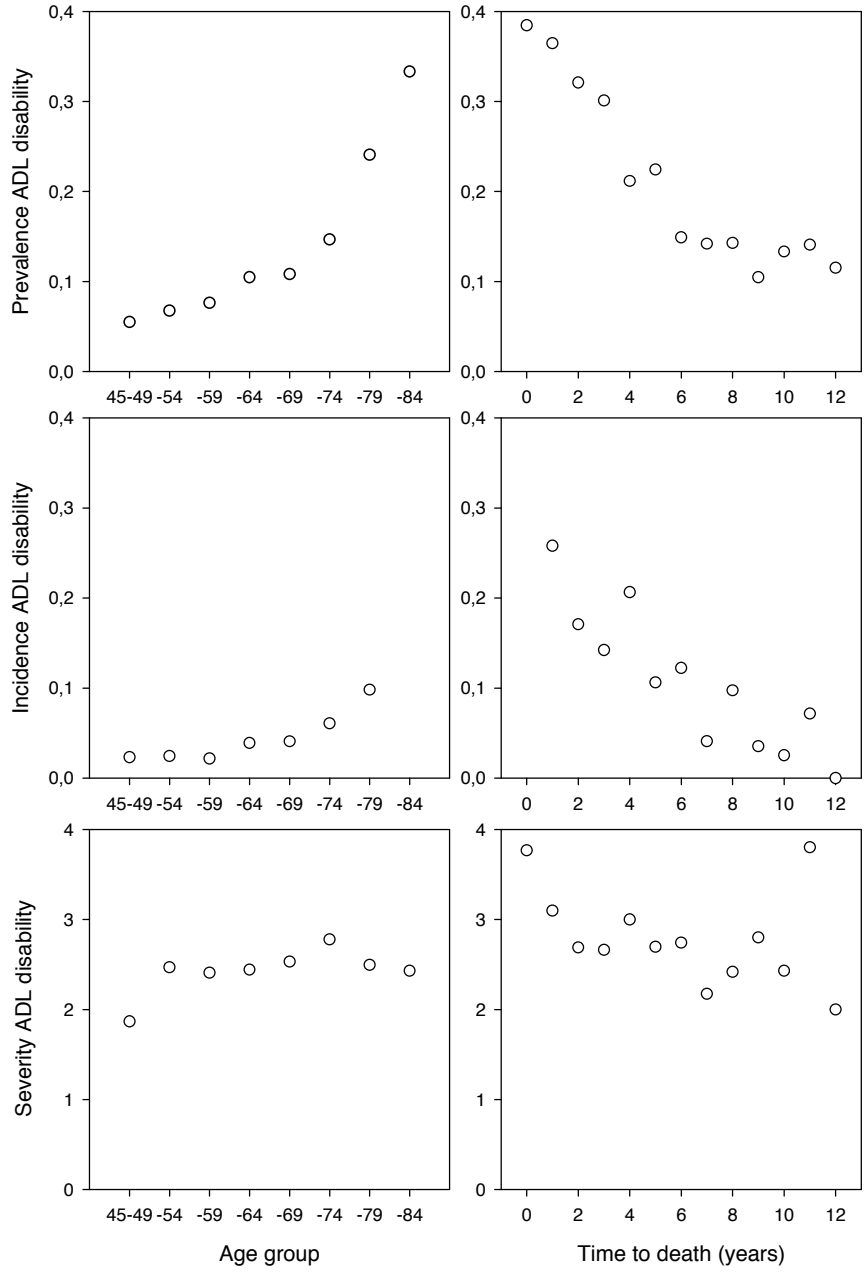


Figure 3.1.1 Prevalence, incidence and severity of ADL disability by age and time to death.

Table 3.1.2 presents wald chi2 values that express the goodness of fit of regression models with, respectively, age, proximity to death and these two factors combined. For OECD disability prevalence and incidence, goodness of fit values were higher for the age model (350 and 129) as compared to the proximity to death model (220 and 80) indicating a closer relationship of OECD disability with age. ADL disability, on the other hand, showed goodness of fit values higher for models with proximity to death (309 and 198) as to models with age (187 and 64), indicating that ADL disability was more closely associated with proximity to death. For severity of disability, goodness of fit values were the highest for models with proximity to death, for both OECD and ADL disability.

Table 3.1.2 Goodness of fit and regression coefficients of models relating disability to age and proximity to death.

	Goodness of fit (wald chi2)			Regression estimate with 95% CI (% increase per year)	
	Age	Proximity to death	Age + proximity to death	Age	Proximity to death
Prevalence					
ADL	187	309	359	4.7 (3.7-5.7)	20.0 (14.8-25.4)
OECD	350	220	424	4.3 (3.7-4.8)	7.1 (3.7-10.7)
Incidence					
ADL	64	198	214	2.7 (1.6-3.8)	18.9 (10.4-28.0)
OECD	129	80	169	2.9 (2.4-3.6)	11.2 (4.9-18.0)
Severity					
ADL	22	44	50	0.6 (0.1-1.2)	4.1 (1.9-6.3)
OECD	77	162	181	0.8 (0.5-1.2)	4.7 (3.4-6.1)

The regression coefficients in Table 3.1.2 show that increases of both OECD and ADL disability prevalence were higher with increasing proximity to death (7.1 and 20.0) as compared to increases with age (4.3 and 4.7). Increases of incidence and severity were also higher with increasing proximity to death as compared to increases with age, for both ADL and OECD disability.

An additional analysis, defining disability as having at least two (instead of one) items with much difficulty' or 'no/just with help', showed goodness of fit values of 350 (age model) and 220 (proximity to death model) for OECD prevalence and 187 (age model) and 309 (proximity to death model) for ADL prevalence and values. Thus, using a more strict definition of disability showed more clearly a stronger association with age for OECD disability and a stronger association with proximity to death than with age, for ADL disability.

In Table 3.1.3, goodness of fit values are presented for models with age and proximity to death among groups of patients with asthma/COPD, heart disease and diabetes. Similar estimates are also presented for people without any of these diseases. For all groups with a chronic disease, the prevalence of ADL disability showed a better fit with proximity to death than with age. For the prevalence of OECD disability in heart disease and diabetes patients, the goodness of fit was similar with age as with proximity to death, whereas for asthma/COPD patients the best fit was with age. With approaching death, increases of prevalence of ADL disability varied from 19.5 in heart disease patients to 25.1 in asthma/COPD patients. Increases in OECD disability prevalence varied from 4.6 in heart disease patients to 11.6 in asthma/COPD patients. Increases with age were lower and varied from 4.7 to 6.3 for ADL disability and from 4.0 to 4.4 for OECD disability.

Table 3.1.3 Goodness of fit and regression coefficients of models relating disability to age and proximity to death, stratified to chronic disease.

	Goodness of fit (wald chi2)			Regression estimate with 95% CI (% increase per year)	
	Age	Proximity to death	Age + proximity to death	Age	Proximity to death
Asthma/COPD					
ADL	66	107	126	5.7 (3.8-7.6)	25.1 (16.4-34.5)
OECD	101	78	128	4.4 (3.3-5.6)	11.6 (5.4-18.1)
Heart disease					
ADL	46	86	94	4.7 (2.1-7.4)	19.5 (11.9-27.6)
OECD	43	44	62	4.1 (2.3-5.9)	4.6 (-1.1-10.7)
Diabetes					
ADL	25	39	45	6.3 (2.8-9.9)	22.7 (10.1-36.7)
OECD	24	23	35	4.0 (1.8-6.2)	9.0 (1.0-17.7)
No disease					
ADL	47	51	76	3.8 (2.4-5.1)	11.0 (1.4-21.6)
OECD	145	48	155	4.0 (3.2-4.7)	3.5 (-2.9-10.4)

Figure 3.1.2 presents estimates of the prevalence of ADL disability over the last 12 years of life for asthma/COPD, heart disease and diabetes patients calculated from regression models including proximity to death, age and sex. For the calculations, a constant age of 70 years was assumed and sex was set as the average of values for male and female. The dichotomous variable indicating whether subjects from the original dataset had died at the end of follow-up (1) or where still alive (0) was set at 0.5. From 12 years prior to death to the year prior to death, disability prevalence increased from around 0.10 up to 0.48 in diabetes patients, up to 0.54 in patients with heart disease and up to 0.60 in patients with asthma/COPD.

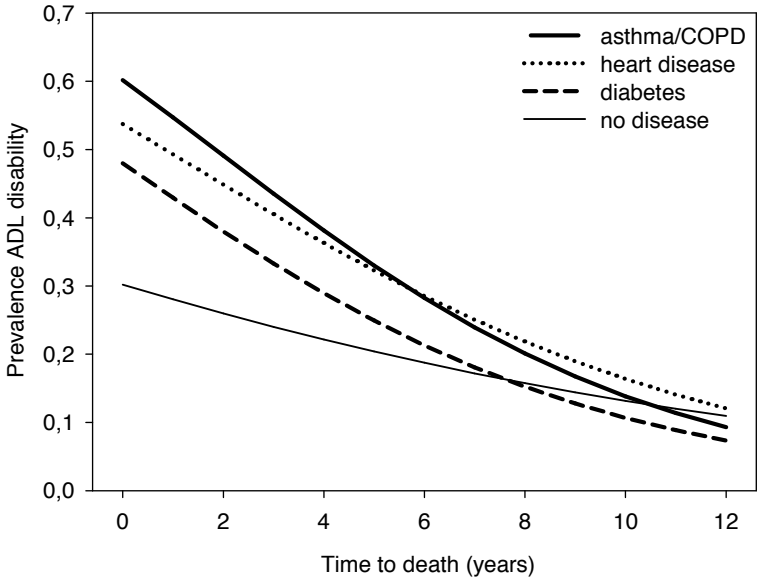


Figure 3.1.2 Regression-based estimates of ADL disability prevalence by time to death stratified by chronic disease.

Table 3.1.4 presents wald chi2 values that expresses the goodness of fit of regression models for different age strata and for males and females separately and combined. For ADL disability prevalence, goodness of fit values were higher for the oldest age category (110), as compared to the youngest age category (67). The goodness of fit for OECD disability was better for the youngest age category (172) as compared to the oldest age category (24). This pattern was not different for males and females.

Table 3.1.4 Goodness of fit and regression coefficients of models relating disability prevalence to proximity to death, stratified to age categories.

	Goodness of fit (wald chi2)			Proximity to death regression estimate with 95% CI (% increase per year)		
	Males + females	Males	Females	Males + females	Males	Females
All						
ADL	343	204	176	19.1 (13.9-24.4)	27.0 (19.1-35.3)	14.2 (7.2-21.6)
OECD	394	218	194	7.8 (6.0-9.7)	7.3 (2.9-11.9)	6.6 (1.2-12.4)
<60 years						
ADL	67	40	28	6.4 (-3.2-17.0)	9.5 (-3.3-24.0)	3.1 (-10.9-19.3)
OECD	172	83	92	6.3 (-1.3-14.5)	5.4 (-4.4-16.2)	8.0 (-3.8-21.1)
60-69 years						
ADL	66	62	19	16.0 (8.3-24.3)	24.3 (12.8-37.0)	6.6 (-3.6-17.9)
OECD	38	42	9	6.4 (1.1-11.9)	7.1 (0.6-14.1)	6.3 (-2.6-15.9)
>=70 years						
ADL	110	73	53	23.0 (13.9-32.7)	38.1 (21.4-57.1)	17.2 (6.2-29.3)
OECD	24	20	9	7.5 (1.6-13.6)	10.0 (1.7-19.0)	7.0 (-1.6-16.3)

The regression coefficients in Table 3.1.4 show that increases of the prevalence of ADL disability with approaching death were stronger in the oldest age category (23.0) as compared to the youngest age category (6.4), also for males and females separately. Increases of OECD disability were also higher for the oldest age category (7.5) as compared to the youngest age category (6.3).

Figure 3.1.3 presents estimates of the prevalence of ADL disability over the last 12 years of life for age strata younger then 60 years, 60–69 years and older than 70 years, calculated from regression models including proximity to death, age and sex. For the calculations, a constant age of 55, 65 and 75 years was assumed for the respective age categories. Sex and the value indicating death at the end of follow-up were set identical as was done for Figure 3.1.2. From 12 years prior to death to the year prior to death, disability prevalence increased from below 0.15 up to 0.25 for ages younger than 60 years, up to 0.39 for ages 60–69 years and up to 0.59 for ages older than 70 years.

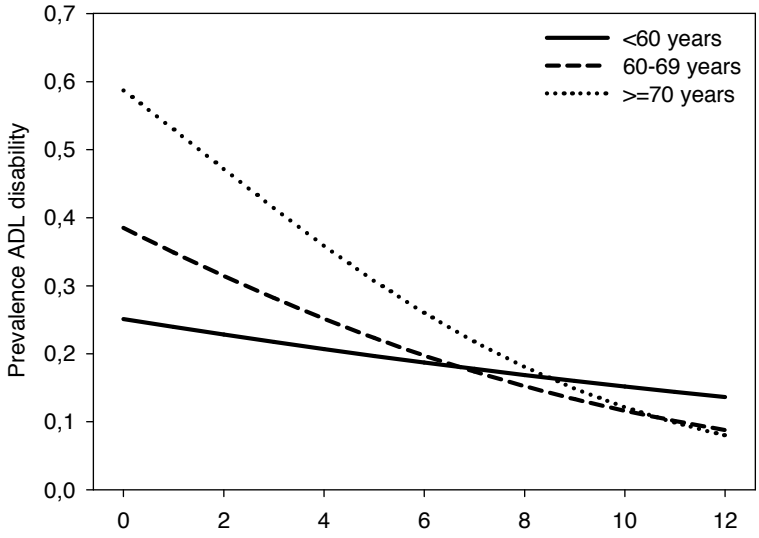


Figure 3.1.3 Regression-based estimates of ADL disability prevalence by time to death stratified by age.

DISCUSSION

Summary of results

The concept of proximity to death dependence has widely been applied in the field of health economics and has led to important new insights in expectations of future health care expenditures. Previous research suggested that disability occurrence is also partly related to approaching death. However, no previous study compared age and proximity to death with regards to their associations with disability occurrence. Our results showed that ADL disability was more strongly related to proximity to death than to age, also within specific patient groups and among different age groups. Functional impairments, as measured with the OECD list, were however more strongly related to age.

Evaluation of data and methods

Our data has some limitations that need proper attention. If non-response during follow-up was related to disability occurrence, this may have influenced the estimation of proximity to death parameters. To evaluate this possibility of attrition bias, we compared mortality during follow-up between non-responders and the rest of the study population. Age-standardised mortality among nonresponders was 12.9% versus 16.4% among the rest of the population. The lower mortality ratio among non-responders could be indicative of a lower disability prevalence among this group. In order to evaluate whether this might have biased our estimates of proximity to death dependence, we compared the original prevalence plots with plots in which missing disability values imputed from last available observations. The new plots hardly differed from the original plots. The relatively unchanged plots indicate that bias related to sample attrition or item non-response is probably small.

Opposite to the (small) effect of attrition in our study, exclusion of part of the institutionalised population from the baseline survey could have been associated with a lower prevalence of disability due to exclusion of the relatively more disabled nursing home population. As admission to a nursing home occurs often at the end of life, exclusion of the institutionalised might have led to some degree of underestimation of the proximity to death dependence of disability.

The use of self-reported measures of disease and disability might have led to some information bias. This would particularly be problematic if, independent from the status of disability, reporting behaviour was related to proximity to death. With the available data, these effects cannot be studied, and, as far as we know, no studies exist that describe such effects. One could imagine that being in the last phase of life could both positively (by increased relativism) and negatively (by increased pessimism) affect one's perception and reporting of disability. If the latter, pessimistic tendency were to predominate, this could

in part explain the relationship with proximity to death observed in this study. Nevertheless, as the significant increases of health care costs the last years of life (11,20-22) are to at least some extent related to disability occurrence (28-29), it seems unlikely that reporting tendencies alone would explain much of this strong increase in disability occurrence.

Comparison to previous studies

Our finding that disability prevalence increases as death approaches is in general agreement with a substantial amount of literature reporting terminal trajectories of functional decline at the end of life (12-19). Similar to our results, trajectories of functional decline were also reported among terminal patients with different diseases (12,17,19), e.g., COPD, diabetes and cerebrovascular accident (19). In line with our finding of a stronger association of disability prevalence with proximity to death at older ages, it was found that disability rates prior to death were higher at increased ages of death (15). Hubert et al. (30) found increasing disability scores with approaching death as from 10 years prior to death. As with our finding of a relationship over 12 years of time, their results suggest that death casts its shadow remotely over life.

In the health economics field, the principle of relating health care expenditures to proximity to death has been applied for more than 20 years (29). International studies found that health care expenditures during the last year of life are four to six times higher than expenditures for survivors (22,28) and ten times higher compared to expenditures 5 years earlier before death (21). In the Netherlands, 10% of total health expenditure has been found to be associated with health care use during the last year of life (20). To compare, we calculated the share of lifetime ADL disability burden (prevalence times severity) that occurred during the last year of life and during the last 5 years of life, assuming an 80 years lifespan. We estimated that 18% of the lifetime disability burden would occur during the last year of life and 66% of the burden would occur during the last 5 years of life. This suggests that ADL disability burden is at least as strongly related to the end of life as health care costs.

Interpretations of other findings

A remarkable difference was observed between the dominant proximity to death dependence of ADL disability on the one hand and the dominant age dependence of functional impairments (as measured in the OECD measure) on the other hand. This difference may perhaps be explained to the different physical domains that these scales represent: ADL mainly represents the locomotor domain, and functional impairments also represent visual, auditive and lingual domains. Ageing is associated with degeneration and lack of maintenance and repair of physiological and metabolic systems (31–33). As a result of damage to these systems, disability can occur, and, if a life maintaining system is involved, chances for death increase. As compared to ADL disability, functional impairments as measured in the OECD

list may be more associated to damage to systems that are not life maintaining (e.g., hearing and vision) and that therefore are more dependent on age.

Our finding that the prevalence of disability is more strongly associated to proximity to death in males as compared to females may be explained by the fact that females tend to suffer to a larger extent from non-lethal chronic disabling conditions like arthritis and back complaints (34–37) whereas lethal disabling conditions like cardiovascular disease and cancer are more common in males (34–37).

Implications

Current projection models of the future prevalence of disability either assume that age specific prevalence rates are constant or that past trends in age-specific disability prevalence rates will continue at the same rate in the future (38). Scenarios for health care expenditures show that age based models overestimate future expenditures as compared to models that take into account dependence on proximity to death. The latter models project about 10% less increase (20). Estimating to what extent past disability trends will be prolonged in the future remains a difficult exercise. In order to improve projections, we strongly recommend incorporating proximity of death parameters in future projection models. This would enable to directly relate future disability occurrence to expectations of increasing life expectancy (2–5) and could therefore lead to importantly improved estimations. The different results for ADL disability and for functional impairments, plea for incorporation of multiple domains of disability in projections of future trends in disability burden.

Our results suggest that, together with ongoing increases of the life expectancy, the prevalence of functional limitations, as measured by the OECD list, may increase in particular. Thus, in the coming decades, the number of elderly people with problems in movement or communication is likely to increase rapidly. This would result in an increased demand for care and rehabilitation to compensate for such functional limitations. In addition, the presence of functional limitations may increasingly complicate treatment of other diseases in elderly people, due to problems of co-morbidity. Sound projections, taking into account age at death, are needed to explore the pace and extent to which demand for rehabilitation and care will expand in the next decades (39,40).

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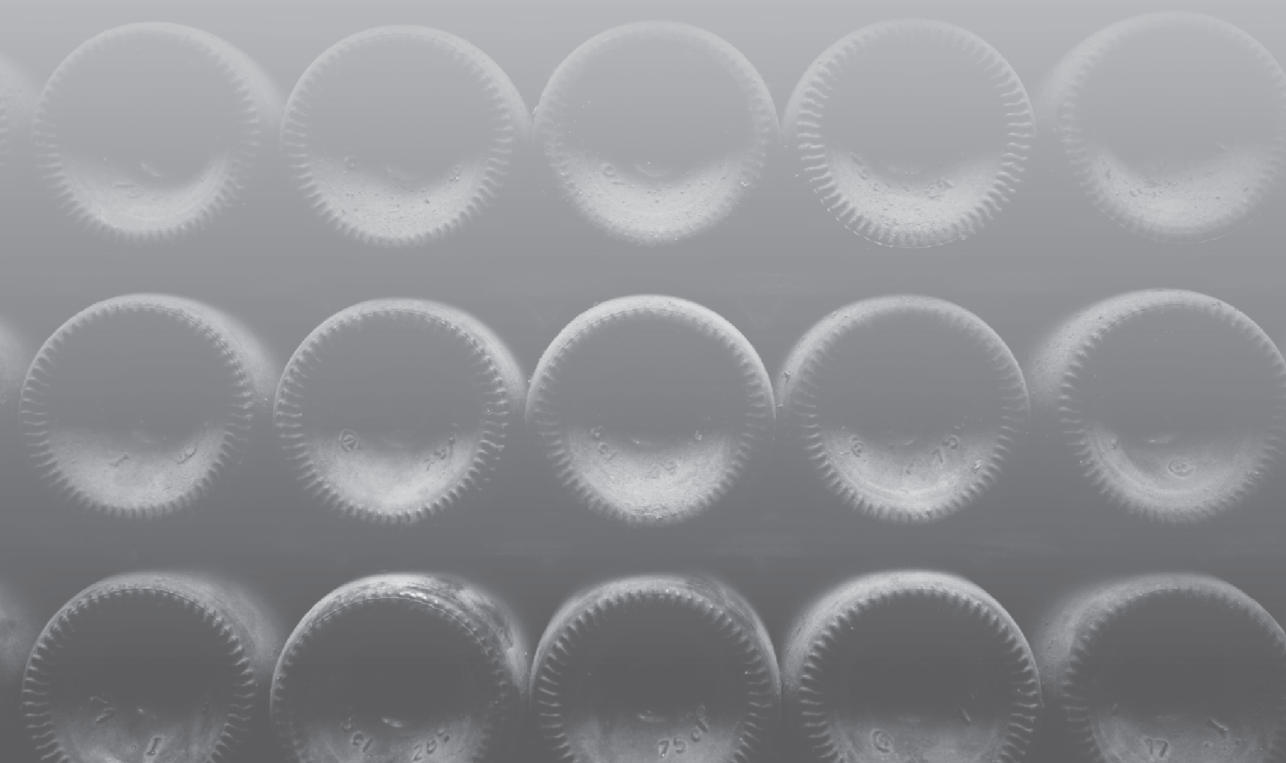
3.2

Disability occurrene and proximity to death in disability projections

Klijs B, Mackenbach JP, Kunst AE. Future disability projections could be improved by connecting to the theory of a dynamic equilibrium. J Clin Epidemiol. 2011, 64(4):436-43.



Introduction Projections of future trends in the burden of disability could be guided by models linking disability to life expectancy, such as the dynamic equilibrium theory. This article tests the key assumption of this theory that severe disability is associated with proximity to death, whereas mild disability is not.

Methods Using data from the GLOBE study (Gezondheid en Levensomstandigheden Bevolking Eindhoven en omstreken), the association of three levels of self-reported disabilities in activities of daily living with age and proximity to death was studied using logistic regression models. Regression estimates were used to estimate the number of life years with disability for life spans of 75 and 85 years.

Results Odds ratios of 0.976 (not significant) for mild disability, 1.137 for moderate disability, and 1.231 for severe disability showed a stronger effect of proximity to death for more severe levels of disability. A 10-year increase of life span was estimated to result in a substantial expansion of mild disability (4.6 years) compared with a small expansion of moderate (0.7 years) and severe (0.9 years) disability.

Conclusion These findings support the theory of a dynamic equilibrium. Projections of the future burden of disability could be substantially improved by connecting to this theory and incorporating information on proximity to death.

INTRODUCTION

In the coming decades, human life expectancy is likely to further increase (1,2). The issue whether this increase of life expectancy will correlate with either compression of disability (3) or expansion of disability (4,5) has been the subject of debate ever since the publication of Fries' (3) seminal article on compression of morbidity. A compression, that is, a decrease in the number of years that people may expect to live with disability, can only occur when the increase in life expectancy is surpassed by a stronger increase in the mean age of the onset of disability. When the increase in the age of the onset of disability will not keep pace with rising life expectancy, expansion will occur, that is, an increase in the number of years that people may expect to live with disability. Explorative analyses of future compression or expansion in disability are needed to prepare future health care systems to cope with the health effects of ageing of the population.

Projections of future trends in the total burden of disability have been applied that were based on past trends of disability (6,7). Unfortunately, application of these methods involved some difficulties. Past trends of disability were often not unambiguously pointing toward one direction and therefore constituted a weak basis for projections (6,8). Furthermore, studies do not present univocal methods to extrapolate trends, as it is not clear to what extent past trends will keep pace in the future (6,7). The complex mechanisms that simultaneously drive the life expectancy and the expectancy of life with disability are still not fully understood. This complicates the modelling of the effect of increasing life expectancy on the future burden of disability (9).

The extent to which gained life years will be spent in disability will greatly be determined by the relative part of disability in the population that is specifically related to end-of-life processes and will therefore shift to older ages as life expectancy increases. Assuming that most severe disability is reserved to the end of life (10-12), but that mild disability mostly occurs independent to the end-of-life processes, it is to be expected that with increase of life expectancy most severe disability will shift to older ages, but that mild disability will mostly expand. This scenario, which is expressed in the theory of a dynamic equilibrium, is graphically represented in Figure. 3.2.1 (13). Severe disability is fully dependent on proximity to death and, consequently, with increase of life expectancy, the onset of severe disability equivalently shifts to older ages. Mild disability is fully dependent on age and, therefore, the onset of mild disability does not change as life expectancy increases. The years spent in severe disability did not change, whereas the years in mild disability expanded.

The present article aims to assess whether the theory of a dynamic equilibrium (13) provides a valid framework for projections of the future burden of disability. We will test the key assumption of this theory that the occurrence of severe disability is associated with proximity to death, whereas the occurrence of mild disability is not. Based on estimates of associations of disability with age (time since birth) and proximity to death, we will calculate to what extent the lifetime burden of mild, moderate, and severe disability will expand in the hypothetical case of a 10-year increase of life span.

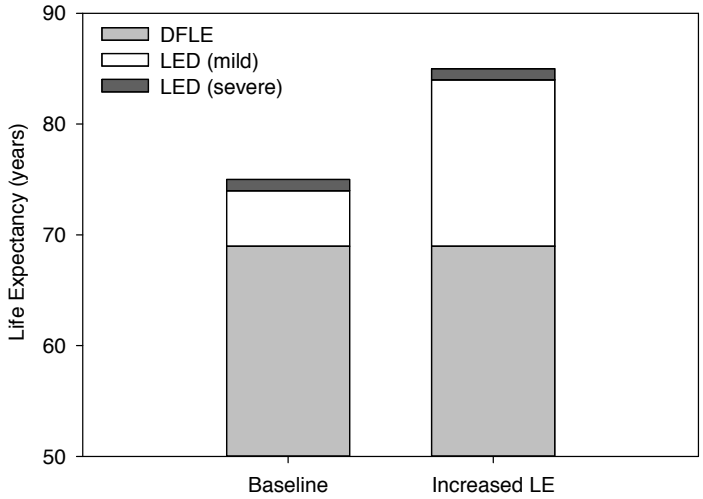


Figure 3.2.1 Effects of increasing life expectancy on LED(mild) and LED(severe) according to the theory of a dynamic equilibrium.

METHODS

Study population

We used data from the GLOBE study (Gezondheid en Levensomstandigheden Bevolking Eindhoven en omstreken), a prospective cohort study investigating the explanation of inequalities in health in The Netherlands (14). The study comprised a baseline postal survey in 1991, conducted among a stratified random sample of 27,070 inhabitants of the city of Eindhoven (40%) and surrounding municipalities (60%). The age range was set at 15-74 years with overrepresentation of 45 years and older. Institutionalized persons were excluded in Eindhoven but not in the surrounding municipalities. The response to the baseline questionnaire was 70.1% (n=18,973).

A subsample (n=3,968) of the initial cohort was invited for an oral interview and received annual follow-up questionnaires until 1997 (except for 1996). The subsample overrepresented subjects suffering from asthma/chronic obstructive pulmonary disease (COPD), heart disease,

and diabetes mellitus. The response to the oral interview was 72.2% (n=2,867). All analyses in the present article were based on data from the subsample.

The mean age of the subsample at baseline was 52.6 years, and 34% of the subjects had mild, moderate, or severe activities of daily living (ADL) disability. At the moment of the last administrative follow-up in 2004, 16% of the sample had died. Among subjects being ADL disabled at baseline, this was 26% compared with 11% among nondisabled subjects.

Attrition and item non-response

The maximal number of questionnaires that could have been obtained during follow-up of the GLOBE subsample was six waves times the 2,867 initial respondents = 17,202 questionnaires. However, 3,337 questionnaires were not returned during follow-up, leaving a total of 13,865 questionnaires.

Among questionnaires that were returned, 572 had incomplete data on ADL disability. Information was missing for only one item of ADL disability in 226 cases. In these cases, we imputed the missing item with the value of the preceding year or (for 1991) the next year. Single instead of multiple imputation was justified because of the small amount of missing values. Three hundred forty-six cases with information missing for more than one item were excluded from the analysis. In total, 13,519 questionnaires with information on ADL disability were available.

Disability measure

Disability was measured by means of 10 ADL items. The items were "walking down/upstairs, moving outdoors, leaving/entering house, sitting down/getting up from chair, moving on same floor, getting in/out of bed, eating/drinking, getting (un)dressed, washing face/hands and washing completely." For each item, subjects were asked whether they were able to perform the actions "without difficulty," "with minor difficulty," "with major difficulty," "only with help." Mild disability was defined as at least one item answered with "with minor difficulty," moderate disability as at least one item answered with "with major difficulty," and severe disability as at least one item answered with "only with help." Overall disability was considered as at least one item answered with any of these three categories.

Data analysis

The variables "mild disability," "moderate disability," "severe disability," "overall disability," and "proximity to death" were created for the six waves of data collection separately. The four disability variables indicated whether mild, moderate, severe, and overall disability were reported at the time the data were collected. "Proximity to death" was calculated as the difference in time between the moment of death, available from linkage to population registers,

and the moment of the survey. Information on age and sex was obtained from the baseline survey.

For all statistical analyses, Stata 10.0 was used (Stata-Corp, College Station, TX, USA). Generalized estimating equations (GEE) models were used to account for the interdependence of observations from one individual that would not be possible by using Cox proportional hazards models. Logistic regression analyses were applied using an exchangeable correlation matrix. By subsequently using overall, mild, moderate, and severe disabilities as dependent variables, four different models were fitted. All models included "age" and "proximity to death" as independent continuous variables, and all were adjusted for sex. Furthermore, a dichotomous variable was added to the models indicating whether or not subjects had died during follow-up and to capture differences in disability between those who died and those who survived until the end of follow-up. Consequently, the relationship of disability to proximity to death could be estimated only from subjects who died during follow-up. Following the approach in previous studies on disability trajectories in the GLOBE cohort, no weights were applied (15,16).

Using the different regression models and drawing on associations with age and proximity to death, we estimated age-specific prevalence rates for mild, moderate, severe, and overall (sum of mild, moderate, and severe) disability for life spans of 75 and 85 years. A Sullivan type of method was used to estimate the total number of years that a person might expect to live with disability over a life span of 75 and 85 years, respectively. In this particular approach, the years of life lived was assumed to be the same for each age-group considered. That is, the age-specific prevalence rates were summed to estimate the total number of years that are expected to be lived in disability (life with disability, LED). Confidence intervals (CI) around the estimated years with disability were estimated using probabilistic sensitivity analyses (17-19). That is, thousand times, regression coefficients were drawn randomly from each regression model, assuming multivariate normal distribution. For each draw, the corresponding transition rates and years with disability were calculated. The 25th and 975th of the ordered values indicated the boundaries of the CI's.

RESULTS

Table 3.2.1 shows the odds ratios (ORs) for all variables that were included in the models to estimate the prevalence of mild, moderate, severe, and overall disability. In case of the continuous variables age and proximity to death, the ORs indicate the extent to which the o odds for disability increase if age or proximity to death increases with one year. Results from models with and without proximity to death are shown together with their goodness

Table 3.2.1 Parameter estimates from models with and without proximity to death predicting the prevalence of overall, mild, moderate and severe ADL disability.

	Mild disability	Moderate disability	Severe disability	Overall disability‡
		age and proximity to death model		
OR age (continuous)	1.027 (1.022 – 1.032)	1.032 (1.022 – 1.042)	1.095 (1.072 – 1.117)	1.039 (1.033 – 1.044)
OR proximity to death (continuous)	0.976 (0.945 – 1.009)	1.137 (1.081 – 1.196)	1.231 (1.144 – 1.326)	1.108 (1.075 – 1.143)
OR deceased (dummy; 0=survived, 1=died)	1.479 (1.127 – 1.941)	0.967 (0.609 – 1.535)	0.500 (0.227 – 1.106)	1.072 (0.823 – 1.397)
OR sex (dummy; male=0, female=1)	1.134 (0.999 – 1.287)	1.387 (1.111 – 1.733)	2.110 (2.110 – 0.421)	1.353 (1.185 – 1.544)
Goodness of fit (wald chi2)	152	182	215	422
		age model		
OR age (continuous)	1.029 (1.024 – 1.034)	1.045 (1.035 – 1.054)	1.126 (1.104 – 1.149)	1.046 (1.041 – 1.052)
OR sex (dummy; male=0, female=1)	1.114 (0.983 – 1.263)	1.228 (0.989 – 1.524)	1.740 (1.186 – 2.550)	1.244 (1.092 – 1.417)
Goodness of fit (wald chi2)	143	90	150	332

‡Based on estimates from separate model

Table 3.2.2 Life years in mild, moderate and severe disability for life spans of 75 and 85 years and percentages of disability occurring the last and last five years of life.

	Mild disability	Moderate disability	Severe disability	Overall disability‡
		age and proximity to death model		
Years with disability, 75 yrs lifespan	11.6 (8.0 – 18.7)	2.4 (0.9 – 5.6)	0.8 (0.5 – 1.3)	14.8 (10.7 – 20.0)
Years with disability, 85 yrs lifespan	16.2 (10.7 – 28.0)	3.1 (1.1 – 6.8)	1.7 (1.1 – 2.7)	21.0 (15.0 – 34.0)
Increase	4.6 (2.5 – 9.4)	0.7 (0.3 – 1.2)	0.9 (0.5 – 1.5)	6.2 (3.9 – 11.1)
% in last life year, 75 yrs lifespan	1.4 (0.5 – 3.1)	12.6 (9.9 – 13.9)	23.6 (18.2 – 28.4)	4.4 (2.5 – 6.8)
% in last life year, 85 yrs lifespan	1.3 (0.4 – 2.9)	12.0 (9.7 – 13.2)	21.3 (16.2 – 26.1)	4.5 (2.5 – 6.7)
% in last five life years, 75 yrs lifespan	7.1 (2.6 – 14.6)	50.2 (41.0 – 54.5)	75.3 (64.5 – 82.3)	17.8 (9.9 – 27.8)
% in last five life years, 85 yrs lifespan	6.4 (2.2 – 13.8)	48.9 (40.5 – 52.9)	72.7 (61.3 – 80.5)	18.0 (10.0 – 27.6)
		age model		
Years with disability, 75 yrs lifespan	14.9 (14.8 – 15.1)	2.9 (2.5 – 3.4)	0.8 (0.6 – 1.1)	18.6 (17.4 – 20.0)
Years with disability, 85 yrs lifespan	19.2 (17.9 – 20.4)	4.4 (3.8 – 5.1)	2.5 (1.9 – 3.2)	26.0 (24.5 – 27.6)
Increase	4.2 (3.9 – 4.6)	1.5 (1.2 – 1.8)	1.6 (1.2 – 2.2)	7.4 (6.8 – 8.1)
% in last life year, 75 yrs lifespan	2.6 (2.4 – 2.9)	4.2 (3.5 – 4.9)	10.7 (9.1 – 12.3)	3.2 (2.9 – 3.5)
% in last life year, 85 yrs lifespan	2.4 (2.2 – 2.6)	4.0 (3.4 – 4.7)	9.9 (8.5 – 10.9)	3.4 (3.0 – 3.7)
% in last five life years, 75 yrs lifespan	12.5 (11.5 – 13.7)	19.3 (16.5 – 22.5)	43.6 (38.1 – 48.4)	15.0 (13.9 – 16.2)
% in last five life years, 85 yrs lifespan	11.5 (10.6 – 12.6)	18.6 (15.8 – 21.6)	41.3 (36.5 – 44.9)	15.5 (14.2 – 16.9)

‡Based on summed estimates for mild, moderate and severe disability.

of fit. As represented by ORs of 0.976 for mild disability, 1.137 for moderate disability, and 1.231 for severe disability, the effect of proximity to death was stronger for more severe levels of disability. Only for mild disability, the association with proximity to death was not statistically significant. Compared with the models that did not include proximity to death, the goodness of fit of the model with proximity to death was only slightly better for mild disability, whereas the fit substantially improved for moderate and severe disability.

Table 3.2.2 shows calculated LEDs for mild, moderate, and severe disability for life spans of 75 and 85 years and percentages during the last and last five years of life, based on the respective regression models. For a life span of 75 years, it was estimated that 11.6 (8.0-18.7) years were spent with mild disability, 2.4 (0.9-5.6) years with moderate disability, and 0.8 (0.5-1.3) years with severe disability. A 10-year increase in life span resulted in 4.6 (2.5-9.4) extra years in mild disability, 0.7 (0.3-1.2) extra years in moderate disability, and 0.9 (0.5-1.5) extra years in severe disability. Models with information on age only (thus excluding time to death) projected a much smaller increase in LED with mild disability, whereas they projected larger increases in LED with moderate or severe disability.

Percentages of LED occurring in the last year of life ranged from 1.4% for mild disability to 12.6% for moderate disability to 23.6% for severe disability, for life spans of 75 years. A 10-year increase of life span resulted in lower percentages of LED occurring in the last year of life for mild (0.1% lower), moderate (0.6% lower), and severe disability (2.3% lower). The percentages of LED occurring in the last five years decreased with 0.7% for mild disability, 1.3% for moderate disability, and 2.6% for severe disability.

Figure. 3.2.2 visually represents the calculated prevalence of mild, moderate, severe disability for life spans of 75 and 85 years. To also display the prevalence of overall disability, the prevalences for the different levels of severity are shown cumulatively. Increase of life span resulted in a strong shift of the burden of disability to older ages, especially for moderate and severe disability. Thirteen percent of LED mild was spent during the 10 years that were gained, as compared with 75% and 94% for LED moderate and LED severe, respectively. Age-specific prevalences of disability at younger ages generally declined.

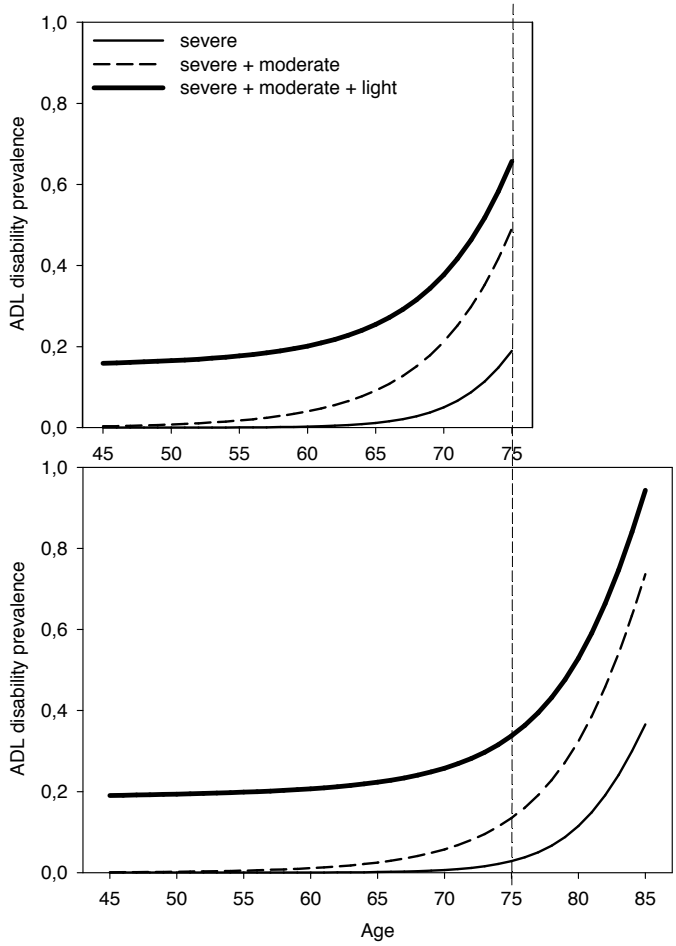


Figure 3.2.2 Age-specific prevalence of ADL disability by level of severity for life spans of 75 and 85 years. Estimates derived from regression models.

DISCUSSION

Summary of results

Our results confirm the hypothesis that the occurrence of severe disability is associated with proximity to death and the occurrence of mild disability is not. Based on the associations with age and proximity to death and assuming a 10-year increase of life span, we showed that mild disability greatly expanded, but that moderate and severe disability showed much lesser expansion. Current findings support the theory of a dynamic equilibrium (13).

Evaluation of data and methods

Our data has some limitations that need proper attention. If non-response during follow-up was related to disability occurrence, this may have influenced the estimation of proximity-to-death parameters. To evaluate this possibility of attrition bias, we compared mortality during follow-up between non-responders and the rest of the study population. Age-standardized mortality among non-responders was 12.9% vs. 16.4% among the rest of the population. The lower mortality ratio among non-responders could be indicative of a lower disability prevalence among this group. To evaluate whether this might have biased our estimates of proximity-to-death dependence, we compared the original regression estimates with estimates in which missing disability values were imputed from last available observations. The new estimates hardly differed from the original one. This indicates that bias related to sample attrition is probably small.

Exclusion of part of the institutionalized population from the baseline survey could have been associated with a lower prevalence of disability because of exclusion of the relatively more disabled nursing home population. As admission to a nursing home occurs often at the end of life, exclusion of the institutionalized population might have led to some degree of underestimation of the relationship between proximity to death and disability, especially for moderate and severe disability.

The use of self-reported measures of the different levels of disability might have led to some information bias. This would particularly be problematic if, independent from the status of disability, reporting behaviour was related to proximity to death. Again, especially moderate and severe levels of disability may have been influenced, because these levels are more likely to occur close to death. With the available data, these effects cannot be studied, and, as far as we know, no studies exist that describe such effects. One could imagine that being in the last phase of life could both positively (by increased relativism) and negatively (by increased pessimism) affect one's perception and reporting of disability. If the latter pessimistic tendency were to predominate, this could in part explain the relationship with proximity to death observed in this study. Nevertheless, also in view of an increase of health care costs during the last years of life (20-23), it seems unlikely that reporting tendencies alone would explain much of this strong increase in disability occurrence.

The association of proximity to death and disability is likely to be mediated by other factors, such as health status/disease and demographic factors. If our aim had been to gain insight into causal chains that relate disability with time to death, or to provide a model with an optimal predictive power, it would have been useful to include more covariates. However, our aim was only to demonstrate the relevance of proximity to death for predicting the prevalence of disability. To keep the models simple and transparent, we decided not to include any

other covariates except sex. Moreover, variables other than sex, age, and time to death are not routinely distinguished in projections of future demographic trends of many countries.

We chose to use GEE instead of other statistical models, for example Cox proportional hazards or ordered logit models, because this allowed us to account for interdependence of observations. Postestimated intraindividual correlations that were 0.442 for mild disability, 0.407 for moderate disability, and 0.675 for severe disability, showed that interdependences were strong. Using statistical models that did not account for these interdependences would have substantially affected the model estimates.

To test whether adding polynomial terms on age or proximity to death would have improved the fit of the models, we used quasi-information criterion (QIC). QIC is a Stata program that has been developed as an aid for model selection in GEE analyses (24). Adding polynomial terms did not substantially improve the goodness of fit for models of overall, moderate, and severe disability. For mild disability, however, the model fit did improve by adding a quadratic term for proximity to death (the QIC value decreased from 16062 to 15050). Nevertheless, to use the same model for different types of severity, we decided not to include any polynomial terms.

We modelled the prevalence of disability as dependent on proximity to death, but the converse may also be applied, that is, modelling proximity to death as dependent on the prevalence of disability. This raises the issue of reverse causality that is relevant especially to studies that construct statistical models with the aim of identifying associations and making inferences about the causality of the associations observed. Our aim, however, was not to make inferences about causality but to test for the existence of a set of associations as predicted by a descriptive theory (i.e., the theory of a dynamic equilibrium).

In the article in which Manton introduced his theory of a dynamic equilibrium, he stated that slowing down the progression rate of a disease would lead to a longer life, an increasingly longer period spent in disease, but a relatively constant number of years spent in "highly morbid" state. Although Manton did not define this "highly morbid" state, we applied a distinction according to the severity of disability. Similar distinctions have been applied by other researchers (25). In our calculations, mild disability showed rapid expansion, whereas the occurrence of moderate and severe disability shifted toward older ages with increase of life span. This shift resembles the trends in the "highly morbid state" that Manton postulated.

Comparison with past trends

Between 1990 and 2003, life expectancy has increased by approximately 1 year in females and 2.5 years in males (26,27). In accordance with the theory of a dynamic equilibrium, one would

expect an increasing life expectancy in mild disability but much smaller increases for more severe disability. In addition, if disability occurrence would be strongly related to proximity to death, one would expect increasing of life expectancy to be related to decreasing age-specific disability prevalence rates (instead of constant prevalences; see Figure. 3.2.2).

Although the evidence is not completely unambiguous, generally, stable or decreasing age-specific disability prevalence rates were observed for a variety of disability indicators (6,8). Simultaneous trends of increasing life expectancy and decreasing age-specific disability rates were also found for the United States, Japan, and various European countries (6,28-30). Thus, evidence from The Netherlands and other countries generally supports the expectation of decreasing age-specific prevalence rates.

Studies for The Netherlands estimate that between 1989 and 2000 a gain in life expectancy in males from 14.3 to 15.3 years at age 65 was accompanied by an increase of years in mild disability from 3.7 to 6.2 years, whereas the number of years in moderate and severe disability decreased from 5.1 to 4.5 years (31). Similar patterns were observed for females (31). Research from other countries showed similar results. In the United States, between 1992 and 2002, a half-year gain in life expectancy at age 65 was accompanied with constant expectations of years in instrumental activities of daily living (IADL) disability and moderate ADL disability and a decrease of life expectancy in severe ADL disability from 2.1 to 1.7 years (32). In New Zealand, between 1981 and 1996, life expectancy at age 65 increased from 13.3 to 15.5 in males and from 17.2 to 19.0 years in women. During the same period, the life expectancy with major mobility restrictions in male remained 0.8 years, but life expectancy with moderate mobility restrictions more than doubled from 0.7 to 1.6 years. In females, the life expectancy with major mobility restrictions moderately increased from 2.0 to 2.6 years, whereas the life expectancy with moderate mobility restrictions sharply increased from 1.2 to 2.7 years (33).

Cohort differences

We found that disability is associated with age and proximity to death. In theory, these associations may partially reflect cohort effects. Cohort differences could for instance occur if differences in living conditions at birth substantially affect the onset of disability and mortality within specific generations. In a study on cohort differences in disease and disability in the young-old (in the United Kingdom), Jagger et al. (34) showed that the number of chronic conditions and especially the presence of arthritis and COPD were reported more frequently in more recent cohorts. Nevertheless, these cohort differences did not appear to be reflected in similar differences in functional limitation or disability, whereas survival too was similar between cohorts. This suggested that cohort effects in disability occurrence might be only small. However, more definite answers should be derived from studies that, like in the field

of mortality (35), could distinguish between period and cohort effects by using long observation periods.

Implications for modelling future developments in disability

Together with evidence from past disability trends, the results from the present article provide empirical support to the theory of a dynamic equilibrium. This theory may provide a useful framework for projecting changes in disability occurrence in relationship to increases in life expectancy. Prediction models could connect to this framework by incorporating information on proximity to death. Using a proximity-to-death term would allow the modelling of a shift of disability toward older ages when life expectancy increases. To further connect to the theory of a dynamic equilibrium, prediction models should distinguish for different levels of severity of disability. According to our estimates, these new prediction models are likely to predict a smaller increase in the burden of moderate and severe disability than traditional age-based models.

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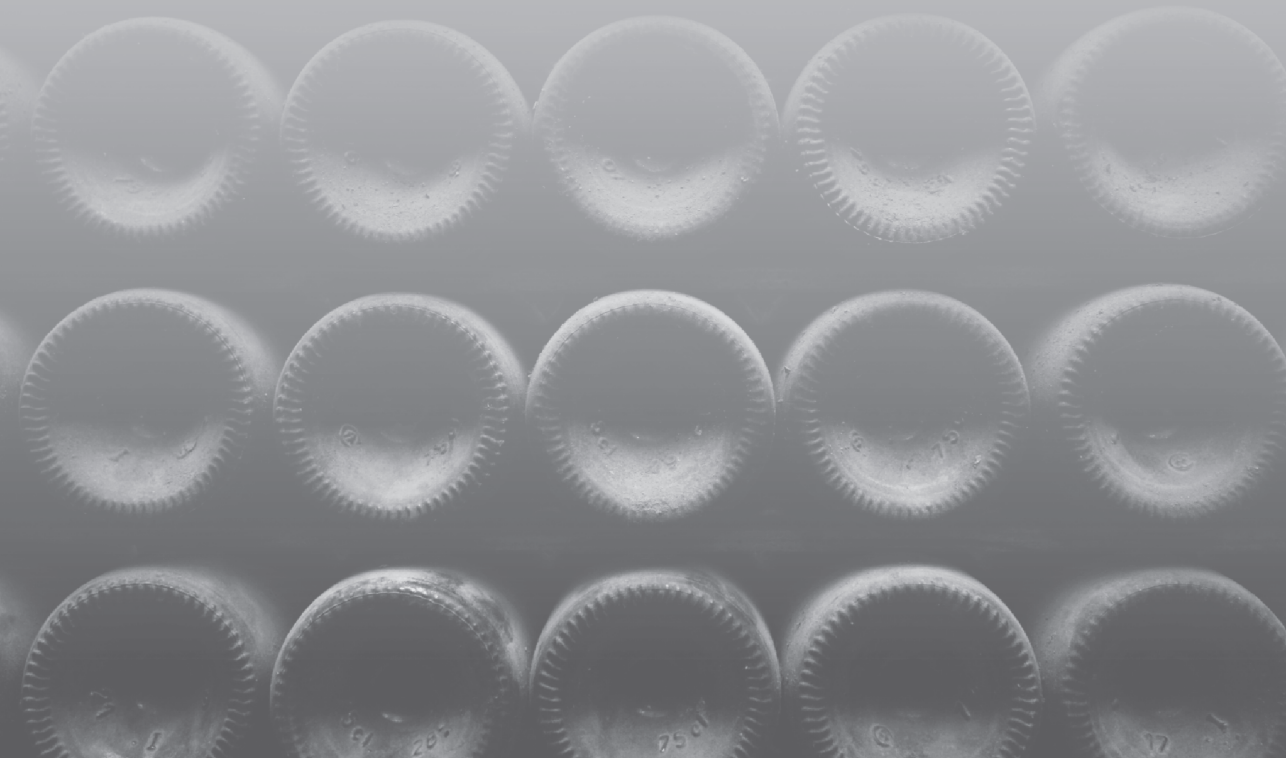
Part II

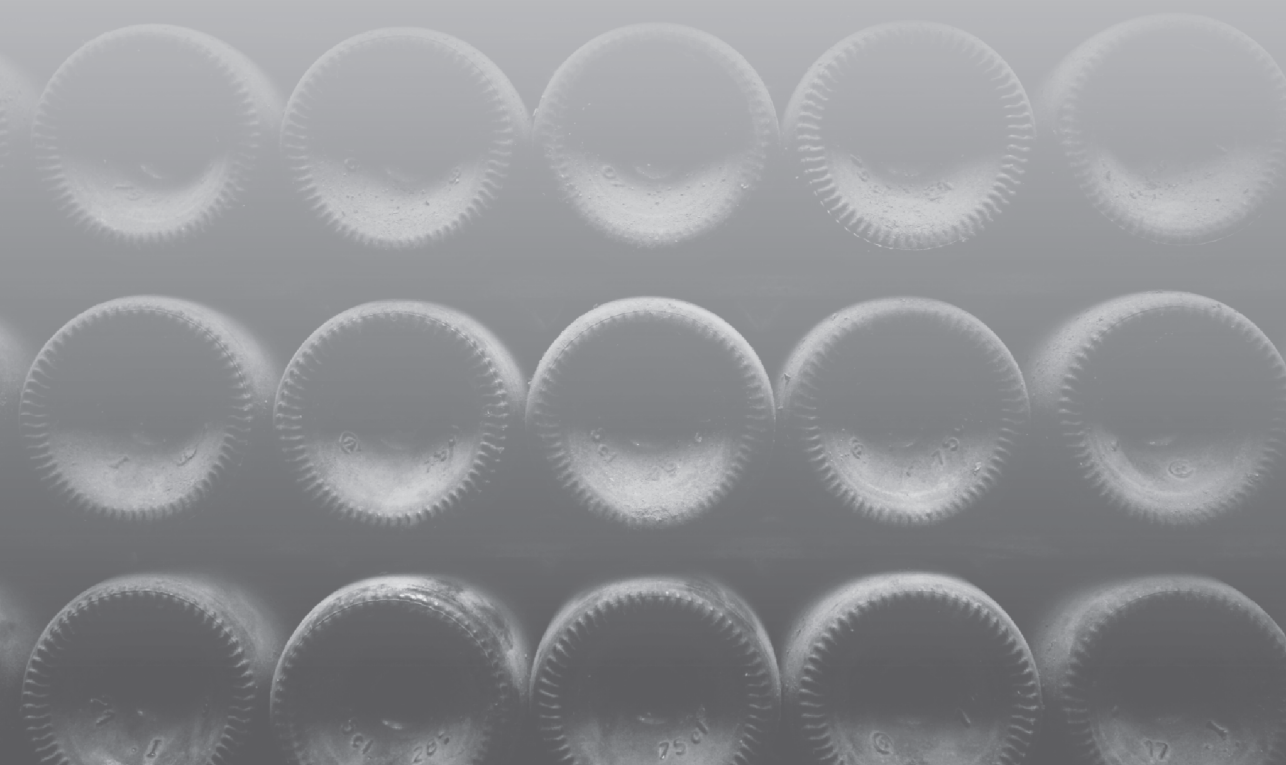
Explaining the burden of disability



4

The contribution of chronic disease to the burden of disability

Klijs B, Nusselder WJ, Looman CW, Mackenbach JP. Contribution of chronic disease to the burden of disability. PLoS One. 2011, 6(9):e25325.



Introduction Population ageing is expected to lead to strong increases in the number of persons with one or more disabilities, which may result in substantial declines in the quality of life. To reduce the burden of disability and to prevent concomitant declines in the quality of life, one of the first steps is to establish which diseases contribute most to the burden. Therefore, this paper aims to determine the contribution of specific diseases to the prevalence of disability and to years lived with disability, and to assess whether large contributions are due to a high disease prevalence or a high disabling impact.

Methods Data from the Dutch POLS-survey (Permanent Onderzoek Leefsituatie, 2001-2007) were analyzed. Using additive regression and accounting for co-morbidity, the disabling impact of selected chronic diseases was calculated, and the prevalence and years lived with ADL and mobility disabilities were partitioned into contributions of specific disease.

Results Musculoskeletal and cardiovascular disease contributed most to the burden of disability, but chronic non-specific lung disease (males) and diabetes (females) also contributed much. Within the musculoskeletal and cardiovascular disease groups, back pain, peripheral vascular disease and stroke contributed particularly by their high disabling impact. Arthritis and heart disease were less disabling but contributed substantially because of their high prevalence. The disabling impact of diseases was particularly high among persons older than 80.

Conclusion To reduce the burden of disability, the extent diseases such as back pain, peripheral vascular disease and stroke lead to disability should be reduced, particularly among the oldest old. But also moderately disabling diseases with a high prevalence, such as arthritis and heart disease, should be targeted.

INTRODUCTION

Population ageing is expected to lead to a sharp increase in the occurrence of disability. Disability is associated with an increased need for social services, e.g. healthcare, and a loss in quality of life (1-3). To enable the future health care system to cope with increasing demands, and to avoid strong decrements in the quality of life, it is crucial to develop strategies that effectively lead to reductions in the burden of disability. One of the first steps crucial in developing these strategies is to identify which diseases contribute most to the total burden of disability, but also to clarify whether large contributions are related with a high prevalence of disease or with a high disabling impact, i.e. a high extent the disease leads to disability.

To date, only a limited number of studies have assessed the contribution of specific diseases to the burden of disability (4-14). Unfortunately, most of these studies were based on relatively old data (4-9). As both the prevalence of chronic diseases and their disabling impacts change over time, the results of these studies may be outdated (13,14). Furthermore, only two studies explicitly addressed the role of disease prevalence and disabling impact in contributions to disability (5,6). The most comprehensive study assessing burden of disease has probably been WHOs Global Burden of Disease study (GBD) (12). In this study, however, disease burden is quantified on the basis of panel valuations of health states rather than actual presence of physical or mental disabilities (12).

Most of the previous studies were based on cause elimination techniques, which provide outcome measures that reflect the reduction in the prevalence of disability if the disease would no longer be present (4,7,8,11). Drawbacks of this method are that the results may be inconsistent in a situation of co-morbidity, as they depend on the ordering of the elimination, and that contributions of all diseases do not add up to the total disability prevalence. Recently, Nusselder et al. developed a methodology, based on an additive regression technique, that enables exact partitioning of the burden of disability into additive contributions of disease in the presence of co-morbidity (5,15).

The aim of this study was to investigate the current contribution of specific chronic diseases to the total burden of disability in mobility and activities of daily living among the elderly, both in terms of disability prevalence and years lived with disability. This study is among the first to highlight the role of both the prevalence and the disabling impact of specific diseases to determine their contribution to the burden of disability.

METHODS

Study population

The study population consisted of subjects from seven successive years (2001-2007) of the POLS health and labour survey, which is being conducted by Statistics Netherlands. The survey does not include the institutionalized population. To account for selective non-response and to ensure representativeness for the Dutch non-institutionalized population, weights were used that were attached to the data.

Information on disabilities in mobility and activities of daily living was collected through face-to-face interviews and information on the presence of chronic disease through written questionnaires. From 2001-2007, 110,766 subjects were approached and the response was 62%. For our analyses selected elderly subjects who were 55 years and older (n = 17,404) were selected. 22% of these subjects could not be included in the study population because they lacked disease information. Table 4.1 provides further detailed information on numbers of persons in the study population and Figure 4.1 on the difference between the source and study population.

Table 4.1 Numbers of subjects in the study sample.

	Males			Females		
	55-64	65-79	>=80	55-64	65-79	>=80
Total	3412	2873	478	3187	3005	680
Elementary education	531	695	149	680	1160	359
Secondary education	1928	1499	232	2003	1546	265
Tertiary education	932	656	95	495	286	52
Education missing	21	23	2	9	13	4
DM	262	365	55	168	353	97
Stroke	130	233	50	88	159	53
Heart disease	330	599	116	107	297	100
PVD	119	207	50	72	183	67
Cancer	130	278	66	244	306	80
CNSLD	229	283	61	239	314	67
Back pain	414	258	46	380	407	102
Arthritis	580	629	147	868	1254	358
Disorder neck/arm	432	316	46	623	577	127
Other	600	487	118	918	906	269
No disease reported	1620	1014	119	1283	845	131
ADL disabled	137	263	96	200	472	254

Abbreviations: CNSLD = chronic non-specific lung disease; DM = diabetes mellitus; PVD = peripheral vascular disease (upper extremity excluded). Numbers of persons with diseases do not add up to total because of co-existence of diseases.

Disability

Subjects were asked if they were able to 'walk up and down the stairs', 'walk outside', 'enter/leave the house', 'sit down/get up from a chair', 'move around on the same floor', 'get in/out of bed', 'eat/drink', 'get dressed/undressed', 'wash face/hands' and 'wash completely' and could answer with 'without difficulty', 'with minor difficulty', 'with major difficulty' and 'only with help'. Someone was considered disabled if he or she opted for one of the latter two answers at least once.

Definition of disease groups

Information on the presence of a range of diseases was collected in the questionnaire. From the original questions 'cardiovascular disease' (CVD) was compiled, containing 'stroke', 'heart disease' and 'peripheral vascular disease (PVD)', and 'musculoskeletal disease' was compiled, containing 'back pain', 'arthritis' and 'disorder neck/arm'. Furthermore, 'diabetes mellitus (DM)', 'cancer', 'chronic non-specific lung disease (CNSLD)' and 'other' were distinguished. Appendix 4.1 shows the original questions and the diseases that were distinguished. Skin cancer was not included because it is not associated with disability. PVD did not include vascular disease of the upper extremity. In subjects who had suffered from back pain or disorders of the neck/arm but indicated that they currently did not suffer anymore, the condition was regarded as no longer present. If a disease was defined on the basis of multiple questions and information on any of the questions was missing while none of the questions indicated the presence of a disease, the disease information was considered missing.

Statistical methods

Disability prevalence by cause was estimated from individual information on the presence or absence of disability, the presence or absence of the selected disease groups, gender and age. A method based on a multivariate additive regression model was used, which is described in more detail elsewhere (5,6,16). This method takes into account that persons who do not report a disease may be disabled (this risk is referred to as "background") and that persons can have more than one disease (co-morbidity). Disability in persons without a reported disease is entirely attributed to background. Disability in persons with at least one disease is attributed partly to background and partly to the disease(s). We assume that causes of disability (diseases and background risk) act as independently competing causes. Assuming independence, the hazard of someone having disease A and B (and zero background risk) equals hazard A + hazard B. In a situation of no competing risk (one disease and zero background risk) the hazard can be easily converted to a probability of being disabled (1-exp(- disease hazard)). When more causes are competing, the probability of being disabled from the specific disease is lower than in the situation of no competition. In the footnote of Table 4.2, a calculation example is given of how was dealt with co-morbidity.

To estimate cause-specific disability prevalence from cross-sectional data the following assumptions were made. First, the distribution of disability by cause is explained entirely by diseases that are (still) present at the time of the survey and the risk of disability in absence of any reported diseases. Second, this distribution is proportional to the distribution of the risk of becoming disabled in the time-period preceding the survey. Thirdly, causes of disability (diseases and background) act as independently competing causes.

The regression model is specified as follows:

$$\hat{y} = 1 - \exp(-\eta:)\ Y : \text{b}inomial$$

$$\eta = \alpha_a + \sum_d \beta_d X_d$$

where $\hat{y}$ is the estimated probability that the person has disability, e is the base of the natural logarithm and η the linear predictor. The latter is defined as the sum of the background rate by age (α_a) and the cause-specific rates of disability (β_d, labelled as "disabling impact") for the disease groups (d) that are present in the respondent (given by the dummy variables X_d). Background was handled as a cause that is prevalent for everyone; the rate of background is age dependent (5-year age groups). The disabling impact β_d may also vary by age. As the full age-interaction term would require n (number of age classes) times m (number of diseases) different parameters, the rank of the interaction was reduced to one, which means that the age-specific disabling impact of each disease, β_{da}, is estimated as the product of an age pattern γ_a which is equal for each disease, and a disease effect δ_d, which varies by disease, but not by age (Reduced Rank Regression) (17,18). While a one rank solution restricts the age pattern to be the same for all diseases, also second rank solutions were fitted ($\beta_{da} = \gamma_{a1}.\delta_{d1} + \gamma_{a2}.\delta_{d2}$) and scaled deviances were compared to test for differences in age patterns for different diseases. Adding a one rank interaction improved the fit of the model (log-likelihood ratio test with *P*-value of 0.05), indicating that the disabling impact varies by age. Because adding a second rank did not further improve the fit of the model, the same age pattern for all diseases was used. Models were fitted using a quasi-Newton method that was programmed for the statistical package R version 2.7.1. (19). All analyses were done separately for men and women, as the log-likelihood ratio test indicated that both the rates of background and the disease-specific rates given sex-specific rates of background differed significantly by sex. The significance of the differences in the disabling impact between males and females was assessed by assuming normal distribution of the parameters with the mean of the original ones as the standard error.

Calculation of number of disabled by cause across subgroups

Disability prevalence by cause depends on the prevalence of the disease (X_d) and the disabling impact of the disease (β_d or β_{da}). Analogous to using the proportional distribution of mortality rates to obtain probabilities of death in the presence of competing causes (so called "crude probabilities"), the attribution of disease d is $(\beta_{da} X_d/\eta).y$ and of background is $(\alpha_a/\eta).y$ (5,6). Applying these formulas gives for every individual the probability of being disabled caused by background *or* disease (if present). Adding the cause-specific probabilities of an individual gives the probability of being disabled for that individual. Adding the cause-specific probabilities of all persons in the dataset, or in a specific age group, gives the total number of disabled by cause in the population, or in that age group. Dividing the number of disabled persons by cause by the total number of persons gives the proportion of disability by cause.

Years lived with disability at age 55 by cause were obtained using the Sullivan method (20). The Sullivan method uses the prevalence of disability in each age group to divide the number of person-years into years lived with and without disability (20). Instead of using the age and sex specific prevalence of disability, we used age, sex and cause specific prevalence of disability, yielding the years with disability by each cause. Adding the years with disability by each cause yields the life expectancy with disability, as the sum of the cause-specific disability add to the total prevalence. A life table for the Dutch population 2001-2007, available from the EHEMU database, was used (21).

Confidence intervals around the estimates of disabling impacts, prevalences of disability by cause and contributions to LED at age 55 were obtained with bootstrapping based on 1000 replicas (22). For the disabling impacts and prevalences by cause we used non-parametric bootstrapping. For the bootstrap of life expectancy, which is used in combination with prevalence by cause to calculate LED, we used parameterized bootstrap, assuming Poisson distribution of the numbers of deaths.

The software for additive regression and for calculation of disability prevalence by cause is available from the authors on request.

RESULTS

In males, the prevalence of disability increased from 4% at ages 55-59 to 20% at ages older than 80. In females, this was from 6% to 37% (Figure 4.1). Also persons without any disease reported disability.

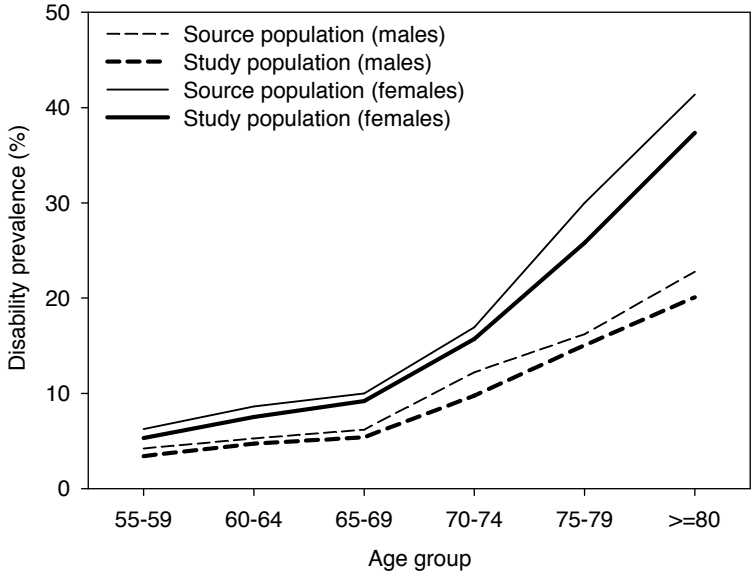


Figure 4.1 Prevalence of disability by age.
The source population consisted of all respondents to the POLS health and labor survey, the Netherlands, 2001-2007, aged 55 and older (n=17,404). The study population equals the source population minus all subjects who had information missing on the presence of diseases (n=13,635).

The contribution of diseases to the prevalence of disability depends both on the prevalence and disabling impact of disease. Among males, arthritis, heart disease and other, and at younger ages also back pain, had the highest prevalences (Table 4.2). Among females these were arthritis, other, disorder neck/arm and back pain, and at older ages also DM and heart disease.

Table 4.2 Prevalences and disabling impacts of disease.

	Disease prevalences (%)			Disabling impacts of disease (hazard)		
	55-64	65-79	>=80	55-64	65-79	>=80
			males			
DM	7.7 (6.9-8.7)	12.6 (11.5-13.9)	10.8 (1.6-9.0)	0.01 (0.00-0.02)	0.02 (0.00-0.05)	0.03 (0.00-0.08)
Stroke	3.8 (3.2-4.4)	8.1 (7.2-9.1)	10.9 (8.4-14.1)	0.08 (0.05-0.12)	0.16 (0.10-0.23)	0.28 (0.17-0.42)
Heart disease	9.6 (8.7-10.6)	20.9 (19.4-22.4)	23.3 (19.8-27.2)	0.01 (0.00-0.03)	0.03 (0.01-0.06)	0.05 (0.01-0.10)
PVD	3.4 (2.9-4.1)	6.9 (6.1-7.9)	10.6 (8.1-13.7)	0.09 (0.05-0.13)	0.17 (0.10-0.26)	0.30 (0.17-0.47)
Cancer	3.7 (3.1-4.4)	9.7 (8.7-10.9)	14.3 (11.4-17.8)	0.01 (0.00-0.03)	0.02 (0.00-0.05)	0.04 (0.00-0.09)
CNSLD	6.6 (5.8-7.5)	10.2 (9.1-11.4)	12.6 (9.9-15.9)	0.08 (0.05-0.11)	0.15 (0.10-0.20)	0.26 (0.16-0.38)
Back pain	11.9 (10.9-13.0)	8.7 (7.7-9.8)	8.9 (6.7-11.7)	0.08 (0.05-0.11)	0.16 (0.11-0.22)	0.29 (0.17-0.42)
Arthritis	16.7 (15.5-18.0)	21.9 (20.4-23.5)	31.0 (27.0-35.3)	0.03 (0.02-0.05)	0.07 (0.04-0.09)	0.12 (0.06-0.19)
Disorder neck/arm	12.7 (11.6-13.8)	10.9 (9.8-12.1)	9.5 (7.2-12.4)	0.00 (0.00-0.02)	0.01 (0.00-0.04)	0.01 (0.00-0.08)
Other	17.3 (16.1-18.6)	17.4 (16.0-18.8)	25.1 (21.4-29.2)	0.03 (0.01-0.04)	0.05 (0.02-0.08)	0.09 (0.04-0.15)
No disease reported	48.1 (46.4-49.8)	35.4 (33.6-37.1)	25.8 (22.1-30.0)			
			females			
DM	5.4 (4.7-6.2)	11.7 (10.6-12.9)	14.7 (5.9-16.0)	0.07 (0.04-0.10)	0.11 (0.06-0.16)	0.23 (0.13-0.37)
Stroke	2.6 (2.1-3.2)	5.2 (4.5-6.1)	7.9 (6.1-10.2)	0.10 (0.05-0.16)	0.16 (0.08-0.24)	0.35 (0.18-0.55)
Heart disease	3.2 (2.7-3.9)	9.9 (8.9-11.0)	14.4 (11.9-17.2)	0.06 (0.03-0.10)	0.10 (0.05-0.15)	0.22 (0.11-0.36)
PVD	2.3 (1.8-2.8)	6.4 (5.6-7.4)	9.9 (7.9-12.4)	0.11 (0.06-0.18)	0.17 (0.09-0.27)	0.38 (0.21-0.60)
Cancer	7.6 (6.7-8.5)	10.2 (9.2-11.4)	11.5 (9.3-14.0)	0.01 (0.00-0.03)	0.01 (0.00-0.04)	0.03 (0.00-0.09)
CNSLD	7.4 (6.6-8.4)	10.5 (9.4-11.6)	10.2 (8.1-12.8)	0.06 (0.03-0.10)	0.10 (0.05-0.15)	0.22 (0.10-0.34)
Back pain	12.1 (11.0-13.3)	13.7 (12.5-15.0)	15.3 (12.7-18.2)	0.12 (0.09-0.16)	0.20 (0.14-0.26)	0.44 (0.30-0.60)
Arthritis	27.1 (25.6-28.7)	41.6 (39.9-43.4)	53.6 (49.9-57.3)	0.07 (0.05-0.09)	0.11 (0.08-0.14)	0.24 (0.17-0.32)
Disorder neck/arm	19.8 (18.4-21.2)	19.4 (18.0-20.8)	19.7 (16.8-22.9)	0.03 (0.01-0.05)	0.04 (0.01-0.07)	0.09 (0.03-0.17)
Other	29.3 (27.7-30.9)	30.4 (28.8-32.1)	39.0 (35.4-42.7)	0.04 (0.02-0.05)	0.06 (0.03-0.09)	0.13 (0.07-0.20)
No disease reported	40.0 (38.3-41.7)	27.9 (26.4-29.6)	19.7 (16.8-22.8)			

Abbreviations: CNSLD = chronic non-specific lung disease; DM = diabetes mellitus; PVD = peripheral vascular disease (upper extremity excluded).

5 year age groups were used to calculate the disabling impact of diseases and the prevalence of disability by cause (table 3). To summarize and as is shown in the table, disabling impacts were also calculated using three age-aggregated groups (55-64.9, 65-79.9, >=80). 'Background', representing presence of disability irrespective of disease presence, is preferably modelled according to 5 year age groups and could therefore not be shown in the table.

The disabling impact represents the rate of disability from a specific cause given that the disease is present. Adding these specific disability rates for the diseases present and the background rate of disability (by age and gender) gives the total disability rate for a specific exposure group. The proportion of the cause-specific rate in total rate is used to divide the probability of disability in this group by cause. For example, for males aged 75-79 with PVD and arthritis, adding the background rate (0.03), the rate for PVD (0.17), and the rate for arthritis (0.07) yields a total disability rate of 0.27 and a total probability of disability of 0.24 ($1 - \exp(-0.27) = 0.24$). The probability of disability from background in this group is 0.03 (0.03 / 0.27 * 0.24), that of PVD is 0.15 (0.17 / 0.27 * 0.24), and that of arthritis is 0.06 (0.07 / 0.27 * 0.24).

The disabling impact for males and females was significantly different ($P<0.05$) for DM, heart disease, cancer, arthritis and disorder neck/arm.

Among males, PVD had the highest disabling impact (Table 4.2). Furthermore, stroke, CNSLD and back pain showed high disability risks. Among females, back pain had the highest disabling impact, but stroke and PVD also showed high impacts. In both sexes, cancer did not lead to much disability, as was the case for DM and heart disease in males. The disabling impacts of DM, heart disease, arthritis and disorder neck/arm were significantly higher among females than among males ($p<0.05$). Although the disabling impact of cancer was low, it was significantly higher among males. The disabling impact of the diseases increased with age ($P<0.05$).

Table 4.3 Contributions of disease to prevalence of disability and to life expectancy with disability at age 55.

	Contribution to prevalence of disability (% points)			Contribution to LED at age 55 (years)
	55-64	65-79	>=80	
			males	
DM	0.08 (0.00-0.19)	0.24 (0.00-0.55)	0.33 (0.00-0.77)	0.06 (0.00-0.14)
Stroke	0.28 (0.17-0.42)	1.14 (0.73-1.58)	2.27 (1.37-3.26)	0.34 (0.23-0.46)
Heart disease	0.16 (0.06-0.30)	0.66 (0.27-1.15)	1.17 (0.46-2.02)	0.18 (0.08-0.31)
PVD	0.28 (0.15-0.42)	1.07 (0.63-1.51)	2.34 (1.33-3.38)	0.33 (0.20-0.46)
Cancer	0.04 (0.00-0.09)	0.19 (0.00-0.42)	0.44 (0.00-1.08)	0.06 (0.00-0.13)
CNSLD	0.45 (0.30-0.66)	1.35 (0.92-1.84)	2.49 (1.49-3.63)	0.40 (0.27-0.53)
Back pain	0.92 (0.62-1.26)	1.25 (0.84-1.72)	1.91 (1.09-2.86)	0.39 (0.27-0.52)
Arthritis	0.55 (0.31-0.81)	1.41 (0.83-1.92)	3.07 (1.59-4.74)	0.45 (0.26-0.62)
Disorder neck/arm	0.04 (0.00-0.23)	0.07 (0.00-0.38)	0.09 (0.00-0.60)	0.02 (0.00-0.11)
Other	0.41 (0.19-0.67)	0.82 (0.38-1.31)	1.82 (1.82-1.82)	0.27 (0.12-0.45)
Back ground	0.73 (0.28-1.20)	0.97 (0.43-1.61)	4.37 (1.36-7.91)	0.51 (0.29-0.77)
Total	3.93 (3.33-4.62)	9.07 (8.08-10.18)	20.37 (16.98-24.24)	3.01 (2.68-3.31)
			females	
DM	0.33 (0.18-0.51)	1.14 (0.62-1.66)	2.45 (1.30-3.78)	0.44 (0.24-0.65)
Stroke	0.21 (0.10-0.35)	0.69 (0.37-1.08)	1.65 (0.89-2.46)	0.28 (0.15-0.42)
Heart disease	0.17 (0.08-0.28)	0.85 (0.41-1.30)	2.04 (0.90-3.18)	0.34 (0.16-0.52)
PVD	0.19 (0.08-0.31)	0.86 (0.41-1.30)	2.12 (1.08-3.27)	0.35 (0.18-0.52)
Cancer	0.05 (0.00-0.19)	0.11 (0.00-0.41)	0.22 (0.00-0.83)	0.04 (0.00-0.16)
CNSLD	0.42 (0.21-0.63)	0.93 (0.47-1.43)	1.52 (0.77-2.44)	0.32 (0.17-0.48)
Back pain	1.30 (0.94-1.74)	2.30 (1.70-2.94)	4.07 (2.92-5.44)	0.86 (0.64-1.08)
Arthritis	1.72 (1.27-2.17)	4.35 (3.36-5.25)	9.72 (7.27-12.17)	1.75 (1.36-2.11)
Disorder neck/arm	0.46 (0.13-0.84)	0.72 (0.21-1.28)	1.25 (0.35-2.33)	0.27 (0.07-0.48)
Other	1.06 (0.66-1.49)	1.78 (1.13-2.58)	3.97 (2.38-5.94)	0.75 (0.46-1.09)
Back ground	0.61 (0.21-1.07)	2.04 (1.21-3.00)	8.96 (5.18-13.35)	1.23 (0.82-1.72)
Total	6.48 (5.66-7.40)	15.65 (14.39-16.99)	38.07 (34.48-41.80)	6.64 (6.20-7.06)

Abbreviations: CNSLD = chronic non-specific lung disease; DM = diabetes mellitus; PVD = peripheral vascular disease (upper extremity excluded).

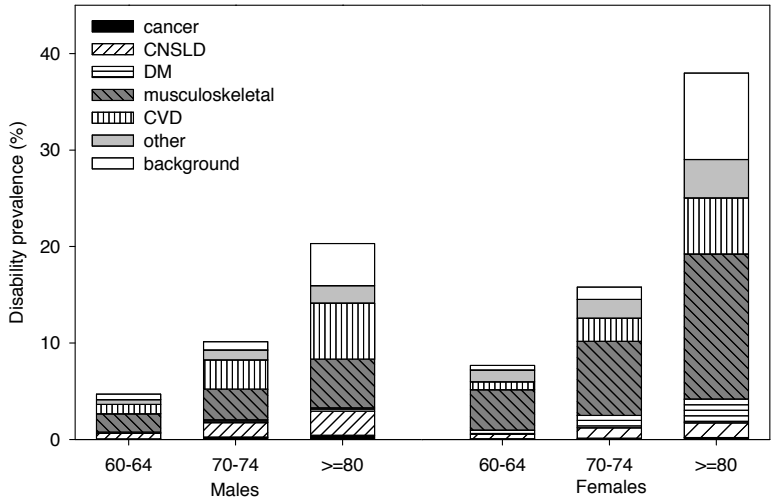


Figure 4.2 Prevalence of disability by cause.

Abbreviations: CNSLD = chronic non-specific lung disease; CVD = cardiovascular disease; DM = diabetes mellitus; PVD = peripheral vascular disease (upper extremity excluded). Contributions of specific diseases to the prevalence of disability were estimated on the basis of diseases prevalence and disabling impact in the study sample from the POLS health and labor survey, the Netherlands, 2001-2007. The disabling impact represents the rate of disability from a specific cause given that the disease is present. Adding specific disability rates for the diseases present and the background rate of disability (by age and gender) gives the total disability rate for a specific exposure group. The contributions of specific diseases presented in the figure add up to the total prevalence of disability.

In males, the most important contributors to the prevalence of disability were musculoskeletal disease and CVD (Table 4.3, Figure 4.2). Musculoskeletal disease accounted for 40% of the prevalence of disability below age 65, which was about twice the contribution of CVD. At older ages the two conditions contributed equally. Most of the disability attributed to CVD was caused by stroke and PVD. In males younger than 65, most disability attributed to musculoskeletal disease was caused by back pain. At older ages, the largest part was caused by arthritis. CNSLD contributed less than musculoskeletal disease and CVD, but was still responsible for 10-15%. In females, musculoskeletal disease was by far the most important contributor and accounted for 40-50% of the disability burden. Disability attributed to musculoskeletal disease was mostly caused by arthritis, but back pain was also an important cause. The second important cause was CVD, contributing more than 15% in females aged 80 and older. Stroke, heart disease and PVD all three contributed importantly to the disability attributed to CVD. DM was also important and contributed 5-8%.

Diseases contributions to years lived with disability were similar to contributions to the prevalence of disability (Table 4.3, Figure 4.3). Of the 3.01 years with disability in males, 0.85 were contributed by CVD and 0.86 by musculoskeletal disease. CNSLD contributed 0.40

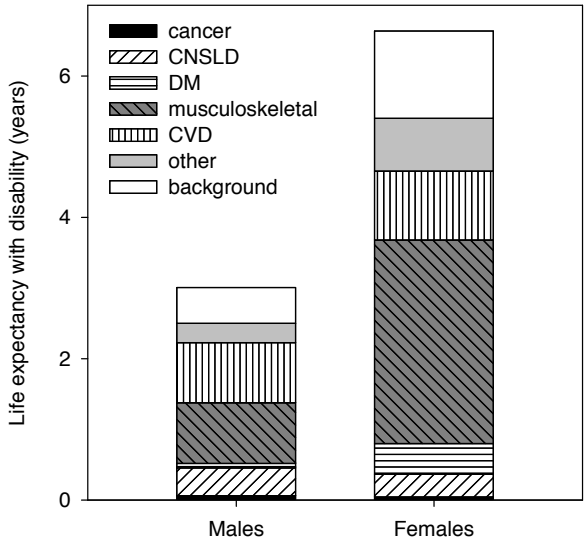


Figure 4.3 Life expectancy with disability at age 55 by cause.
Abbreviations: CNSLD = chronic non-specific lung disease; CVD = cardiovascular disease; DM = diabetes mellitus; PVD = peripheral vascular disease (upper extremity excluded). Contributions of specific diseases to the life expectancy with disability were estimated on the basis of estimated contributions of specific disease to the prevalence of disability in the study sample from the POLS health and labor survey, the Netherlands, 2001-2007, in combination with life table information for the Dutch population 2001-2007, available from the EHEMU database. Methods of decomposition are described elsewhere (5).

years. In females, musculoskeletal diseases were responsible for 2.93 of the 6.64 life years with disability. The contribution of arthritis alone (1.75 years) was about 0.8 years more than the contribution of all CVDs together (0.97 years). DM contributed 0.44 years.

DISCUSSION

This study is among the first to investigate contributions of various chronic diseases to the prevalence of disability and is the first to present years lived with disability by cause. Musculoskeletal disease is the main contributor and CVD, particularly important among males, is a second. CNSLD is the third contributor among males and DM among females. Within the group of musculoskeletal disease, arthritis-disorder neck arm contributes mostly by a high prevalence and back pain by a high disabling impact, although the prevalence of this condition is also high. Within the group of CVD, heart disease contributes mostly by its high prevalence and PVD and stroke by its high disabling impact. The disabling impact of all diseases increases with age.

Evaluation of data and methods/limitations

Selection bias may limit the external validity of the results. Possible selection bias caused by non-response (38%) was minimized by using individual weights to adjust for selection effects by age, gender, marital status, urbanization grade, province, employment, health- and smoking status (23).

Twenty two percent of all subjects aged 55 and older lacked disease information and were excluded from the analysis, which led to a slight underestimation of disability in our study (Figure 4.1). The higher prevalence of disability among non-responders may suggest a slight underestimation of the prevalence and/or disabling impact of some diseases, and hence, that our results should be regarded as conservative.

Our results may not be generalizable to the institutionalized population, which has a higher prevalence of disability and also the relative contribution of specific diseases to the total burden of disability inside institutions may differ from our estimates (24,25). However, in the Netherlands only a minor part of elderly people lives in an institution (i.e. 90% of those aged 80-85 still live at home), hence, bias due to excluding the institutionalized population is probably small and negligible at younger ages (25).

Due to differences in the extent diseases have remained undiagnosed in the population and due to differences in the reference periods used in the questionnaire, some variation may exist in the extent the prevalences derived from the POLS survey reflect true prevalences. Previous literature showed that self-report of most chronic conditions is fairly accurate, except for arthritis, which may be underestimated as well as overestimated (26). If the prevalence of arthritis or another disease in our study was underestimated, subjects with less severe forms of the disease would be most likely to be uncounted and, hence, the disabling impact would be overestimated. This implies that although there may be some bias in the estimates of disease prevalence, this is nullified by a bias in opposite direction in the disabling impact. Hence, the bias in the estimates of contributions of specific diseases to the prevalence of disability and life expectancy with disability is likely to have remained small. Self-report of ADL disability has been found to correlate well with performance based measures and, hence, is expected not to have affected the results substantially (27).

Using a less stringent definition of disability, defined as one or more items answered with "at least minor difficulty" resulted in a lower percentage of disability explained by the diseases included. Our substantive conclusions regarding which diseases contributed most remained unaffected. Due to a lack of power, using a more stringent cut-level could not be evaluated.

The cross-sectional nature our methods and data did not allow identifying cases in which disability was present prior to the onset of the disease. In these cases the disability might be falsely attributed to the disease.

It was decided not to exclude conditions such as 'dizziness with falling' and 'involuntary loss of urine', which have an intermediate position between diseases and disability, but to add them in a separate category. Adding this group mainly reduced the contribution of background, but did not affect the contribution of the other diseases substantially. In both sexes only 'dizziness with falling' and 'involuntary loss of urine' had a high disabling impact and therefore accounted for most of the contribution of other (data available on request).

Mental health conditions are a strong predictor of disease burden and disability onset (12,28). Unfortunately, mental conditions were not included in the checklist of diseases in the POLS survey. To obtain an impression of the extent mental health issues contribute to the burden of disability, in an additional analysis, we included a score of 60 or lower on the RAND Mental Health Inventory (MHI-5) to the diseases, representing (light or severe) mental health problems (29). In this analysis, 8-13% of the prevalence of disability was attributed to mental health conditions, at the expense of contributions of most other disease groups and background (Figure S4.4). Together with findings from previous studies, these results suggest that a substantial part of the burden of disability may be associated with mental health problems (10,12). However, as the MHI-5 is particularly useful for assessing mental health status of the general population and may lack validity to diagnose individual cases, the results need to be interpreted with caution. We decided to provide the results including mental health as supplementary material instead of presenting them in the main analysis.

Comparison with previous studies

In most previous studies musculoskeletal and cardiovascular disease were reported as the most important contributors to disability (4-9,11). Our study confirmed these results also for the oldest old (80+). Additionally, it was shown that the high prevalence of disability at this age is caused by a high prevalence of diseases, but even more by the high extent these diseases lead to disability at older age. This age dependence was not studied in most earlier studies. Furthermore, the current study was the first to identify PVD as an important contributor to the burden of disability, which is associated with much disability mainly by a high disabling impact.

Compared with WHOs Global Burden of Disease study, our method was substantially different (12). Most importantly, WHOs approach uses disability weights to quantify burden of disease that are based on panel valuations and do not refer to physical (or mental) disabilities only, but represent a broader spectrum of health loss. Additionally, in this approach, each case of

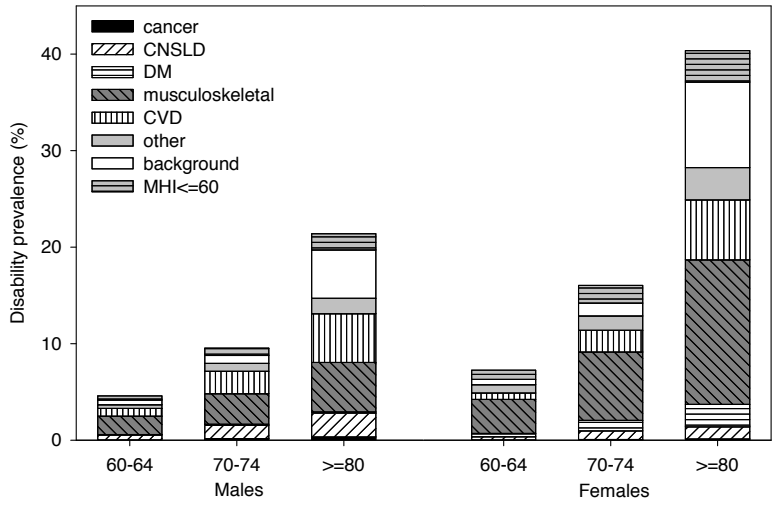


Figure S4.4 Prevalence of disability by cause, including ill mental health.

Abbreviations: CNSLD = chronic non-specific lung disease; CVD = cardiovascular disease; DM = diabetes mellitus; PVD = peripheral vascular disease (upper extremity excluded); MHI-5 = RAND mental health inventory. Contributions of specific diseases to the prevalence of disability were estimated on the basis of diseases prevalence and disabling impact in the study sample from the POLS health and labor survey, the Netherlands, 2001-2007. The disabling impact represents the rate of disability from a specific cause given that the disease is present. Adding specific disability rates for the diseases present and the background rate of disability (by age and gender) gives the total disability rate for a specific exposure group. The contributions of specific diseases presented in the figure add up to the total prevalence of disability. The total prevalence for females aged>=80 is higher than in the original analysis, which may be related with exclusion of subjects who had information missing on items for MHI-5.

disease is assigned a disability weight, irrespective of individual factors such as age and sex which may affect disabling consequences of diseases, and, hence, the estimated burden of disease. In the Global Burden of Disease study, unipolar depressive disorders, alcohol use disorders, hearing loss (adult onset) and Alzheimer and other dementias were associated with most years lost due to disability in high income countries (12). Differences in methodology and diseases included hampers further comparison with our results.

Interpretation of results

The high prevalence of disability at older ages reflects both an increase in the presence of disabling diseases with increasing age and an increase of the disabling impact. The increasing contributions of background suggest that at older ages also frailty or age-related diseases not included in our study may have contributed (30). This could for instance be dementia, of which the prevalence by age shows considerable resemblance with the pattern of disability attributed to background in our study (31). Also conditions that caused persisting disability but are no longer 'present', e.g. falls, might have contributed (32).

Gender differences in the disabling impact of heart disease, DM, cancer, arthritis and disorder neck/arm were found. In addition to differences by gender in self-reporting behaviour, differences in physiological, psychosocial and environmental factors may explain these variations. For heart disease, a higher disabling impact among females may be related to a more pronounced decline in lethality among females than males during the last decades, or to gender differences in the nature of heart disease causing better survival among disabled females than among disabled males (33,34). For DM, a more negative interference of the disease with protective mechanisms in the vascular wall causing thrombogenesis, and a negative influence of female gender on the effect of some cardiovascular risk factors are potential causes of the greater risk for vascular complications in females than in males (35-37). Via cardiovascular complications, these mechanisms may also be responsible for the larger disabling impact among females. Due to differences in hormonal factors, coping styles and anxiety, females are more sensitive to pain than males (38-40). These differences therefore may also explain the differences in the disabling impact of arthritis and disorder neck/arm.

IMPLICATIONS; CONCLUSION

This study clearly shows that diseases contribute to the burden of disability by high disabling impacts, e.g. stroke in males, by moderate disabling impacts but high prevalences, e.g. arthritis, or by both high prevalences and disabling impacts, e.g. back pain in females. Diseases that only have a high disabling impact, e.g. stroke in females, or only a high prevalence, e.g. heart disease in males, do not necessarily contribute much to the burden of disability. The current results showed that the largest contributors are musculoskeletal disorders, particularly arthritis, and CVD. For policy makers this means that the largest reductions in the burden of disability can be obtained by interventions that prevent the primary cause of disability, i.e. that prevent disease onset. Further reductions can be achieved by diminishing disabling impacts. Evidence is accumulating that effective interventions to reduce the extent diseases cause disability, such as home visit and exercise programs, are increasingly available (41,42). As frail elderly are particularly vulnerable to disability, this group should receive priority (43,44). The coming decades, the population of oldest old will increase massively, i.e. in 2050 about a quarter of the population of 50 years and older is expected to be older than 80 (45). The large burden of disability at this age shows that reductions are urgently needed.

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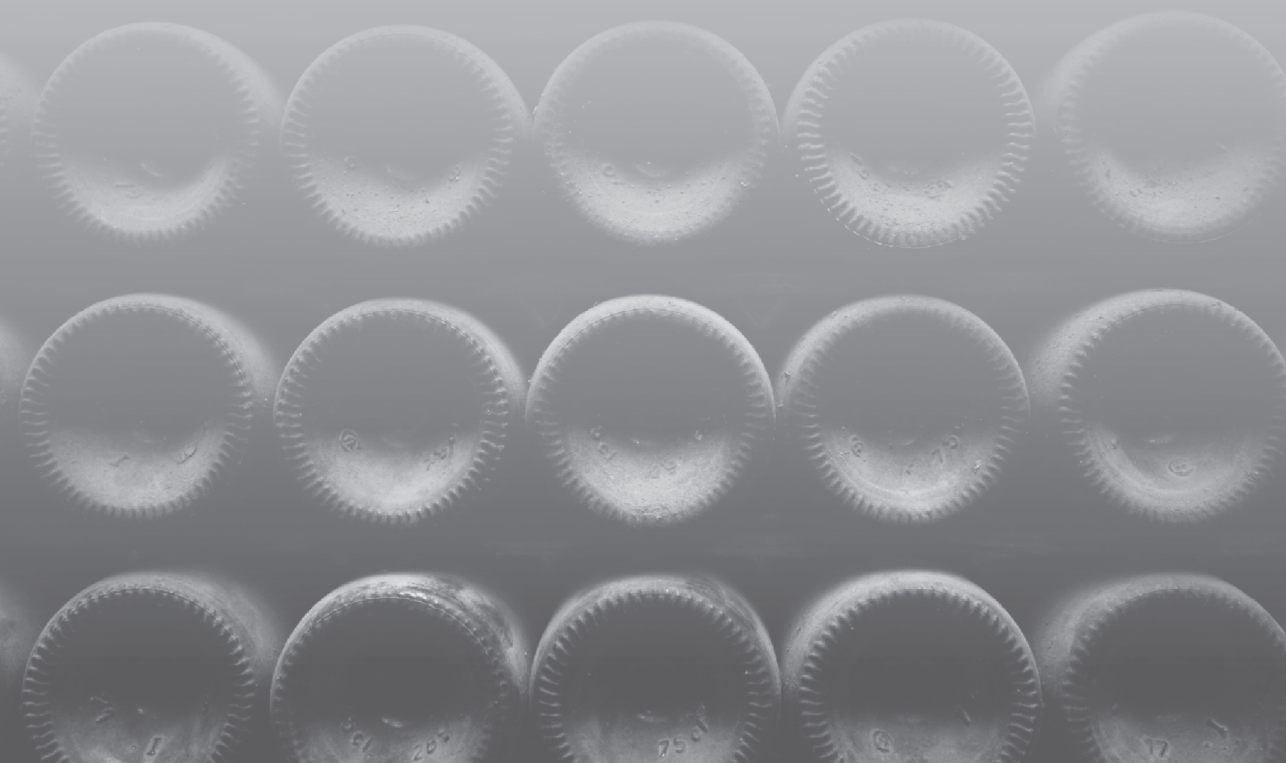
Appendix 4.1 Disease groups and original questions they were compiled from.

	Disease group	Original questions
	Diabetes mellitus (DM)	1. Do you have diabetes?
CVD	Stroke	2. Have you ever had stroke, cerebral bleeding or cerebral infarction?
CVD	Heart disease	4. Have you ever had a myocardial infarction? 5. Have you suffered from any severe myocardial disorder (e.g. cardiac failure or angina pectoris)
CVD	Peripheral vascular disease (PVD)	6. Have you suffered from narrow arteries in legs or abdomen during past twelve months?
	Cancer	7. Have you ever had any form of cancer? 8. Have you suffered from cancer during past twelve months? (please indicate the type)
	Chronic non-specific lung disease (CNSLD)	9. Have you suffered from asthma, chronic bronchitis, emphysema of lung or CNSLD during past twelve months?
Musculoskeletal	Back pain	10. Have you suffered from severe or persistent back disorder during past twelve months? Are you still suffering?
Musculoskeletal	Arthritis	11. Have you suffered from joint degeneration during past twelve months? 12. Have you suffered from chronic joint inflammation during past twelve months?
Musculoskeletal	Disorder neck/arm	13. Have you suffered from any disorder of neck or shoulder during past twelve months? Are you still suffering? 14. Have you suffered from any disorder of elbow, wrist or hand during past twelve months? Are you still suffering?
	Other	15. Have you suffered from migraine or frequent severe headache during past twelve months? 16. Have you suffered from dizziness with falling during past twelve months? 17. Have you suffered from severe or persistent disorder of intestine for more than three months during past twelve months? 18. Have you suffered from involuntary loss of urine (incontinence) during past twelve months? 19. Have you suffered from psoriasis during past twelve months? 20. Have you suffered from chronic eczema during past twelve months?
	RAND Mental Health inventory (MHI-5; only used in supplemental analysis)	During the past four weeks, how much of the time… 21. have you been a nervous person? 22. have you felt so down in the dumps that nothing could cheer you up? 23. have you felt calm and peaceful? 24. have you felt downhearted and blue? 25. were you a happy person?

5

The contribution of chronic disease to educational inequalities in the burden of disability

Klijs B, Nusselder WJ, Looman CW, Mackenbach JP. Contribution of chronic disease to educational inequalities in the burden of disability. Manuscript



Introduction Although socioeconomic inequalities in non-fatal health outcomes such as disabilities are large, explanations including the role of chronic conditions have remained limited. We investigated to what extent specific chronic conditions contribute to educational inequalities in the prevalence of disability. As diseases may contribute to disability inequalities either through prevalence differences or through differences in disabling impact we also assessed to what extent contributions are due to differences in diseases' disabling impact.

Methods Pooled data from seven subsequent years (2001-2007) of the Dutch POLS-survey were used, comprising self-reported information on disability (including mobility, hearing and seeing limitations), selected chronic diseases and the highest completed level of education for 24,833 subjects aged 40-97. A multivariate additive regression model that accounted for co-morbidity was used to calculate disabling impacts of selected diseases by age, sex and level of education. These disabling impacts and information on individual disease presence were used to calculate the contribution of diseases to the prevalence of disability. It was assessed to what extent contributions were explained by differences in the disabling impact.

Results Large absolute differences in the prevalence of disability of 18% (points) in males and 15% in females existed between the highest and lowest level of education. 64% of the inequalities in males and 69% in females were due to the diseases included. For mobility limitations only, these percentages were 90% and 84%. In males, diseases that contributed most to the inequalities were back pain (17 %), disorder neck / arm (13%), other (11%) and peripheral vascular disease (7%). In females, arthritis (18%), other (17%), back pain (13%) and chronic non-specific lung disease (7%) contributed most. In males and females, 49% and 51% of the total inequality in disability prevalence was explained by diseases' disabling impact.

Conclusion Disability inequalities can substantially be reduced by preventing the onset of back pain, disorder neck /arm, other and peripheral vascular disease in males and of arthritis, other, back pain, and chronic non-specific lung disease in females among low educated groups. When disease prevention is not completely feasible, further substantial reductions can be achieved by reducing the disabling impact of these conditions.

INTRODUCTION

Social inequalities in health are large and are one of the main challenges in public health (1-3). In the Netherlands, females with an elementary education only can currently expect to live 6.4 years less than their tertiary educated counterparts and for males the difference is even more than 7 years (1). A first step important for reducing inequalities is to assess which diseases contribute most to the health differences. Studies that aimed to resolve this issue show that inequalities in total mortality are explained by mortality differences for a variety of diseases, but that cardiovascular disease, cancer, HIV, trauma, diabetes mellitus and COPD contribute most to the inequalities (2-4). Other studies show that mortality inequalities have recently not declined, but persisted, mainly due to a relative stagnation of cardiovascular mortality declines among low socioeconomic groups (5).

Although health inequalities are large in terms of mortality, they are often even larger when also non-fatal health outcomes are included. Nonetheless, studies aiming to explain inequalities in non-fatal health outcomes, such as disabilities, have remained limited (6). A number of studies show substantial differences in the prevalence and incidence of various diseases according to socioeconomic position (7-10). Studies investigating to what extent these differences in disease occurrence contribute to socioeconomic inequalities in the burden of disability suggest that knee and hip osteoarthritis and cardiovascular disease contribute most in females and that musculoskeletal conditions contribute most in males (11-12). However, diseases may not only contribute to disability inequalities by differences in their occurrence, but also by differences in the extent they lead to disability once present (disabling impact). Until now, only one study assessed disease contributions to the burden of disability while taking into account these both aspects (13). This study showed that, indeed, substantial differences exist in the prevalence as well as in the disabling impact of chronic conditions and that both contribute to inequalities in the years lived with disability (13). Unfortunately, also this study did not investigate what percentage of the inequalities is due to differences in disease prevalence and what percentage due to differences in disabling impact (13). Such insight would importantly help to target public health interventions as it would show whether interventions should fully focus on disease prevention or whether health inequalities may also be reduced by targeting disease impacts.

The aim of the current study is to assess the contribution of specific diseases to educational inequalities in the prevalence of disability (14). Another aim is to assess to what extent disease contributions are due to differences in the disabling impact. Using an approach that is based on competing risks, we estimate disabling impacts while adjusting for co-morbidity and attribute the prevalence of disability to selected chronic conditions. Attributions by level

of education are performed for OECD disability, including limitations in mobility, hearing and seeing, and for mobility limitations in isolation.

METHODS

Study population

The study population consisted of subjects from seven successive years (2001-2007) of the POLS survey, which is being conducted by Statistics Netherlands. The survey does not include the institutionalized population. To account for selective non-response and to ensure representativeness for the Dutch non-institutionalized population, weights were used that were attached to the data. The POLS data are available via Data Archiving and Networked Services (DANS; http://www.dans.knaw.nl/).

Information on education was collected trough face-to-face interviews and information on disability and the presence of chronic disease through written questionnaires. From 2001-2007, 110,766 subjects were approached and the response was 62%. For our analyses, subjects who were 40 years and older (n=32,233) were selected. 23 % of these subjects could not be included to the study population because they lacked information on education (n=186), disability (n=4,761) or disease (n=6,681). Table 5.1 provides further detailed information of the study population.

Table 5.1 Numbers in study population, and numbers disabled and diseased.

	Males				Females			
	Tertiary	Upper secondary	Lower secondary	Elementary	Tertiary	Upper secondary	Lower secondary	Elementary
Total	3381	4350	2583	1874	2214	3527	4092	2862
Disabled	260	550	449	554	231	496	843	1173
DM	169	273	174	217	38	123	220	327
Stroke	83	153	115	123	32	65	116	150
Heart disease	228	374	273	294	46	118	170	232
PVD	62	114	102	142	27	61	120	159
Cancer	138	180	113	107	146	217	279	227
CNSLD	179	289	191	219	149	248	306	320
Back pain	221	461	284	261	202	368	443	418
Arthritis	355	618	446	397	403	729	1050	1035
Disorder Neck/arm	256	474	332	304	320	663	749	603
Other	581	800	474	382	667	1169	1267	1044

Abbreviations: DM = diabetes mellitus, PVD = peripheral vascular disease, CNSLD = chronic non-specific lung disease.
Numbers diseased do not add up to total because of co-existence of conditions.

Disability

Subjects were asked if they were able to 'follow a conversation in a group of 3 persons', 'have a conversation with one other person', '(is your vision sufficient to) read the small letters in the newspaper', 'recognize someone at 4 meters distance', 'carry a 5 kg object for 10 meters', 'from an upward position, bend forward and take something from the ground', 'walk 400 meters without interruption'. To the vision questions 'using spectacles or contacts if necessary' was added and to the hearing questions 'using hearing aids if necessary'. Persons could answer 'without difficulty', 'with minor difficulty', 'with major difficulty' and 'no, I can't' and someone was considered disabled if he or she opted for one of the latter two answers at least once. In an additional analysis, mobility disability was assessed in isolation excluding hearing and seeing problems.

Definition of disease groups

Information on the presence of a range of diseases was collected in the questionnaire. From the original questions 'cardiovascular disease' (CVD) was compiled, containing 'stroke', 'heart disease' and 'peripheral vascular disease (PVD)', and 'musculoskeletal disease' was compiled, containing 'back pain', 'arthritis' and 'disorder neck/arm'. Furthermore, 'diabetes mellitus (DM)', 'cancer', 'chronic non-specific lung disease (CNSLD)' and 'other' were distinguished. Appendix 5.1 shows the original questions and the diseases that were distinguished. Skin cancer was not included because it is not associated with disability. PVD did not include vascular disease of the upper extremity. If subjects suffered from back pain or disorders of the neck/arm but indicated that they were currently free of complaints, the condition was regarded as no longer present. If a disease was defined on the basis of multiple questions and information on any of the questions was missing while none of the questions indicated the presence of a disease, the disease information was considered missing.

Education was measured according to the highest completed level and was classified as 'elementary', 'lower secondary', 'upper secondary' and 'tertiary'.

Statistical analysis

Disability prevalence by cause was estimated from individual information on the presence or absence of disability, the presence or absence of the selected disease groups, gender, age and level of education. A method based on a multivariate additive regression model was used, which is described in more detail elsewhere (13-15). This method takes into account that persons who do not report a disease may be disabled (this risk is referred to as "background") and that persons can have more than one disease (co-morbidity). Disability in persons without a reported disease is entirely attributed to background. Disability in persons with at least one disease is attributed partly to background and partly to the disease(s). We assume that causes of disability (diseases and background risk) act as independently competing causes.

Assuming independence, the disability hazard of someone having disease A and B (and zero background risk) equals hazard A + hazard B. In a situation of no competing risk (one disease and zero background risk) the hazard can easily be converted to a probability of being disabled (1-exp(- disease hazard)). When more causes are competing, the probability of being disabled from a specific disease is lower than in a situation of no competition. In the footnote of Table 5.3, a calculation example is given of how was dealt with co-morbidity.

To reconstruct the process of one or more diseases leading to disability, taking into account the competing risk principle and using cross-sectional data, additive hazards can be estimated. To estimate cause-specific disability prevalence from cross-sectional data the following assumptions were made. First, the distribution of disability by cause is explained entirely by diseases that are (still) present at the time of the survey and the background risk of disability. Second, this distribution is proportional to the distribution of the risk of becoming disabled by the diseases in the time-period preceding the survey. Thirdly, causes of disability (diseases and background) act as independently competing causes.

The regression model is specified as follows:

$$\hat{y} = 1 - \exp(-\eta:) \qquad Y \sim \text{b}inomial$$

$$\eta = \alpha_{ae} + \sum_{d} \beta_{Ade} X_d$$

$$\beta_{Ade} = \gamma_A . \delta_{de}$$

where $\hat{y}$ is the estimated probability that the person has disability, e is the base of the natural logarithm and η the linear predictor. The latter is defined as the sum of the background hazard by age and education (α_{ae}) and the cause-specific hazards of disability (β_{Ade} , labelled as "disabling impact") for the disease groups (d) that are present in the respondent (given by the dummy variables X_d). Background was handled as a cause that is prevalent for everyone; the hazard of background is age (5-year age groups) and education dependent. As a likelihood ratio test indicated that disease hazards differed significantly by age, the disabling impact β_{Ade} was modelled varying by age. As the full age-interaction term would require n (number of age classes) times m (number of diseases times 4 education groups) different parameters, the rank of the interaction was reduced to one, which means that the age- and education-specific disabling impact of each disease, β_{Ade} , is estimated as the product of an age pattern γ_A (three age categories) which is equal for each disease, and a disease effect δ_{de} , which varies by disease and education, but not by age (Reduced Rank Regression) (16-17). All analyses were done separately for men and women, as the likelihood

ratio test indicated that both the hazards of background and the disease-specific hazards given sex-specific hazards of background differed significantly by sex. The significance of differences in the disabling impact between males and females was assessed by assuming normal distribution of the parameters with the mean of the original ones as the standard error. Using a likelihood ratio test, it was tested whether an RRR improved the model and if the disabling impact varied by age. Because adding parameters indicating variation in the age pattern by level of education did not further improve the fit of the model, the same age pattern γ_A was used for each level of education. Models were fitted using a quasi-Newton method that was programmed for the statistical package R version 2.7.1. (18).

Calculation of the proportion disabled by cause across subgroups

Disability prevalence by cause depends on the prevalence of the disease (X_d) and the disabling impact of the disease (β_{Ade}). Analogous to using the proportional distribution of mortality rates to obtain probabilities of death in the presence of competing causes (so called "crude probabilities"), the attribution of disease d is $(\beta_{Ade}X_{de}/\eta).y$ and of background

is $(\alpha_{ae}/\eta).y$ (13,15). Applying these formulas gives the probability of being disabled caused by background or disease (if present) for every disabled individual. Adding the cause-specific probabilities of all persons in a group with a specific age and level of education, gives the total number of disabled by cause in that group. Adding the number of disabled persons by cause gives the total number disabled by cause. Dividing this number by the total number of persons gives the proportion of disability by cause. Standard methods were used to calculate confidence intervals and p-values for differences by level of education in disease prevalence and disabling impact. Confidence intervals around diseases' contributions to the prevalence of disability could not be provided as no standard methods are available and bootstrapping would require excessive calculation time. Contributions of diseases to the prevalence of disability across education groups were age standardized to the weighted study population for males and females separately. The contribution of a specific disease to the educational inequality in disability prevalence was calculated as the difference in the contribution among elementary and tertiary educated persons.

Using a counterfactual approach, it was calculated to what extent disease contributions to the total difference in disability prevalence are due to differences in diseases' disabling impact. In this approach, it was assumed that the disabling impact among persons with an elementary education was equal to that among those with a tertiary education.

The software for additive regression and for calculation of disability prevalence by cause is available from the authors on request.

RESULTS

Large differences by level of education existed in the prevalence of disability (Figure 5.1). Diseases contributed to these inequalities by differences in their prevalence as well as in their disabling impact.

The prevalence of all diseases except cancer differed significantly across the four levels of education (Table 5.2). The absolute differences in disease prevalence for tertiary and elementary educated males were largest for disorders neck/arm (difference of 9.2% points), back

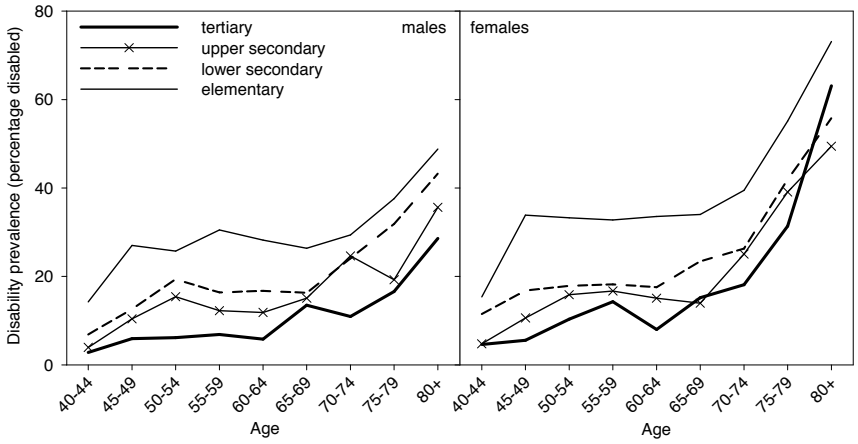


Figure 5.1 Prevalence of disability by level of education.

pain (7.6% difference) and arthritis (7.4% difference). In females, these differences were largest for other (7.5% difference), disorder neck/arm (6.3% difference), arthritis (6.1% difference) and DM (5.8 % difference).

Table 5.2 Disease prevalence with confidence intervals by level of education.

	Tertiary	Upper secondary	Lower secondary	Primary	P-value overall difference
			males		
DM	5.1 (4.4 – 5.9)	6.6 (5.9 – 7.4)	6.5 (5.6 – 7.5)	9.0 (7.9 – 10.3)	0.000
Stroke	2.4 (2.0 – 3.0)	3.7 (3.1 – 4.3)	4.2 (3.5 – 5.1)	4.8 (4.0 – 5.7)	0.000
Heart disease	7.4 (6.5 – 8.4)	6.7 (5.9 – 7.6)	9.6 (8.6 – 10.7)	11.2 (10.0 – 12.5)	0.000
PVD	1.8 (1.4 – 2.3)	2.7 (2.3 – 3.3)	3.7 (3.0 – 4.5)	5.5 (4.7 – 6.5)	0.000
Cancer	4.2 (3.5 – 4.9)	4.4 (3.8 – 5.1)	4.1 (3.4 – 4.8)	3.9 (3.2 – 4.7)	0.780
CNSLD	5.4 (4.7 – 6.3)	6.7 (5.9 – 7.4)	7.5 (6.5 – 8.6)	10.3 (9.1 – 11.7)	0.000
Back pain	6.5 (5.7 – 7.4)	10.2 (9.3 – 11.1)	11.0 (9.8 – 12.3)	14.1 (12.6 – 15.7)	0.000
Arthritis	10.4 (9.4 – 11.5)	14.3 (13.3 – 15.4)	16.8 (15.4 – 18.3)	17.8 (16.2 – 19.4)	0.000
Disorder Neck/arm	7.4 (6.5 – 8.3)	10.9 (10.0 – 11.8)	13.3 (12.0 – 14.7)	16.6 (15.0 – 18.4)	0.000
Other	17.3 (16.0 – 18.6)	18.5 (17.4 – 19.7)	19.3 (17.8 – 20.9)	21.1 (19.3 – 23.0)	0.009
			females		
DM	2.3 (1.7 – 3.2)	4.4 (3.7 – 5.2)	5.4 (4.7 – 6.1)	8.1 (7.3 – 9.0)	0.000
Stroke	1.9 (1.3 – 2.6)	2.3 (1.8 – 2.9)	2.7 (2.3 – 3.3)	3.7 (3.1 – 4.3)	0.001
Heart disease	2.9 (2.2 – 3.8)	4.4 (3.7 – 5.3)	4.2 (3.6 – 4.8)	5.3 (4.6 – 6.0)	0.001
PVD	1.7 (1.2 – 2.5)	2.3 (1.8 – 3.0)	3.1 (2.6 – 3.7)	3.8 (3.2 – 4.4)	0.000
Cancer	7.5 (6.4 – 8.8)	7.0 (6.2 – 8.0)	6.4 (5.7 – 7.2)	6.7 (5.9 – 7.6)	0.428
CNSLD	7.0 (6.0 – 8.2)	7.4 (6.6 – 8.4)	7.4 (6.6 – 8.2)	10.7 (9.6 – 11.9)	0.000
Back pain	9.7 (8.5 – 11.1)	10.9 (9.9 – 12.0)	10.8 (9.9 – 11.8)	13.5 (12.4 – 14.8)	0.000
Arthritis	22.2 (20.4 – 24.1)	24.6 (23.1 – 26.1)	25.3 (24.0 – 26.6)	28.3 (26.7 – 29.8)	0.000
Disorder Neck/arm	14.7 (13.3 – 16.3)	19.5 (18.2 – 20.9)	18.4 (17.2 – 19.6)	21.0 (19.6 – 22.5)	0.000
Other	29.6 (27.7 – 31.5)	32.8 (31.3 – 34.4)	31.9 (30.5 – 33.4)	37.1 (35.3 – 38.9)	0.000

Abbreviations: DM = diabetes mellitus, PVD = peripheral vascular disease, CNSLD = chronic non-specific lung disease.
Estimates are age-standardized to the male and female study populations

In males, the disabling impact was higher for lower levels of education for most diseases and differed significantly by level of education for cancer, back pain and disorder neck/arm (Table 5.3). For back pain, which was the most disabling condition among elementary educated males, there was a gradient by level of education, which was also true for disorder neck/arm. The disabling impact of cancer was particularly high among males with an upper secondary education, which also resulted in a significant difference by education. In females, the disabling impact differed significantly for back pain, arthritis and other. For these three diseases, there was a gradual increment in disabling impact towards lower levels of education.

Large absolute differences in the prevalence of disability existed. That is, the prevalence for the highest and lowest level of education differed by 18% (points) in males and by 15% in females. 64% of the inequality between males and 69% between females with the highest and lowest level of education were due to the diseases included (Table 5.4, Figure 5.2). 31% of the inequality in males and 32% in females were caused by musculoskeletal disease. Cardiovascular disease was responsible for 15% of the inequalities in males and for (only) 4%

in females. In males, diseases that contributed most to the inequalities in males were back pain (18 %), disorder neck / arm (13%), other (11%) and peripheral vascular disease (7%). In females, arthritis (18%), other (17%), back pain (13%) and chronic non-specific lung disease (7%) contributed most.

Table 5.3 Disabling impact with confidence intervals by level of education.

	Tertiary	Upper secondary	Lower secondary	Primary	P-value overall difference
			males		
DM	0.00 (0.00 – 0.00)	0.05 (-0.01 – 0.11)	0.03 (-0.05 – 0.10)	0.07 (-0.03 – 0.18)	0.091
Stroke	0.14 (0.02 – 0.26)	0.22 (0.10 – 0.33)	0.23 (0.08 – 0.39)	0.31 (0.13 – 0.50)	0.503
Heart disease	0.06 (0.00 – 0.12)	0.03 (-0.02 – 0.07)	0.15 (0.06 – 0.23)	0.12 (0.02 – 0.22)	0.086
PVD	0.08 (-0.04 – 0.20)	0.23 (0.08 – 0.38)	0.24 (0.06 – 0.42)	0.38 (0.18 – 0.57)	0.139
Cancer	0.01 (-0.05 – 0.06)	0.13 (0.04 – 0.22)	0.00 (0.00 – 0.00)	0.03 (-0.08 – 0.14)	0.011
CNSLD	0.12 (0.04 – 0.19)	0.07 (0.01 – 0.13)	0.14 (0.04 – 0.24)	0.16 (0.05 – 0.28)	0.473
Back pain	0.05 (-0.01 – 0.11)	0.20 (0.13 – 0.27)	0.24 (0.14 – 0.34)	0.41 (0.25 – 0.56)	0.000
Arthritis	0.03 (-0.01 – 0.08)	0.13 (0.07 – 0.18)	0.04 (-0.02 – 0.11)	0.04 (-0.04 – 0.12)	0.064
Disorder Neck/ arm	0.02 (-0.02 – 0.07)	0.07 (0.02 – 0.13)	0.09 (0.01 – 0.17)	0.23 (0.11 – 0.35)	0.006
Other	0.05 (0.01 – 0.08)	0.06 (0.03 – 0.10)	0.06 (0.01 – 0.11)	0.18 (0.09 – 0.28)	0.085
			females		
DM	0.00 (0.00 – 0.00)	0.08 (-0.03 – 0.19)	0.17 (0.07 – 0.28)	0.14 (0.04 – 0.25)	0.198
Stroke	0.17 (-0.07 – 0.40)	0.30 (0.09 – 0.51)	0.14 (0.00 – 0.28)	0.29 (0.10 – 0.48)	0.688
Heart disease	0.30 (0.06 – 0.54)	0.22 (0.07 – 0.37)	0.18 (0.06 – 0.30)	0.22 (0.07 – 0.36)	0.859
PVD	0.19 (-0.06 – 0.31)	0.13 (0.19 – 0.57)	0.38 (0.19 – 0.57)	0.27 (0.06 – 0.48)	0.501
Cancer	0.02 (-0.04 – 0.08)	0.07 (0.00 – 0.13)	0.07 (0.00 – 0.15)	0.23 (0.10 – 0.36)	0.053
CNSLD	0.09 (0.02 – 0.16)	0.09 (0.02 – 0.16)	0.12 (0.04 – 0.20)	0.22 (0.09 - 0.34)	0.102
Back pain	0.15 (0.07 - 0.24)	0.25 (0.16 - 0.33)	0.36 (0.26 - 0.47)	0.49 (0.34 - 0.63)	0.002
Arthritis	0.07 (0.01 - 0.12)	0.16 (0.11 - 0.21)	0.16 (0.11 - 0.21)	0.25 (0.18 - 0.33)	0.003
Disorder Neck/ arm	0.10 (0.04 - 0.16)	0.11 (0.06 - 0.16)	0.18 (0.11 - 0.24)	0.09 (0.00 - 0.18)	0.444
Other	0.01 (-0.02 - 0.03)	0.03 (0.00 - 0.05)	0.06 (0.02 - 0.09)	0.14 (0.08 - 0.21)	0.001

Abbreviations: DM = diabetes mellitus, PVD = peripheral vascular disease, CNSLD = chronic non-specific lung disease.
Age specific disabling impacts for the age groups 40-54, 55-69 and >=70 can be obtained by multiplying with 0.781, 0.735 and 1.483 for males and with 0.822, 0.843 and 1.335 for females. The disabling impact represents the hazard of disability from a specific cause given that the disease is present. Hazards are used to reconstruct the occurrence of disability during the life courses prior to the survey, assuming that the entire population was initially non-disabled. Adding these specific disability hazards for the diseases present and the background hazard of disability (by age and gender) gives the total disability hazard for a specific exposure group. The proportion of the cause-specific hazard in total hazard is used to divide the probability of disability in this group by cause. For example, for tertiary educated males aged 70-74, the hazard for background is 0.040 (not shown), the hazard for PVD is 0.120 (0.081*1.483), and the hazard for arthritis is 0.050 (0.033*1.483). Adding these hazards yields a total hazard of 0.210 (0.040+0.120+0.050) and a total probability of disability of 0.188 (1-exp(-0.210)). The probability of disability from background in this group is 0.036 (0.040/0.210*0.188), that of PVD is 0.107 (0.120 /0.210 * 0.188), and that of arthritis is 0.045 (0.050/0.210*0.188).

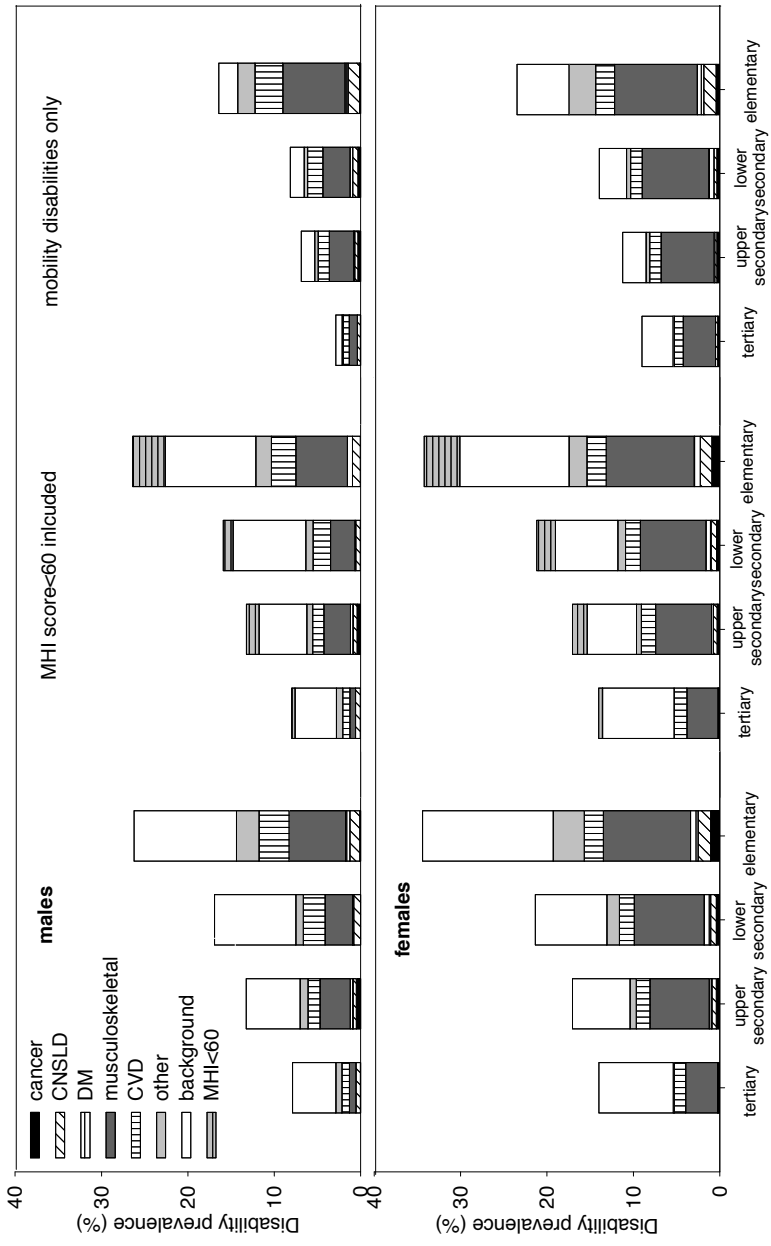


Figure 5.2 Contribution of disease to educational inequalities in the prevalence of disability.
Abbreviations: DM = diabetes mellitus, PVD = peripheral vascular disease, CNSLD = chronic non-specific lung disease, MHI = mental health inventory.
Estimates are age-standardized to the male and female study populations

When hearing and seeing limitations were excluded and mobility disabilities were investigated in isolation, the contribution of each disease remained about equal, but the percentage of disability attributed to background decreased substantially (Figure 5.2). That is, 90% of the mobility inequalities in males and 84% of the inequalities in females were explained by the diseases. Thus, a substantial part of the inequality attributed to 'background' was related with disabilities in the hearing and seeing domain.

Table 5.4 Contribution of diseases to educational differences in prevalence of disability.

	Contribution to prevalence of disability (%points)				Contribution to total inequality in disability prevalence (elementary-tertiary)	
	Tertiary	Upper secondary	Lower secondary	Elementary	Total contribution, by difference in prevalence and disabling impact*	Contribution by disabling impact only‡
				males		
DM	0.00	0.31	0.14	0.48	0.48 (3%)	0.48 (3%)
Stroke	0.35	0.65	0.75	1.11	0.76 (4%)	0.50 (3%)
Heart disease	0.39	0.21	1.12	0.98	0.58 (3%)	0.39 (2%)
PVD	0.14	0.52	0.63	1.40	1.26 (7%)	1.02 (6%)
Cancer	0.03	0.50	0.00	0.10	0.08 (0%)	0.08 (0%)
CNSLD	0.53	0.40	0.80	1.16	0.63 (4%)	0.22 (1%)
Back pain	0.28	1.46	1.77	3.51	3.24 (18%)	2.96 (16%)
Arthritis	0.32	1.46	0.58	0.55	0.23 (1%)	0.06 (0%)
Disorder Neck/arm	0.13	0.60	0.85	2.46	2.33 (13%)	2.17 (12%)
Other	0.69	0.90	0.88	2.62	1.92 (11%)	1.82 (10%)
Background	5.01	6.25	9.40	11.84	6.83 (37%)	-0.78 (-4%)
Total (disability prevalence)	7.88	13.25	16.92	26.22	18.34 (100%)	8.93 (49%)
				females		
DM	0.00	0.29	0.75	0.87	0.87 (4%)	0.87 (4%)
Stroke	0.27	0.53	0.31	0.71	0.44 (2%)	0.23 (1%)
Heart disease	0.76	0.81	0.60	0.82	0.06 (0%)	-0.43 (-2%)
PVD	0.28	0.25	0.83	0.68	0.40 (2%)	0.09 (0%)
Cancer	0.12	0.39	0.39	1.03	0.91 (5%)	0.93 (5%)
CNSLD	0.13	0.53	0.66	1.48	1.35 (7%)	1.29 (6%)
Back pain	1.19	2.02	2.64	3.88	2.69 (13%)	2.31 (11%)
Arthritis	1.33	3.21	3.15	4.93	3.60 (18%)	3.41 (17%)
Disorder Neck/arm	1.18	1.64	2.31	1.26	0.08 (0%)	-0.36 (-2%)
Other	0.13	0.73	1.43	3.59	3.46 (17%)	3.44 (17%)
Background	8.58	6.65	8.29	15.15	6.57 (32%)	-1.39 (-7%)
Total (disability prevalence)	13.97	17.03	21.35	34.41	20.44 (100%)	10.40 (51%)

Abbreviations: DM = diabetes mellitus, PVD = peripheral vascular disease, CNSLD = chronic non-specific lung disease.

Estimates are age-standardized to the male and female study populations

‡Percentages are relative to the total inequality in disability prevalence, i.e. 18.34 for males and 20.44 for females.

In males and females, 49% and 51% of the inequalities in the total prevalence of disability were explained by differences in the disabling impact of diseases (Table 5.4). In males, the difference in the disabling impact of back pain and disorders neck/arm together was responsible for 28% of the total inequality in disability prevalence. In females, 28% of the inequality in the prevalence of disability was due to the difference in the disabling impacts of arthritis and back pain.

DISCUSSION

Summary of most important findings

The aim of this study was to investigate to what extent chronic conditions contribute to educational inequalities in the prevalence of disability and to what extent contributions are explained by differences in diseases' disabling impacts. Large absolute inequalities in the prevalence of disability exist that, to a large extent, are explained by differences in disease prevalence and disabling impact. Diseases that contribute most to the inequalities in males are back pain, disorder neck/arm, other and peripheral vascular disease. Arthritis, other, back pain and chronic non-specific lung disease contribute most in females. About half of the disability inequality is due to differences in diseases' disabling impact.

Evaluation of data and methods

Selection bias may limit the external validity of the results. Possible selection bias caused by non-response (38%) was minimized by using individual weights to adjust for selection effects by age, gender, marital status, urbanization grade, province, employment, health- and smoking status (19).

Item non-response was 23% and possible bias associated was evaluated by comparing self-assessed health and ADL disability (55+) in the source and study population. The prevalence of less than good self-assessed health and ADL disability was slightly higher in the source population, suggesting that the prevalence estimates of disability are conservative in our study. However, the level of underestimation did not differ substantially by level of education, suggesting that selection bias has not affected our substantive conclusions to a great extent.

Our study population did not include persons living in institutions. As the burden of disease and disability is expected to be higher in institutions, our results may not be generalizable to the institutionalized population (20-21). However, in the Netherlands, only a minor part of the population lives in institutions (i.e. 90% of those aged 80-85 still live at home) and there is no consistent evidence that institutionalization is affected by educational level (21-22). Hence, bias due to excluding the institutionalized population has probably remained small.

Studies investigating the validity of self-report of chronic conditions show that this is generally fairly accurate and that level of education has no significant effect on reporting behaviour (23-25). Self-report of disability has been shown to strongly correlate with performance-based measures independent of the level of education (26-28). Therefore, self-report is expected not to have affected our substantive conclusions regarding which disease contributed most to the inequalities.

Using a less stringent definition of disability, defined as one or more items answered with "at least minor difficulty" resulted in a larger part of the inequalities explained by background. Relative contributions of diseases to educational inequalities in the burden of disability, however, remained unchanged. Due to a lack of power, using a more stringent cut-level could not be evaluated.

The cross-sectional nature of our methods and data did not allow identifying cases in which disability was present prior to the onset of the disease. In these cases the disability might be falsely attributed to the disease. However, as the risk for disability prior to the onset of a particular disease is equal to among persons without onset of this disease, such false attribution is expected not to have biased our results.

It was decided not to exclude conditions such as 'dizziness with falling' and 'involuntary loss of urine', which have an intermediate position between diseases and disability, but to add them in a separate category. The main contributors to the educational inequalities in males were 'dizziness with falling', 'migraine or frequent severe headache' and 'involuntary loss of urine'. In females, these were 'involuntary loss of urine' and 'migraine or frequent severe headache' (data available on request).

Mental health problems are a strong predictor of disability and are unequally distributed across the social spectrum, and therefore may contribute to educational inequalities in the burden of disability (29-30). Unfortunately, we lacked a valid indicator of mental conditions in the data used. To obtain an impression of the contribution of mental health issues to disability inequalities, we included a score of 60 or lower on the RAND Mental Health Inventory (MHI-5) as a disease, representing (light or severe) mental health problems (31). In this analysis, 19% of the inequalities in males and 18 % in females were attributed to ill mental health (Figure 5.2). Contributions of the original diseases were all attenuated, except for back pain in males and contributions of background and other were attenuated most strongly. We conclude that ill-mental health may contribute substantially to educational inequalities in disability. However, these results should be interpreted with caution as the MHI-5 was designed to assess mental health status at population level and may lack validity to diagnose individual mental disorders.

Comparison with previous studies

In earlier studies, Nusselder et al. found that back complaints (2.1 years) and arthritis (1.3 years) in males and arthritis (2.2 years) and CNSLD (1.3 years) in females contributed most to educational inequalities in the life expectancy with functional mobility limitations (13). In a study of Sainio et al., diabetes contributed most to inequalities in stair climbing limitations in males and osteoarthritis of the knee and angina pectoris contribute most in females (17). In another study by Koster et al. knee pain contributed most to an excess hazard for mobility limitations among low educated persons (11). Similar to earlier studies, we show large contributions of back pain and arthritis, but, in addition, we show that disorders of the neck and upper extremity contribute much (12-13). Contrasting with findings from Sainio et al., our study suggests that PVD contributes importantly in males, and in agreement with Nusselder et al. we show that CNSLD is important in females (12-13). What has not been investigated in earlier studies is to what extent contributions to inequalities in disability burden are due to differences in the disabling impact of diseases, as opposed to contributions due to differences in disease prevalence. Our study reveals that for most diseases and particularly for diseases that contribute most, a very substantial part of the contribution is due to differences in the disabling impact. Furthermore, our study shows a gradient by level of education in disease contributions for the diseases that contribute most.

Interpretation of findings

The significantly higher disabling impact of back pain and disorder neck/arm in males and of back pain and arthritis in females has been reported before and has been suggested to reflect increased disease activity and disease severity among less affluent groups (32-37). For the increased disease severity, a variety of explanations have been suggested, including a stronger exposure to behavioural and environmental risk factors, more burdensome occupations, worse adaptation to stress, and less access to and utilisation of health services (38-39). A study of Eachus et al. showed that rheumatoid arthritis patients living in less affluent areas had similar disease processes and equal severity of joint degeneration as compared to patients in more affluent areas, but nonetheless had more disability (33). It was suggested that the excess disability in less affluent areas could be explained by a lower confidence in ones ability to influence the disease, which may lead to worse adaptive strategies (33). Similar mechanisms might have played a role in our study. An unexpected study result was the high disabling impact of cancer in males with an upper secondary education, which resulted in a significant difference of the disabling impact by level of education. We are not aware of similar results in other studies, but we suspect that "cancer" in this group may contain a high proportion of types of cancer that are particularly disabling. Furthermore, differences in cancer incidence and mortality across socioeconomic groups may have contributed to the typical pattern of disabling impacts (40-41). A large part of the disability burden could be attributed to diseases in spite of the lack of longitudinal information but the disability in-

equalities were not completely explained by the diseases included. Factors that may further explain the disability inequality are health behaviours (9, 11-12, 42-43); biomedical factors (11); psychosocial factors (43); work related factors (12,42); and material problems (42).

Implications; conclusion

Our study shows that back pain, disorder neck/arm, other and PVD contribute most to educational inequalities in the burden of disability in males, that arthritis, other, back pain and CNSLD contribute most in females, and that a substantial part of the disability inequality is due to differences in the disabling impact. For health policy aiming to reduce disability inequalities, this implies that a multi focal approach would probably most effective. First, actions are needed to prevent or delay the onset of diseases with a high prevalence among low socioeconomic groups, such as back pain, disorder neck/arm, arthritis etc. Second, for the part that prevention is not completely feasible, efforts are required to reduce the disabling impact of chronic conditions that contribute much to the inequalities. In the hypothetical situation that reducing disease occurrence among low socioeconomic groups would be completely unsuccessful, reducing disabling impacts could still lead to a reduction of the disability inequality of around 50%. Evidence for interventions that effectively may reduce diseases' disabling impacts is becoming increasingly available (44-47). Among others, inpatient rehabilitation for geriatric patients has been shown to improve functional outcomes and community based interventions and home visitation programs can lead to disability reductions (44-47). To be effective among low socioeconomic groups, such interventions would preferably be multidimensional, include multiple follow-up visits and be tailored to meet individual needs and preferences (45-47).

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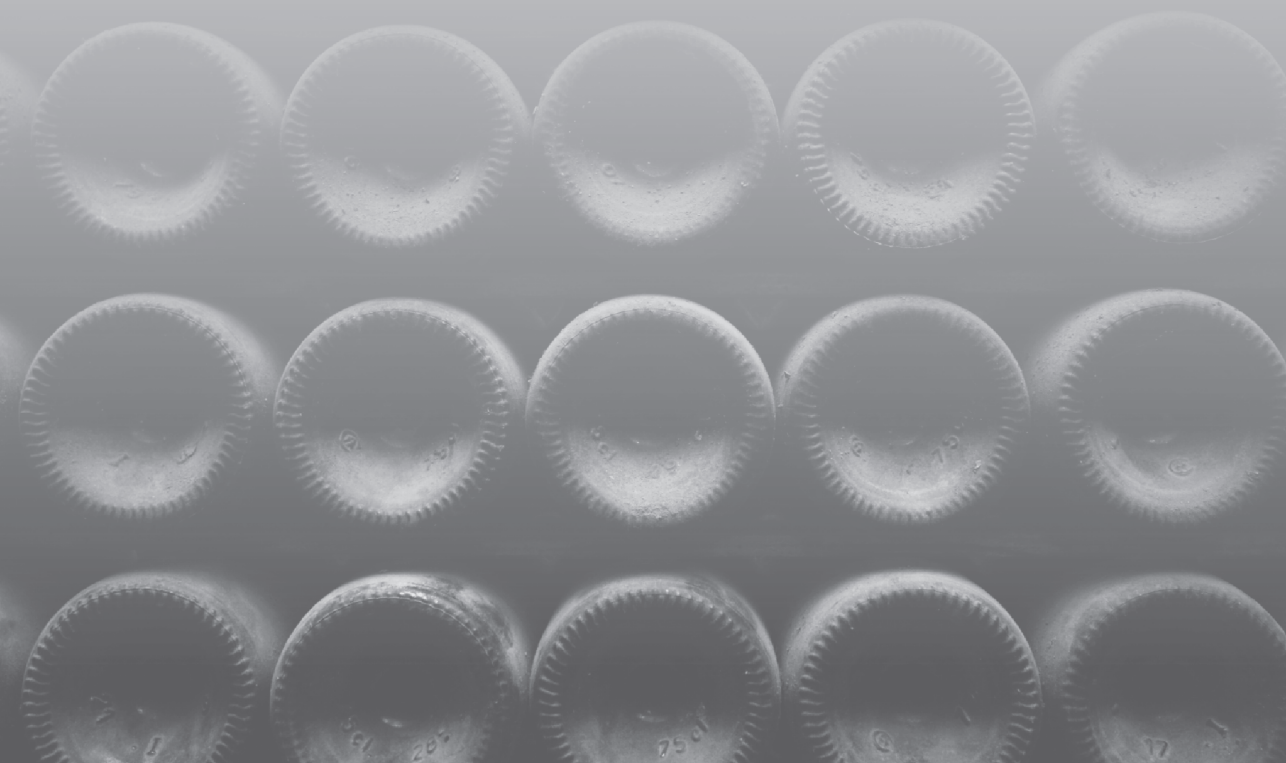
Appendix 5.1 Disease groups and original questions they were compiled from.

	Disease group	Original questions
	Diabetes mellitus (DM)	1. Do you have diabetes?
CVD	Stroke	2. Have you ever had stroke, cerebral bleeding or cerebral infarction?
CVD	Heart disease	4. Have you ever had a myocardial infarction? 5. Have you suffered from any severe myocardial disorder (e.g. cardiac failure or angina pectoris)
CVD	Peripheral vascular disease (PVD)	6. Have you suffered from narrow arteries in legs or abdomen during past twelve months?
	Cancer	7. Have you ever had any form of cancer? 8. Have you suffered from cancer during past twelve months? (please indicate the type)
	Chronic non-specific lung disease (CNSLD)	9. Have you suffered from asthma, chronic bronchitis, emphysema of lung or CNSLD during past twelve months?
Musculoskeletal	Back pain	10. Have you suffered from severe or persistent back disorder during past twelve months? Are you still suffering?
Musculoskeletal	Arthritis	11. Have you suffered from joint degeneration during past twelve months? 12. Have you suffered from chronic joint inflammation during past twelve months?
Musculoskeletal	Disorder neck/arm	13. Have you suffered from any disorder of neck or shoulder during past twelve months? Are you still suffering? 14. Have you suffered from any disorder of elbow, wrist or hand during past twelve months? Are you still suffering?
	Other	15. Have you suffered from migraine or frequent severe headache during past twelve months? 16. Have you suffered from dizziness with falling during past twelve months? 17. Have you suffered from severe or persistent disorder of intestine for more than three months during past twelve months? 18. Have you suffered from involuntary loss of urine (incontinence) during past twelve months? 19. Have you suffered from psoriasis during past twelve months? 20. Have you suffered from chronic eczema during past twelve months?
	RAND Mental Health inventory (MHI-5; only used in supplemental analysis)	During the past four weeks, how much of the time… 21. have you been a nervous person? 22. have you felt so down in the dumps that nothing could cheer you up? 23. have you felt calm and peaceful? 24. have you felt downhearted and blue? 25. were you a happy person?

6

Obesity, smoking, alcohol consumption and years lived with disability

Klijs B, Mackenbach JP, Kunst AE. Obesity, smoking, alcohol consumption and years lived with disability: a Sullivan life table approach. BMC Public Health. 2011, 24;11:378.



Introduction To avoid strong declines in the quality of life due to population ageing, and to ensure sustainability of the health care system, reductions in the burden of disability among elderly populations are urgently needed. Life style interventions may help to reduce the years lived with one or more disabilities, but it is not fully understood which life style factor has the largest potential for such reductions. Therefore, the primary aim of this paper is to compare the effect of BMI, smoking and alcohol consumption on life expectancy with disability, using the Sullivan life table method. A secondary aim is to assess potential improvement of the Sullivan method by using information on the association of disability with time to death.

Methods Data from the Dutch Permanent Survey of the Living Situation (POLS) 1997-1999 with mortality follow-up until 2006 (n=6 446) were used. Using estimated relative mortality risks by risk factor exposure, separate life tables were constructed for groups defined in terms of BMI, smoking status and alcohol consumption. Logistic regression models were fitted to predict the prevalence of ADL and mobility disabilities in relationship to age and risk factor exposure. Using the Sullivan method, predicted age-specific prevalence rates were included in the life table to calculate years lived with disability at age 55. In further analysis we assessed whether adding information on time to death in both the regression models and the life table estimates would lead to substantive changes in the results.

Results Life expectancy at age 55 differed by 1.4 years among groups defined in terms of BMI, 4.0 years by smoking status, and 3.0 years by alcohol consumption. Years lived with disability differed by 2.8 years according to BMI, 0.2 years by smoking and 1.6 by alcohol consumption. Obese persons could expect to live more years with disability (5.9 years) than smokers (3.8 years) and drinkers (3.1 years). Employing information on time to death led to lower estimates of years lived with disability, and to smaller differences in these years according to BMI (2.1 years), alcohol (1.2 years), and smoking (0.1 years).

Conclusion Compared with smoking and drinking alcohol, obesity is most strongly associated with an increased risk of spending many years of life with disability. Although employing information on the relation of disability with time to death improves the precision of Sullivan life table estimates, the relative importance of risk factors remained unchanged.

INTRODUCTION

Due to ageing of the populations, the burden of disability is likely to further increase in the next decades [1]. Persons with one or more disabilities often experience declines in the quality of life and have an increased need for health care services [2-5]. As elderly people often spend at least part of their life while having one or more disabilities, declines in the quality of life are commonly associated with old age, as well as substantial health care expenditures at the end of life [6-9]. To avoid strong declines in the quality of life and to ensure sustainability of the health care system, reductions in the burden of disability are urgently needed.

Such reductions may be achieved by interventions that help persons adopting more healthy lifestyles, as is suggested by studies showing associations between lifestyle factors and years lived with disability [10-6]. Although the results of these studies are promising, there are some caveats. That is, almost all of these studies analyzed one single risk factor in isolation and did not compare effects of risk factors [10. 12-13, 15-16]. Moreover, estimates of the effects of smoking were inconsistent and, to date, estimates for alcohol consumption are lacking [12-14]. Consequently, it is still not fully understood which factor has the largest potential for achieving reductions in years lived with disability. Therefore, the primary aim of the study was to compare the effect of BMI, smoking and alcohol consumption on the life expectancy with disability.

Two standard methods for calculating the life expectancy lived with disability are the Sullivan life table and the multistate life table. The latter method is considered as most appropriate for modelling risk factor and population health dynamics [17-20]. However, the multistate life table method requires data on disability incidence, which are often unavailable or too imprecise due to small numbers of cases [19]. For these situations, one has to recur to the Sullivan life table method. Commonly, the input to the Sullivan table consists of a series of age-specific disability prevalence rates, multiplied with a factor to quantify the effect of exposure to a risk factor. Recently, however, it was demonstrated that the prevalence of ADL disability is not simply a function of age (i.e. time since birth) but that it is even more strongly associated with approaching death (i.e. time to death) [21-22]. The occurrence of disability sharply increases in the about 10 last years of life, and especially in the 5 last years. Using information on disability occurrence in relationship to end of life could result in more realistic estimates of the occurrence of disability across the life course. Consequently, Sullivan life tables could gain in precision by employing this additional information [21-22]. A secondary aim of the study was to assess whether employing information on time to death in the Sullivan life table may lead to substantively different estimates of the relative importance of these risk factors.

METHODS

Study population

The study population consisted of respondents to three successive years (1997-1999) of the POLS health interview survey, which was conducted by Statistics Netherlands. The survey was representative for the Dutch population excluding the institutionalized population. Information was collected through face to face interviews. From 1997-1999, 52 198 subjects were approached and the response was 58%. For our analyses we selected elderly subjects who were 55 years and older (n=6 446) at the time of the survey. Mortality among these subjects was registered until 2006 through linkage with the Dutch causes of death registry. The mean BMI in the study population was 25.0 kg/ m^2 and the mean number of alcohol consumptions per week was 6.0. Further characteristics are presented in Table 6.1. The POLS surveys and mortality data are administered by Statistics Netherlands and Data Archiving and Networked Services (DANS; www.dans.knaw.nl/).

Table 6.1 Characteristics of the study population.

	Number of respondents (%)	Mean age	Percentage males	Percentage married	Number disabled	Number of deaths
Normal weight	2814 (43.7)	67.4	46.9	69.9	293	762
Overweight	2699 (41.9)	66.7	53.5	72.8	297	673
Obese	704 (10.9)	66.2	37.2	66.5	147	179
Missing/other	229 (3.6)	72.3	23.3	48.5	68	113
Never smoker	2041 (31.7)	69.1	16.7	61.3	318	510
Former smoker	2686 (41.7)	67.0	64.4	77.1	289	714
Current smoker	1524 (23.6)	64.9	59.8	68.8	181	445
Missing	195 (3.0)	67.0	50.0	72.8	17	58
1-14 alc cons/wk	3937 (61.1)	66.5	52.2	74.2	330	917
>14 alc cons/wk	647 (10.0)	64.5	78.2	76.7	47	160
Non drinker	1859 (28.9)	69.5	27.6	58.7	428	650
Missing	3 (0.0)	66.0	33.3	100.0	0	0

Disability

Respondents were asked if they were able to 'walk up and down the stairs', 'walk outside', 'enter/leave the house', 'sit down/get up from a chair', 'move around on the same floor', 'get in/out of bed', 'eat/drink', 'get dressed/undressed', 'wash face/hands' and 'wash completely'. For each item, respondents could answer with 'without difficulty', 'with minor difficulty', 'with major difficulty' and 'only with help'. We considered respondents disabled if they reported "with major difficulty" or "only with help" for at least one item.

Risk factors

BMI was calculated as body weight/body length^2 and was classified as 'normal weight' 20-24.9 kg/m^2; 'overweight' 25-29.9 kg/m^2; and 'obesity' ≥30 kg/m^2. On the basis of the questions 'do you smoke?' and 'did you smoke in the past?' subjects were classified as 'never smoker', 'former smoker' or 'current smoker'. A question 'do you ever drink alcohol?' and two questions asking for the number of alcoholic consumptions in the week and at weekends were used to construct the categories 'no drinker', '1-14 alcoholic consumptions per week' and 'more than 14 alcoholic consumptions per week'. Together with age and sex, we controlled for marital status ('married', 'divorced', 'widower' and 'never married') in all analyses. Further analyses revealed that control for educational level or household income level would not substantially change the results.

Mortality analyses

Poisson regression methods were used to calculate the relative risk (RR) for mortality by BMI, smoking and alcohol. Univariate models were fitted that included dummy variables representing the different categories of BMI, smoking and alcohol, respectively. Normal weight, never smoker and 1-14 alcohol consumptions/week were chosen as reference categories. Missing values, and for BMI missing values and BMI<20 kg/m2, were treated as a separate group and were modelled in the regression models using dummy variables. Each model was adjusted for age (continuous), sex, and marital status. The RRs for mortality were used to calculate conversion factors that express the mortality level of exposed individuals in relationship to the average Dutch mortality levels. The conversion factors were applied to age-specific mortality rates for the Netherlands in the period 2000-2004 to construct separate life tables for each category of BMI, smoking and alcohol consumption.

Disability analysis

Univariate logistic regression models were fitted in which disability (a dichotomous variable) was predicted as a function of risk factor exposure (dummies) and age (continuous). Sex and marital status were included to the models as control variables. Quadratic terms on age were significant and were therefore added to the prediction models. Interactions between age and risk factor exposure were not significant and were not included. The fitted models were used to predict the age specific prevalence of disability for each risk factor exposure category. In these predictions, the values of the control variables (sex and marital status) were set at the study population averages.

In further analysis, the age schedules of disability were not predicted on the basis of associations with age only, but also on the basis of associations with both age and time to death. For this analysis, regression models were fitted that were similar to the original models but also contained a variable measuring the time to death for each person that died during follow-up

until 2006. Time to death was defined as the difference in time between the moment of the survey and the moment of death. Further details on this method, including ways to take into account survivors, are given elsewhere [21-22].

Life table analysis

Sullivan life tables were constructed to calculate the years lived with disability (i.e. life expectancy with disability at age 55) for each risk factor exposure category [20]. For constructing these life tables, we utilized the estimated age schedules of mortality and disability, stratified by risk factor exposure category (see above).

In most analyses, the common version of the Sullivan life table method was applied. However, in the additional analyses aimed to take into account relationships between disability and time to death, a refined approach had to be taken. In this approach, annual age specific disability prevalences were estimated conditional on remaining years of life, and remaining years of life adjusted estimates of the age specific disability prevalence were used as input to the life table. As a first step, we stratified the life table population into subpopulations according to their age at death (or length of life). The number of people in subpopulation with length of life *x* was equal to the number who would die at age *x* according to the life table. Next, for each population with the same age at death, we estimated the age-specific schedule of disability, using the estimates of the logistic regression models described above. Finally, we estimated the age-specific prevalence rates of disability for the total life table population as the population-weighted sum of the age-specific prevalence rates in all subpopulations.

The total life expectancy and the years lived with disability were calculated for the aggregate life table population. The years lived without disability (i.e. disability free life expectancy) were calculated as the difference between the total life expectancy and the life expectancy with disability. Confidence intervals (CI) around the estimated life expectancy and years lived with and without disability were estimated using probabilistic sensitivity analyses [23-25]. That is, thousand times, regression coefficients were drawn randomly from each regression model, assuming multivariate normal distribution. For each draw, a life table was set up and total life expectancy and years lived with and without disability were calculated. The 25th and 975th of the ordered values indicated the boundaries of the CIs.

Regression analyses were performed using Stata 10.0 and life tables were constructed in Microsoft Excel 2002.

RESULTS

Of the three factors compared, smoking had the largest effect on mortality (Table 6.2; RR current smoker: 1.62). The effects of alcohol consumption and BMI were substantially smaller (RR >14 cons/wk: 1.19; RR obese: 1.15, not significant).

BMI had a substantial effect on the odds of disability (Table 6.2; OR obese: 2.73). The effect of smoking was smaller but still significant (OR current smoker: 1.58), while the effect of drinking alcohol was not significant. In models that include time to death, the estimated odds ratios were slightly smaller for smoking and alcohol, but not for BMI.

Table 6.2 Relative risks for mortality and odds ratios for disability according to risk groups.

	RR mortality with 95% CI	OR disability in models without time to death with 95% CI	OR disability in models with time to death with 95% CI
Normal weight	1.00	1.00	1.00
Overweight	0.97 (0.87-1.07)	1.24 (1.03-1.48)	1.26 (1.05-1.52)
Obese	1.15 (0.98-1.36)	2.73 (2.16-3.46)	2.76 (2.17-3.51)
Never smoker	1.00	1.00	1.00
Former smoker	1.18 (1.03-1.35)	1.25 (1.02-1.53)	1.19 (0.96-1.46)
Current smoker	1.62 (1.40-1.87)	1.58 (1.25-2.82)	1.36 (1.07-1.72)
1-14 alc cons/wk	1.00	1.00	1.00
>14 alc cons/wk	1.19 (1.00-1.41)	1.17 (0.84-1.62)	1.11 (0.80-1.56)
Non drinker	1.43 (1.29-1.59)	2.38 (2.01-2.82)	2.17 (1.83-2.58)

Separate models were fitted for BMI, smoking and alcohol consumption, but control for age, sex and marital status.

Figure 6.1 estimates how the prevalence of disability increases during the last years of life. These estimates were derived from models that include both age and time to death. For persons who died at age 75, the prevalence of disability increased from below 0.05 to about 0.25 or 0.35 among drinkers and smokers, and to 0.50 among obese persons. Persons who died at an older age (i.e. age 85) had a different age pattern of disability. Their prevalence was about 60% lower at age 75, but towards the end of life, their chances of disability were substantially higher compared with younger decedents' chances at the end of life.

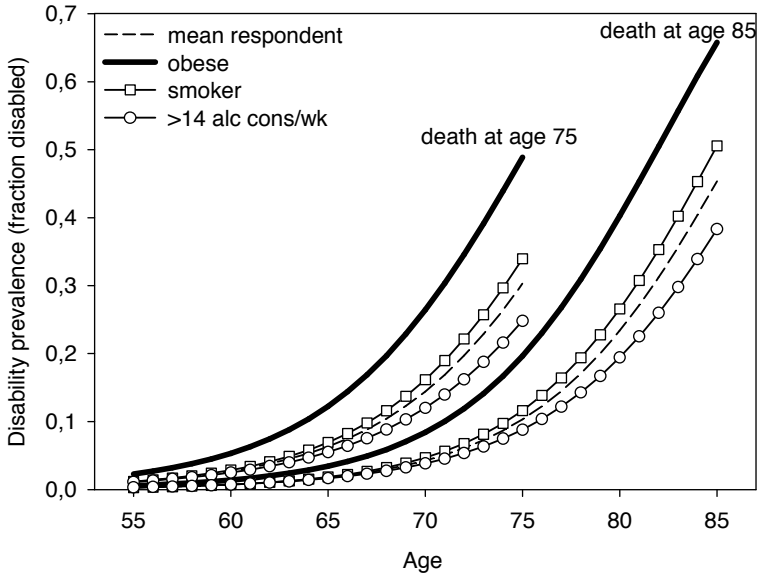


Figure 6.1 Estimated prevalence of disability by age of death and according to risk factor.
Estimates were based on univariate models, controlled for sex and marital status.

Table 6.3 shows the results of life table calculations. The difference in total life expectancy at age 55 was largest according to smoking (4.0 years between). The differences by alcohol consumption (3.0 years) and BMI (1.4 years) were smaller but were still substantial.

The difference between groups in years lived with disability was largest according to BMI (2.8 years between). The difference according to alcohol consumption (1.6 years) was smaller but still substantial and the difference according to smoking was only small (0.2 years). Obese persons spent a much longer period in disability (5.9 years), as compared to smokers and drinkers (3.8 and 3.1 years).
Estimates of the years lived with disability and differences according to risk factor were mostly smaller when calculated using regression models and life tables including time to death. According to this method the difference according to BMI was 2.1 years and according to smoking or alcohol consumption 0.1 and 1.2 years. Obese persons lived 4.3 years with disability, smokers 2.7 years and drinkers 2.3 years. The results regarding which factor was most important remained unchanged.

Table 6.3 Total life expectancy at age 55 and years lived with and without disability.

		Calculations without time to death		Calculations with time to death	
	Total life expectancy	Years without disability	Years with disability	Years without disability	Years with disability
Normal weight	26.0 (25.6 - 26.5)	22.9 (22.4 - 23.3)	3.2 (2.8 - 3.5)	23.8 (23.3 - 24.3)	2.3 (2.0 - 2.6)
Overweight	26.3 (25.8 - 26.8)	22.5 (22.0 - 23.0)	3.8 (3.4 - 4.3)	23.6 (23.0 - 24.1)	2.7 (2.4 - 3.1)
Obese	24.9 (23.8 - 26.1)	18.9 (17.9 - 19.9)	5.9 (5.1 - 6.9)	20.5 (19.5 - 21.6)	4.3 (3.7 - 5.0)
Variation by BMI	1.4 (0.1 - 2.9)	4.0 (2.8 - 5.2)	2.8 (1.9 - 3.8)	3.3 (1.9 - 4.4)	2.1 (1.4 - 2.7)
Never smoker	27.6 (26.9 - 28.5)	23.8 (23.1 - 24.5)	3.8 (3.4 - 4.4)	24.9 (24.2 - 25.7)	2.7 (2.3 - 3.1)
Former smoker	26.2 (25.8 - 26.8)	22.2 (21.7 - 22.7)	4.0 (3.6 - 4.5)	23.4 (22.8 - 23.9)	2.8 (2.5 - 3.2)
Current smoker	23.6 (23.1 - 24.3)	19.8 (19.2 - 20.4)	3.8 (3.3 - 4.4)	20.9 (20.3 - 21.5)	2.7 (2.3 - 3.2)
Variation by smoking	4.0 (2.8 - 5.2)	3.9 (2.9 - 4.9)	0.2 (-0.5 - 0.8)	4.0 (2.9 - 5.1)	0.1 (-0.4 - 0.6)
1-14 alc cons/wk	27.0 (26.7 - 27.4)	23.9 (23.5 - 24.3)	3.1 (2.8 - 3.5)	24.8 (24.3 - 25.2)	2.2 (1.9 - 2.6)
>14 alc cons/wk	25.6 (24.3 - 26.9)	22.5 (21.2 - 23.6)	3.1 (2.4 - 4.2)	23.3 (22.1 - 24.5)	2.3 (1.7 - 2.9)
Non drinker	24.1 (23.5 - 24.6)	19.3 (18.7 - 19.9)	4.8 (4.3 - 5.2)	20.6 (20.0 - 21.2)	3.4 (3.1 - 3.8)
Variation by alcohol	3.0 (2.1 - 3.9)	4.6 (3.8 - 5.4)	1.6 (1.0 - 2.2)	4.2 (3.3 - 5.0)	1.2 (0.8 - 1.6)

DISCUSSION

Summary of results

The current paper is among the first to compare the effect of different life style factors on years lived with disability. Compared with smoking and drinking alcohol, obesity is more strongly associated with an increased risk of spending many years in disability during life. Using information on time to death in the Sullivan life table does not lead to substantively different estimates of the relative importance of the risk factors.

Evaluation of data and methods

Among all subjects approached in the baseline survey, the non-response was 42%. We could not directly evaluate the effect of selective response on our estimates of years lived with disability, but the total mortality in our study sample (3.15% per year) was comparable to the total mortality in the Dutch population (1997-2006) aged 55 and older (3.21% per year) [26]. Although non-response is likely to lead to biased estimates of the prevalence of smoking and alcohol intake, it may not substantially affect associations between these risk factors and health outcomes [27]. None the less, we cannot exclude that selective non-response may have biased our estimates of effects of risk factors on years lived with disability.

The use of self reported measures of disability may have caused some reporting bias, particularly if risk factor exposure was related to reporting behaviour, independently from status of disability. However, in previous studies it was shown that self report of ADL disabilities

correlates strongly with performance based measurement of disability [28], suggesting that it is unlikely that reporting bias could have substantially biased our results.

Self-reported BMI tends to be underreported, particularly by those who have a high BMI [29-30]. Therefore, the risk of disability among persons who had a high BMI may have been overestimated. However, the potential bias has been shown to be acceptable for correlation analyses like in our study [30]. Underreporting in self-reported alcohol consumption may affect prevalence rates, but does not appear to have substantially bias effect on the association between heavy drinking and harmful consequences [31].

The institutionalized population, an old population with a high disability prevalence, was not included in the baseline survey [32-33]. It cannot be excluded that this exclusion may have led to some bias in our estimates of risk factors in relation to years lived with disability. However, in the Netherlands, only a minor part of elderly people live in an institution, e.g. 90% of those aged 80-85 still live at home. Hence, the bias because of excluding the institutionalized population will probably be small [32-33].

Our choice of disability cut-off level was arbitrary. Using a more stringent cut-off level of having "with major difficulty" or "only with help" for at least two items resulted in (non-significantly) higher odds ratios for disability for BMI (OR obesity = 2.96) and alcohol consumption (OR >14 alc cons/wk = 1.52), but in a lower odds ratio for smoking (OR current smoker = 1.48). Years lived with disability differed by 2.0 years according to BMI, 0.2 years by smoking and 1.4 by alcohol consumption. Including time to death to the calculation yielded similar results. It can be concluded that the cut-off level to define disability has had no major influence on our substantive conclusions.

The association of BMI, smoking and alcohol with disability is likely to be mediated by the occurrence of specific diseases or other risk factors such as physical activity. If our aim had been to gain insight into causal chains that relate risk factor exposure with disability, it would have been useful to include more covariates. However, as our analysis had a descriptive purpose, and adjusting for co-morbidities or physical activities would take out part of the effect of lifestyle on disability, we used simple and transparent univariate regression models, adjusted for age, sex and marital status only, to estimate the years lived with and without disability.

Comparison with previous studies

A few other studies compared lifestyle factors with respect to their effect on years lived with disability. Most studies used other outcome measures [14, 34-36]. Comparable with our results, these studies found that, compared to heavy drinking or regular smoking, obesity had a much greater effect on the number of years that people could expect to live with

long-standing illness, with reduced quality of life, or with less than good self-assessed health [34-36]. The only study that compared effects of different lifestyle factors on years lived with disability confirmed our key finding that obesity is more important than smoking [14].

The obesity paradox

We found that smoking is associated with shorter life, whereas obesity is associated with spending more life years with disability. This difference is likely to be related to the fact that a high BMI is more strongly associated with non-lethal disabling diseases, such as osteoarthritis and chronic back pain, whereas smoking is more strongly associated with a series of fatal diseases with a relatively short period of disablement, such as lung cancer and other types of cancer [37-39].

Compared with other risk groups, obese persons on average spend a larger part of their last years of life with disability (Figure 6.1). This observation represents another side of the 'obesity paradox', which refers to the fact that increased BMI is an independent risk factor for heart failure, but that among patients with established heart failure, those who are overweight or obese are at decreased risk for death [40-44]. This suggests that obesity is a 'stretcher of disease and disability', which results in a high prevalence of disability prior to death among obese persons.

Time to death in the Sullivan life table

The occurrence of ADL disability is not only associated with age (time since birth), but even more strongly with time to death [21-22]. A substantial part of disability occurs in relation with end-of-life processes [21-22]. As a result, a longer life is likely to be associated with a shift of the burden of disability towards older ages [21-22]. Conventional Sullivan life table methods do not account for possible shifts of disability towards older ages, but use one age schedule of disability, irrespective of the length of life (i.e. age of death) of individual people. Using an innovative approach, we accounted for the association of disability with length of life by defining schedules of disability not only as a function of age, but also as a function of age of death (Figure 6.1). The new estimates of the number of years lived with disability differed substantially from the original estimates. As expected, the expected years lived with disability were lower according to the new estimates. However, the relative importance of risk factors remained unchanged.

Therefore, this new methodology may be useful for obtaining more precise estimates of the occurrence of disability across the life cycle. It may be especially useful to assess the effect of increasing life expectancies on years with disability, which may have been overestimated in conventional methodologies. On the other hand, conventional methods appear to have yielded valid estimates of the relative importance of different risk factors.

CONCLUSION

Of all risk factors, the variation in years lived with disability was largest for BMI. The largest reductions in the years that are spent with disability can in principle be achieved among obese people. Consequently, curtailing the obesity epidemic is urgently needed to prevent strong increases in the future burden of disability and to increase the prospects for healthy ageing for future generations of elderly.

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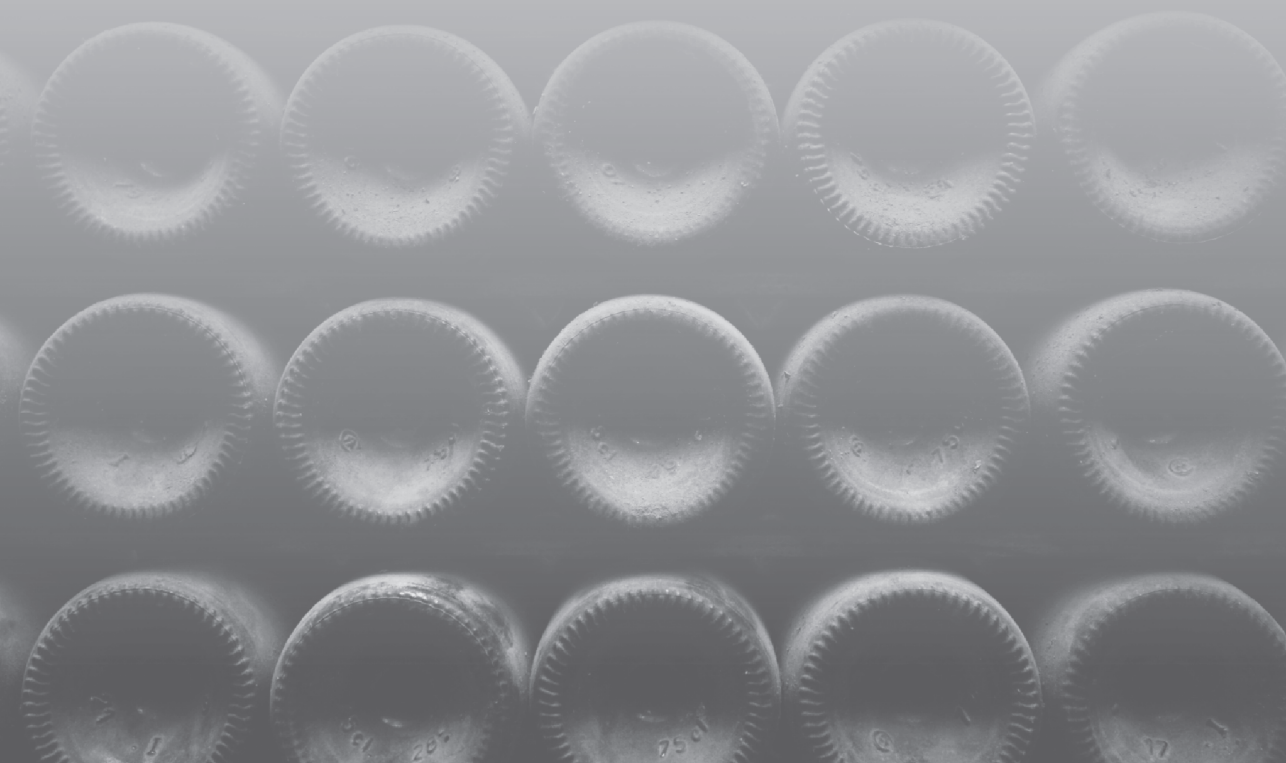
7

General Discussion



Population ageing is one of the great successes of public health, but also poses great challenges to current societies. Among the main challenges are how to secure the sustainability of the health care system and pension system and how to preserve the health and quality of life of the elderly population. Participation of elderly individuals in social and work environments has been proposed essential to a possible solution. The ability to participate and the quality of life of future populations of elderly, however, will greatly depend on the health of these populations and on whether persons will not only live longer, but also longer in good health. For insight in future developments of morbidity and to develop interventions that effectively reduce the burden of disability among the elderly, it is essential to know the current burden of disease and disability, particularly in relationship with the end of life and to know which determinants explain the current burden of disability.

The research questions addressed in this thesis were:

1. What is the current burden of disease and disability?
2. Which determinants explain the current burden of disability?

MAIN FINDINGS

Part I Disease and disability occurrence

Sub question 1: What is the prevalence of diseases and co-occurrences in the last two years of life?

Using individually linked information including multiple causes of death and hospital diagnoses within two years prior to death, it was shown that, in males, diseases most prevalent at the end of life were pneumonia, cancer of trachea, bronchus and lung, acute myocardial infarction, COPD and bronchiectasis, and cerebrovascular disease. In females, these were cerebrovascular disease, pneumonia, dementia, diabetes, and heart failure. The vast majority of all deaths had one or more concurrent condition. It was shown that multiple causes of death do not provide complete information regarding disease occurrence prior to death. Using additional information regarding hospital diagnoses affected the ranking of the most common conditions but did not lead to substantially different conclusions which diseases are most important.

Sub question 2: To what extent is the occurrence of disability associated with age (time since birth) and time to death?

The occurrence of disability was investigated in relationship with age (time since birth) and time to death for ADL disability and OECD disability (functional limitations). Within the last ten years of life, and particularly within the last five years, the prevalence and incidence of

disability increased substantially, but also the severity of disability increased, as the time to death decreased. It was shown that the occurrence of ADL disability is more strongly associated with time to death than with age. This was true among groups in presence of various diseases (chronic non-specific lung disease, heart disease and diabetes) and among various age groups. The association was stronger towards older ages. OECD disability was more strongly related to age. When ADL disabilities were assessed according to level of severity, severe disability defined as major difficulty with one (or more) out of ten ADL activities was particularly associated with approaching death, whereas mild disability, defined as minor difficulty with at least one activity was not at all related with time to death. As was shown in a calculation example, these associations are in accordance with the hypothesis of dynamic equilibrium. This hypothesis poses that when the life expectancy continues to increase, particularly the years lived with mild forms of disability will increase, whereas the years with severe disability will increase to a smaller extent.

Part II Explaining the burden of disability

Sub question 3: Which diseases contribute most to the burden of disability?

To investigate which diseases contribute most to the prevalence of ADL disabilities, data from the Dutch POLS-survey were analyzed. The disabling impact, that is, the extent a disease leads to disability once present, was calculated for a variety of diseases using an additive regression model. This model accounted for possible disability without any disease reported and for competing causes of disability. Musculoskeletal and cardiovascular disease contributed most to the burden of disability, but also chronic non-specific lung disease (males) and diabetes (females) contributed much. Within the musculoskeletal and cardiovascular disease groups, back pain, peripheral vascular disease and stroke contributed particularly by their high disabling impact. Arthritis and heart disease were less disabling but contributed substantially because of their high prevalence. The disabling impact of diseases was particularly high among persons older than 80.

Sub question 4: Which diseases contribute most to educational inequalities in the burden of disability?

Disease contributions to educational inequalities in the prevalence of OECD disability were calculated using a model similar to that used for sub question 3. In the analysis for sub question 4, however, disease contributions to the burden of disability were estimated for groups that differed according to the highest obtained level of education. Large absolute inequalities in the prevalence of disability existed. These differences were largely explained by the diseases included. When disabilities in hearing, seeing were not included to the OECD measure of disability and mobility limitations were assessed in solitude, almost all of the

differences were explained by the diseases. In males, diseases that contributed most to the inequalities were back pain, disorder neck / arm, other and peripheral vascular disease. In females, arthritis, other, back pain and chronic non-specific lung disease contributed most. Half of the total inequality in disability prevalence was explained by diseases' disabling impacts.

Sub question 5: Which lifestyle factor is most important for spending many years with disability: obesity, smoking or heavy drinking?

The analysis for sub question 5 was based on data from the POLS-survey 1997-1999 with mortality follow-up until 2006. Poisson regression methods were used to estimate mortality risks among obese persons, smokers and heavy drinkers. Particularly smoking was associated with a high mortality, whereas the mortality risk for obesity and heavy drinking was only slightly elevated. The odds for ADL disability were high for obese persons, moderate for heavy drinkers and low for smokers. Using the mortality and disability risks in Sullivan life tables, it was estimated that the years lived with disability differed most according to BMI, least according to smoke status, and in between according to alcohol consumption. Obese persons could expect to live at least two years more with disability than smokers and drinkers. Employing information on time to death led to lower estimates of years lived with disability, and to smaller differences in these years according to BMI, alcohol, and smoking. Conclusions regarding which risk factor is most important, however, remained unchanged.

EVALUATION OF DATA AND METHODS

Report of disability, disease and life style variables

Except for chapter 2, the presence or absence of disability, disease and specific lifestyles was assessed on the basis of self-report. Self-reported measures of disability may, in theory, not merely reflect the objective status of disability, but also to some extent the subjective experience of health and disability. This may have introduced some bias to our analyses. However, various studies show that self-report of disability correlates sufficiently well with objective measures of disability, suggesting that the bias related with self-report has remained limited in our study (1-3). In addition, it has been shown that the accuracy of self-report of disability is not influenced by level of education, suggesting that also the possible differential bias by education in chapter 5 has remained small (4). Self-report of most chronic conditions is fairly accurate, except for arthritis, which may be overestimated as well as underestimated (5). Level of education has no significant effect on disease reporting behaviour (6-7). If the prevalence of arthritis or another disease was underestimated in chapters 4 and 5, subjects with less severe forms of the disease would be most likely to be uncounted and, hence, the disabling impact would be overestimated. This implies that although there may be some bias in the estimates

of disease prevalence, this is nullified by a bias in opposite direction in the disabling impact. Thus, the bias in the estimates of contributions of specific diseases to (inequalities in) the prevalence of disability and life expectancy with disability is likely to have remained small. As self-reported BMI tends to be underreported, particularly by those who have a high BMI, the risk of disability among persons who had a high BMI may have been overestimated in chapter 6 (8-9). However, the potential bias has been shown to be acceptable for correlation analyses like in our study (9). Underreporting in self-reported alcohol consumption may have affected prevalence rates, but does not appear to have lead to substantially bias in the association between heavy drinking and harmful consequences (10). In summary, potential bias related with self-reporting of disability, disease and lifestyle is expected to have remained limited and has probably not affected our substantive conclusions.

In chapter 2, disease prevalence was estimated using medical information from cause of death and hospital registries. Cause of death registration comprises the diagnostic process, completion of a death certificate, and coding of the statements on the death certificate (11). It has been shown that some diseases such as cancers are more adequately certified than others, such as COPD, but that cause of death coding practices partly adjusted for inaccurate certification (12). The inter coder agreement of the registration of underlying causes of death such as cancers and acute myocardial infarction is high (>= 90%), but for diseases such as diabetes and hypertension, the agreement is relatively low (53% and 71%) (13). A study on the reliability of the Dutch National Medical Registration showed that that 99% of the diagnoses of discharge was recorded correctly in the register (14). Aiming at information regarding disease presence prior to death as complete as possible, we used nationwide data sources linked at the individual level. As expected, we showed that some non-fatal conditions which were hardly mentioned as a cause of death had a high prevalence according to the full linked data. Nonetheless, as chances for hospitalization are probably lower for conditions that are not very lethal than for highly lethal conditions, it cannot be excluded that the prevalence of some non-lethal conditions to some extent remained underestimated in the full linked data. A decline in the mean number of conditions at age 85 and older suggests that the diagnostic process among the oldest old is less extensive or less accurate than it is for younger persons.

ADL versus OECD disability

Disabilities were assessed as disabilities in ADL (and mobility) (chapters 3.1, 3.2, 4 and 6) and as functional limitations according to the OECD long term indicator of disabilities (chapters 3.2 and 5) (15). In the OECD indicator, mobility, hearing and seeing disabilities are distinguished and hearing and seeing are assessed possibly using hearing aids or spectacles/contacts. ADL disability is a quite severe form of disability and is associated with substantial declines in quality of life and increased demands for health care (16-17). Functional limitations are less severe and generally occur in an earlier stage of the disablement process (18). In each of our

analysis, ADL disabilities were assessed, except for the analysis investigating disease contributions to educational inequalities in the prevalence of disability in chapter 5. In this analysis, there was a lack of power to use ADL disabilities and we decided to use the less severe OECD measure. To analyse the overlap between ADL and OECD disability we selected persons from the POLS survey 2001-2007 who were older than 55 and had complete data for both disability measures. In this sample, 25% was OECD disabled and 11% was ADL disabled. Most persons (81%) who were ADL disabled were also disabled according to the OECD measure, but 64% of those with OECD disability were not disabled according to the ADL measure. Of the persons who only had OECD disability, 41% were disabled in the mobility domain, 46% were disabled in the hearing/seeing domain, and 13% were disabled in both. It was concluded that, the OECD measure largely includes the ADL measure, but expands it with disabilities in mobility and hearing/seeing.

In Figure 7.1, disease contributions to the prevalence of ADL disability are compared with contributions to OECD disability. The prevalence of OECD disability is higher than that of ADL disability, but the largest part of the difference is not due to different disease contributions but due to differences in 'background' which represents disability attributed to other causes than the diseases included. As was explained in chapter 4, the largest part of the OECD disability attributed to background is related with disabilities in hearing/seeing. In males and females aged 60-69, musculoskeletal conditions contribute slightly more to OECD disability than to ADL disability and in females, the contribution of CVD is slightly larger. Given that most of the ADL disabilities are also included in the OECD measure, and that hearing and seeing disabilities are particularly represented as 'background' in the prevalence of OECD disability, these larger contributions are most likely associated with less severe mobility disabilities. In the figure, rather similar conclusions can be drawn for ADL and OECD disabilities. That is, in males, musculoskeletal disease and CVD contribute most to the prevalence of disability and in females, musculoskeletal disease contributes most. The distribution across educational groups of OECD disability was relatively similar to that of ADL disabilities (Figure 7.2). Therefore, it is not expected that using OECD instead of ADL disabilities has substantially affected our conclusions regarding which diseases contribute most to educational inequalities in the prevalence of disability.

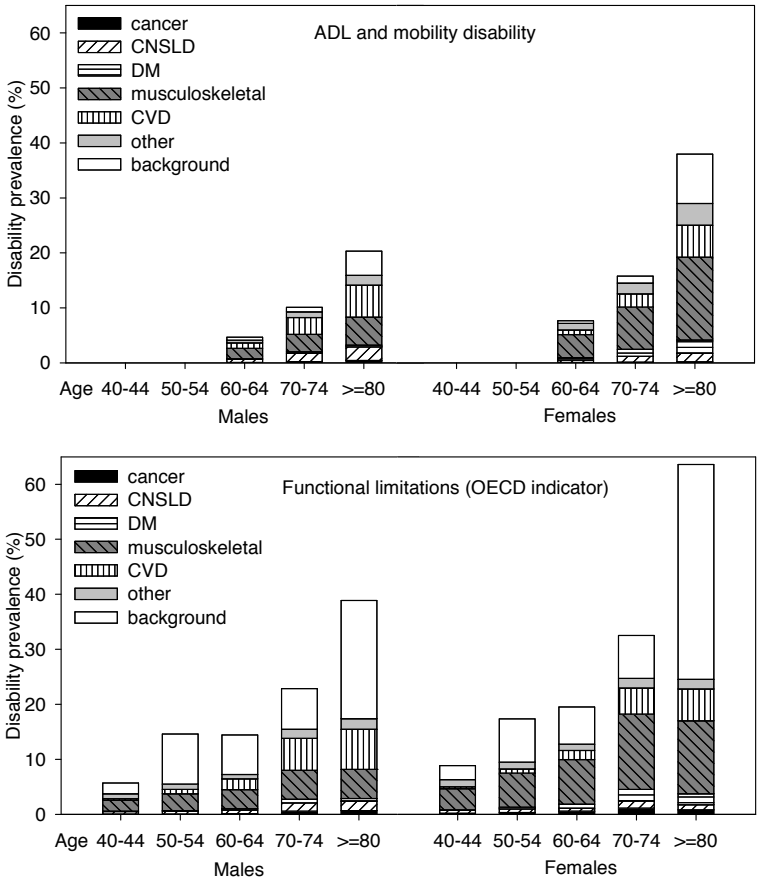


Figure 7.1 Contribution of chronic disease to ADL disability and functional limitations.
Results are for weighted study populations as described in chapters 3.2 and 3.3.

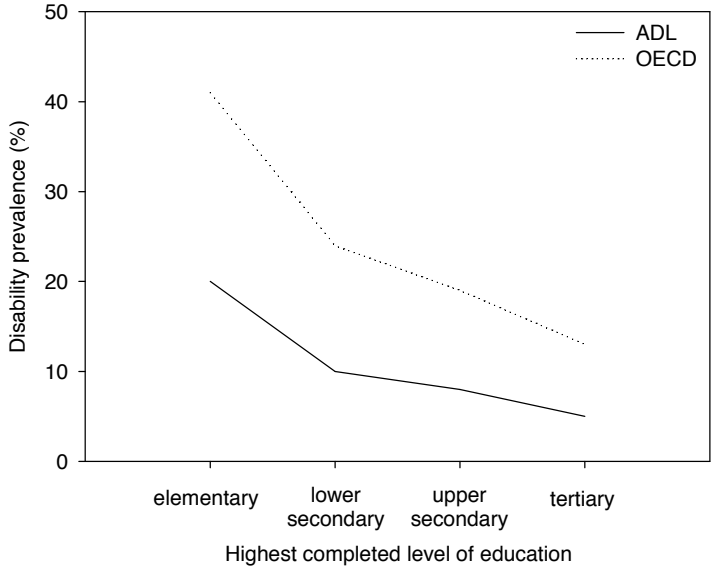


Figure 7.2 Prevalence of ADL and OECD disability by level of education.
Figure is based on data from the POLS-survey 2001-2007.

Generalizability

The study populations that were used to describe disease and disability occurrence and to investigate determinants of disability were not completely representative for the total Dutch population of elderly in the sense that the oldest old and the institutionalized population were not always included. In chapter 2, estimates of the prevalence of diseases and co-occurrences at the end of life were restricted to ages younger than 84, as disease information for older ages was probably incomplete. If complete information at ages older than 84 would have been available, including deaths above age 84 would probably have resulted in a higher prevalence of diseases and co-occurrences (19-20). A study comparing disease prevalence for age 77-84 with that for age 85 and older suggests that the ranking of diseases is not very different for ages above 84, except for mental disorders which have a particularly high prevalence among the oldest old (20). In chapter 3, exclusion of a part of the institutionalized population may have led to a conservative estimate of the association between disability occurrence and proximity to death, particularly for moderate and severe disability. In chapters 4 and 5, the results regarding disease contributions to the burden of disability, and in chapter 6, the estimates of risk factors in relationship with years lived with disability may not be representative for the institutionalized population. However, in the Netherlands, only a minor part of the elderly people lives in an institution and the bias due to excluding the institutionalized population is probably small and negligible at younger ages (21).

Attribution method

In chapters 5 and 6, contributions of chronic diseases to the prevalence of disability were estimated using a methodology that was developed by Nusselder et al. (22-23). According to this methodology, individual cross-sectional information on the presence or absence of selected diseases and disability, gender and age was used to estimate the disabling impact of selected diseases. Estimated disabling impacts and information on diseases present in individuals were used to calculate the contribution of diseases to the prevalence of disability for the Dutch non-institutionalized population.

In principle, there are several options to obtain disability data by cause. One option is to use surveys that already include self-reported information on the main condition causing disability. However, such survey data on causes of disability are not widely available and rely on self-report. Another option is to use prospective data, including information on the time of onset of chronic diseases and disability to reconstruct causes of disability. However, longitudinal data sets of a sufficient size and representative for the population are also scarce. Moreover, as disability prevalence (by cause) depends on incidence and mortality, also information on mortality from the different diseases is required when opting for longitudinal incidence data. The cross-sectional nature of our analysis may have resulted in some (false) attribution of disability in situations where the onset of disease followed the onset of disability. Using longitudinal data might have prevented such false attribution. Nevertheless, false attribution might still have occurred, especially in situations in which multiple diseases were present but only one was the actual cause of disability. Moreover, the risk for disability prior to the onset of a particular disease is expected equal to among persons without onset of this disease. Therefore, in our analysis false attribution is expected not to have biased our results to a large extent. As far as we are aware, no comparative research has been conducted to quantify the bias related with the various methods available to calculate disability data by cause.

In theory, particular combinations of diseases can have a disabling effect that is different than the effects of both diseases added. In other words, there may have been statistical interaction for the diseases. Taking into account such interaction in the model would have been possible by including variables representing the presence or absence of specific combinations of diseases. However, considering the complexity of the models that were used, and as testing for interactions without a priori knowledge would involve problems associated with multiple comparisons, we decided not to include such possible interactions.

Our approach to estimate disease contributions to the burden of disability should be distinguished from Population Attributable Fractions (PAFs, also known as population attributable risks, PARs). PAFs are used to estimate to what extent a specific cause contributes to a burden of ill health assuming counterfactual scenarios (24). In our specific situation, a PAF could

be calculated to answer the question what proportion of disability would be prevented if a specific disease or the disabling effect of a disease were eliminated. However, using this approach to subsequently 'eliminate' a set of diseases from the population, for each disease, the effect of the elimination would depend on the diseases that remain present after elimination of a specific disease and, hence, on the order of the elimination (25). When calculating PAFs for a range of diseases, it is usually assumed for each disease that it is the first in the sequence of elimination (25). In fact, this assumption results in mutually exclusive scenarios that are illogical to sum. As the effect of elimination is largest when a disease is eliminated first in sequence (and smallest if it is eliminated last), the sum of the PAFs is an overestimate of the total proportion of disability prevented. Although solutions have been suggested to avoid this problem, in our view, they are unsatisfying, as the problem of non-additivity of the reductions in risk due to the elimination of different risk factors (in the same person) is a fundamental one, caused by competing risks. Taking an alternative approach by using additive rate models that take into account this competition, the problem was solved at a fundamental level (26). Using additive regression models, we were able to reconstruct how exposure to multiple diseases resulted in the current burden of disability while avoiding problems related with elimination scenarios.

Time to death concept

In chapter 3, the association between disability and time to death was tested and confirmed particularly for ADL disabilities. It may be counterintuitive to model the occurrence of disability dependent on the time to an event occurring later in time, i.e. death. According to rules of causality, an event can only be the cause of a certain effect if it occurred before and not after the effect. In our analysis, a shorter time to death should not be regarded as a real cause of disability, but the association of disability with time to death existed because the occurrence of disability and death have a common cause, namely the deterioration of individuals' health. Although time to death cannot be considered as a 'real cause', it has proven a valuable construct to investigate how health care expenditures or the burden of disability may develop under the assumption of continuing mortality declines and increasing life expectancy (27-30). The association of disability with time to death we found is further substantiated by recent research showing a relationship between disability and mortality (31-32).

In health economics literature, the validity of the conclusion that the strong association of health care costs with time to death would result in a shift of health care costs to older ages rather than to an expansion was questioned, as the relationship might be endogenous (27, 30, 33). If the dependency of health care costs and time to death would, in fact, reflect a delayed moment of death as a result of increased health care spending, an increase of health care spending, rather than postponement, would be most likely (27, 30, 33). Although our

time to death analysis was strongly linked to this recent health economics research, the issue of endogeneity is less relevant as it is unlikely that an increased risk of disability will delay the moment of death.

The association of proximity to death and disability is likely to be mediated by other factors, such as health status/disease and demographic factors. If our aim had been to gain insight into causal chains that relate disability with time to death, or to provide a model with an optimal predictive power, it would have been useful to include more covariates. However, our aim was only to demonstrate the relevance of proximity to death for predicting the prevalence of disability. To keep the models simple and transparent, we decided not to include any other covariates except sex. Moreover, variables other than sex, age, and time to death are not routinely distinguished in projections of future demographic trends of many countries.

The both relationships of ADL disabilities with age and time to death reflect different aspects of the process of ageing. Conceptually, human ageing can be viewed as accumulation of damage due to intrinsic (genetically determined damage, biological factors) and extrinsic (environmental stress) factors and the lack of maintenance and repair (34). It is a continuous not directly observable process over increasing time and age that gives rise to observable, probabilistic events, i.e. the onset of disease, disability and death (34). Damage accumulated to non life maintaining systems is particularly associated with non-fatal disease or disability, whereas damage to life maintaining systems may lead to death, with or without a trajectory of disease and disablement. In terms of associations of disability with age and time to death, damage to non-life maintaining systems is mostly reflected in the association with age, whereas damage to life maintaining systems causing mortality is reflected in the association with time to death. This is also represented in the observation that ADL disabilities, which are quite severe and generally occur later in the disablement process, have a stronger association with time to death than OECD disabilities (chapter 3).

Aiming at improvement of future predictions of the burden of disability, our results suggest that it might be worthwhile to use the both relationships of disability with age and time to death. We found a strong cross-sectional relationship of disability prevalence and incidence with time to death. It should be noted that, similar to the association with age, the association of disability with time to death may change over time, as was for instance suggested by an observed decline in mortality among those with ADL disability (31). Investigating time trends in the relationships of disability with age and time to death as well as investigating determinants (of trends) of these associations could contribute to further understanding of the disablement process and could provide further input to prediction models.

COMPARISON TO PREVIOUS STUDIES

Disease at the end of life

Our study was among the first to investigate whether multiple causes of death provide complete information regarding disease presence prior to death and to provide estimates of the prevalence of diseases and co-occurrences on the basis of individually linked information from cause of death and hospital registrations. Our study confirmed what had been suggested by a few earlier studies, namely that hospital discharge records contain information regarding disease presence prior to death that is not contained in cause of death registrations and that the amount of extra information contained varies according to disease (35-36). Adding to previous studies, we showed that employing the extra information from hospital discharge records results in larger prevalence estimates for each of the twenty conditions most common at the end of life. The ranking of some diseases was substantially affected by including the hospital information, whereas for other diseases, the ranking hardly or not at all affected. Including information from hospital registrations did not lead to substantially different conclusions regarding which diseases are most important according to multiple causes of death.

Disability at the end of life

In the near future, the average length of life is expected to further increase (37-39). One of the key issues in public health is whether the expected extra life years will be years in good health, or, otherwise, will be spent in ill health or disability (40-41). Previous studies described end of life trajectories of functional declines and a recent study showed a strong relationship between disability and mortality for the Dutch population (32, 42-44). Health economics studies showed a strong dependency of health care costs with the end of life (28-30). Together with these studies our results suggest that part of the years gained may be years without (severe) disability. We found that OECD disabilities have a strong dependency with age, whereas ADL disabilities, particularly severe ADL disabilities, are most strongly associated with time to death, which connects most closely to dynamic equilibrium (chapter 2). This confirms findings of a study by Perenboom et al., who found increasing years with mild disability and decreasing years with severe disability in the Netherlands between 1989-2000 (45). Results from a recent meta-analysis investigating trends (1990-2007), however, suggested expansion of both moderate and severe levels of activity limitations in stair climbing, walking and getting dressed (46). Another recent Dutch study found fluctuation in the life expectancy with disability between 1990-2005 and estimated around 60% chance that an absolute compression of disability will have occurred in 2030 (47). Studies in other European countries found evidence for compression, expansion as well as dynamic equilibrium, but it is unclear to what extent these differences represent real differences or refer to differences in methods and disability measurement (48-52). Most studies investigating disability oc-

currence in relationship with the end of life were restricted to a period of maximally three years prior to death (42, 53-54). Our finding of a relationship over 12 years of time suggests that death casts its shadow more remotely over life. As compared to health care costs in the Netherlands, ADL disability is at least as strongly related to the end of life (28).

Contribution disease to disability

The contribution of diseases to the burden of disability was assessed in a number of earlier studies (22-23, 55-63). Of these studies, WHOs Global Burden of Disability study (GBD) is probably most comprehensive and well known. Different to our analysis (chapter 4), WHOs approach uses health state valuations, formerly referred to as disability weights, to quantify disease burden. Health state valuations are panel valuations of the severity of a specific condition instead of actual presence of physical disability. This approach has the advantage that it allows assessing and comparing burden of disease, merely on the basis of disease frequencies. Our approach requires more specific data, but is expected to yield more accurate results as it accounts for effects of individual factors such as age and sex, which were shown to affect the disabling consequences of a disease. In the GBD, unipolar depressive disorders, alcohol use disorders, hearing loss (adult onset) and Alzheimer and other dementias were associated with most years lost due to disability in high income countries. Differences in methodology and diseases included hampers further comparison with our results. In the studies that assessed disability in a way more similar to ours, musculoskeletal and cardiovascular disease were most often reported as the most important contributors to disability. Our study had special attention for variation in disease burden according to age and confirmed these results also for the oldest old (80+). Adding to previous studies, it was shown that the high prevalence of disability at this age is caused by a high prevalence of diseases, but even more by the high extent these diseases lead to disability at older ages. Our study was the first to identify peripheral vascular disease as an important contributor to the burden of disability, which is associated with much disability mainly by a high disabling impact.

Contribution disease to disability inequalities

A few other studies have been conducted to assess disease contributions to disability inequalities (23, 64-65). The results of these studies were not completely consistent, but in each of the studies musculoskeletal conditions such as back complaints, knee complaints and arthritis were among the diseases that contributed most to the inequalities. Our study confirmed the large contributions of back pain and arthritis, but also demonstrated that disorders of the neck and upper extremity contribute substantially (chapter 5). We were the first to show a substantial contribution of peripheral vascular disease. What had not been investigated in earlier studies is to what extent contributions to inequalities in the disability burden are due to differences in disease prevalence or in the disabling impact. Our study revealed that a very substantial part of inequalities in disability is explained by differences in

the disabling impact of chronic conditions. Furthermore, our analysis showed that the gradient by level of education that exists in the prevalence of disability is reflected or explained by gradients in contributions of diseases contributing to the inequalities.

Contribution lifestyle to disability

Studies comparing effects of lifestyle factors on years spent in ill-health found that, compared to heavy drinking or regular smoking, obesity had a much stronger effect on years that people could expect to live with long-standing illness, with reduced quality of life, or with less than good self-assessed health (66-68). Together with other recent evidence, the results of this thesis show that, in addition, obese persons may expect to live more years with one or more disabilities than smokers and drinkers (chapter 6) (69-70). We were the first to assess potential improvement of the Sullivan method by using information on the association of disability with time to death. It was concluded that this new method may be useful for obtaining more precise estimates of the occurrence of disability across the life cycle, but that conventional methods appear to have yielded valid estimates of the relative importance of different risk factors.

Interventions to reduce disability

The results in this thesis show considerable heterogeneity in the burden of disability, suggesting that there is ample room for improvement and prevention of disability. Evidence is becoming increasingly available that effective interventions exist to prevent or delay the onset of disability. In this paragraph we summarize the results of a series of reviews. Supplemental vitamin D reduces the risk of falling among older individuals by 19% and multifactorial fall prevention programmes in primary care, community, or emergency care settings are effective in reducing the number of fallers or fall related injuries (71-72). Exercise programs, particularly long-lasting and high-intensive multicomponent exercise programs may improve physical functioning and can prevent ADL and iADL limitations (73-76). Preventive home visitation programs appear to be effective, provided that the interventions are based on multidimensional geriatric assessment and include multiple follow-up home visits and target persons at lower risk for death (77-79). Community-based multifactorial interventions in elderly people can reduce the risk of not living at home, nursing-home- and hospital admissions and falls and can improve physical functioning (80). General or orthopaedic rehabilitation programmes can increase function and physical condition and can reduce disability (91-83). Compared with conventional care units, admission to acute geriatric units results in a lower risk of functional decline at discharge (84). Furthermore, a number of disease specific reviews suggest that the negative physical consequences of conditions such as back pain, arthritis and myocardial infarction can be limited by targeted interventions (85-88).

IMPLICATIONS

Implications for policy

1. *The associations of disability with age and time to death suggest a development of the disability burden according to dynamic equilibrium.*

As OECD disability (functional limitations) and mild ADL disability have a particular strong association with age, the years lived with these relatively mild forms of disability have a tendency to expand when the life expectancy increases. Severe ADL disabilities are strongly associated with the end of life and, therefore, have a less strong tendency to expand.

2. *To reduce the burden of disability, policy should aim at preventing the onset of disabling conditions, as well as at reducing their disabling impact.*

Diseases may contribute to the burden of disability by high disabling impacts, e.g. stroke in males, by moderate disabling impacts but high prevalences, e.g. arthritis, or by both high prevalences and disabling impacts, e.g. back pain in females. The largest reductions in the burden of disability can be obtained by interventions that prevent the primary cause of disability, that is, by preventing disease onset. Further substantial reductions can be achieved by diminishing disabling impacts. Disease specific interventions should target a broad range of diseases, not only diseases with a high disabling impact, but also those moderately disabling but frequently occurring.

3. *Curtailing the obesity epidemic is essential for reducing the years lived with disability.*

Not all primary prevention interventions that increase the life expectancy and the years lived without disability will at the same time reduce the years lived with disability. Our findings suggest that reducing obesity, smoking and heavy drinking all three will increase the life expectancy and the healthy life expectancy, but that only reducing obesity in the population will at the same time reduce the years lived with disability.

4. *Socially disadvantaged groups should be prioritized in the aim for reductions in the burden of disability.*

Groups with a low socioeconomic position have a substantial higher prevalence of disability than groups with a high socioeconomic position, also among the elderly. Therefore, targeting groups with a low socioeconomic position has great potential for achieving reductions in the burden of disability, while at the same reducing social health inequalities. Reductions among low socioeconomic groups can be achieved by preventing the occurrence of conditions

such as back pain, disorder neck/arm and peripheral vascular disease in males and arthritis, back pain and chronic non-specific lung disease in females. A 50% reduction in the disability inequality can be achieved by eliminating differences in diseases' disabling impacts.

5. *Reducing the burden of disability among persons younger than 65 is essential to allow working until retirement.*

Although disability most occurs most frequently among elderly persons, we showed that the burden of disability among persons younger than 65 is substantial, particularly among those with a lower level of education. As the presence of disability is associated with job loss, preventing the onset of disabling conditions and reducing their disabling impacts among persons younger than 65 is essential to allow working until retirement age. Given the considerable disadvantage in the occurrence of disability among groups with a low socioeconomic position, particular effort is required to reduce diseases and disease impact among these groups.

Implications for research

1. *Future projections of disability could utilise the relationship of disability occurrence with time to death.*

Robust estimates of the future burden of disability are scarce, among others because past trends do not univocally point to increased or decreased years with disability and are a weak basis for projections. Taking an alternative approach by assessing disability occurrence in relationship with age and time to death, we found evidence for a development according to a dynamic equilibrium. We found that models that include age as well as time to death give a better prediction of disability occurrence than models including age only. Therefore, we recommend utilising the both relationships of disability occurrence with age and time to death when using a Sullivan life table approach. When disability incidence data is available and multi state life table modelling is feasible, we recommend investigating different severity levels of disability as our results suggest that trends in disability may vary according to severity level.

2. *It is recommended to expand current research by investigating psychosocial, environmental and socioeconomic factors as determinants of the burden of disability.*

We assessed contributions of diseases and lifestyle factors to the burden of disability as well as socioeconomic differences in diseases' contributions. A review of literature, however, showed that also environmental (neighbourhood depravation, air pollution), social (low frequency of social contacts, childhood living conditions) and mental factors (cognitive

impairment, depression) are risk factors for disability. In addition, occupation, personality, and hospitalisation may play a role in becoming disabled. Targeting such factors may lead to reductions in the prevalence of disability, but is unknown whether such interventions would also affect mortality and would lead to fewer or to more years lived with disability. Therefore, it is recommended to investigate these factors as determinants of years lived with disability and to compare their effects in order to identify further entry points to reduce the disability burden. Furthermore, research is needed to investigate how discrepancies between functional abilities and the environment contribute to the burden of disability and how individual adaptation strategies may influence the disability burden.

3. *It should be unravelled why specific diseases lead to more disability in low socioeconomic groups than in high socioeconomic group.*

A key finding of this thesis was that there is large variation in the disabling impact of specific chronic conditions by level of education. Groups with a low socioeconomic status not only more frequently have conditions such as back pain, arthritis, peripheral vascular disease and chronic non-specific lung disease, but they also have a higher chance to become disabled from these conditions. It could be that groups with a low socioeconomic position tend to have different subtypes of a disease, or that they have more severe forms of the disease which may be associated with more disability. But also a more limited access to revalidation and rehabilitation, smaller use of adaptive device (e.g. walker), less effective coping strategies in general etc. could play a role. Aiming at a reduction of health inequalities, it is recommended to investigate which of these factors play a role and to what extent they are responsible for the difference in disabling impacts.

4. *To reduce the burden of disability, interventions should be developed that effectively postpone the onset of disability, but also lead to a reduction in the years lived with disability.*

As the research presented in this thesis was observational in its nature, the effects cannot directly be translated into effects of interventions, but should be interpreted as maximum potential effects. The real effectiveness of interventions aiming at reductions in the burden of disability should preferably be tested in randomized controlled trials. Commonly, such trials have disability incidence as their main outcome measure, but reductions in the incidence of disability does not necessarily lead to fewer years lived with disability. Therefore, it is recommended to evaluate interventions also in terms of their combined effect on disability and mortality, for instance by effects on years lived with disability, using life table calculations.

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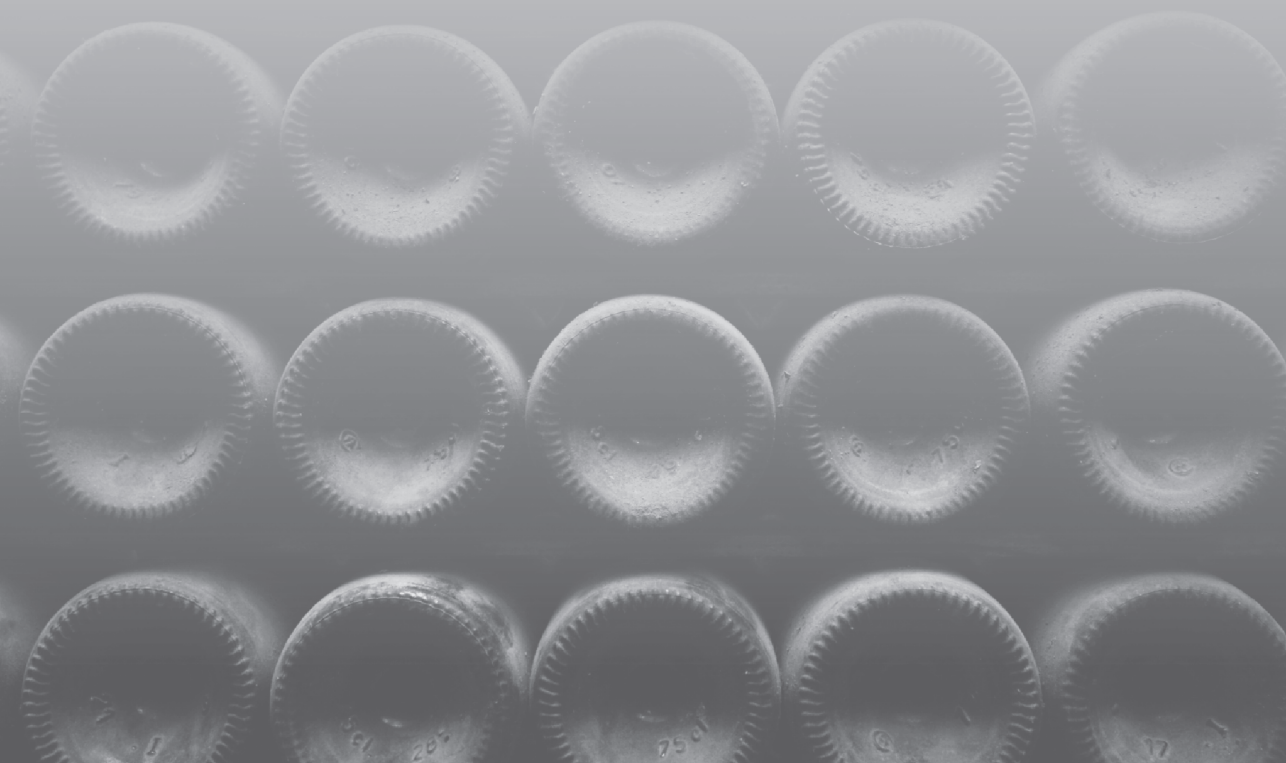
Summary



SUMMARY

Population ageing is the shift in the distribution of a country's population towards older ages. This phenomenon is currently occurring in almost all countries in the world and poses major challenges to current societies. These challenges are importantly related with an increasing group of elderly persons becoming socially and financially dependent on a decreasing group of younger persons. Among the main financial challenges are how to keep health care expenditures within acceptable boundaries and how to ensure the sustainability of the public pension system. Important social challenges are how to keep the growing population of elderly healthy and how to prevent strong declines in the quality of life. "Active ageing" and "participation" have been proposed as a framework to encounter the challenges posed by ageing of the population. However, to remain active and to participate until old age, healthy ageing of individuals is crucial. Furthermore, if the life expectancy continues to increase, as is expected, the extra years of life gained should preferably be years that are spent in good health.

To prepare future societies to cope with the expected increase in the burden of disease, it is essential to quantify the current burden of disease and disability and to know how these may develop in the future. In addition, for developing interventions that may effectively reduce the burden of disability and contribute to a compression of morbidity, it is essential to know which factors, such as diseases and life style factors, contribute most to the current burden of disability. The research questions addressed in this thesis were:

1. What is the current burden of disease and disability?
2. Which determinants explain the current burden of disability?

This thesis consists of two main parts that correspond with these research questions, and a general discussion covering both questions. The first main part has a special focus on the burden of disease and disability in relationship with the end of life. The second part focusses on contributions of diseases and life style factors to the burden of disability and educational inequalities herein. Two measures of disability were used: ADL (and mobility) disability and disability assessed according to the OECD questionnaire (OECD disability). OECD disability is less severe than ADL mobility and comprises functional limitations in mobility, hearing and seeing. In each chapter investigating disability, disability was assessed as ADL disability (or as both disability measures), except for chapter 5.

Part I Disease and disability occurrence

Chapter 2 presents a study investigating the prevalence of diseases most common at the end of life as well as the prevalence of their most common co-occurring conditions. In this study, nation-wide data was used including information on diseases present at the end of life available through multiple causes of death registrations and hospital discharge diagnoses for 86,987 persons aged 50-84. We showed that, in males, diseases most prevalent at the end of life were pneumonia, cancer of trachea, bronchus and lung, acute myocardial infarction, COPD and bronchiectasis, and cerebrovascular disease. In females, these were cerebrovascular disease, pneumonia, dementia, diabetes, and heart failure. The vast majority of all deaths had one or more co-occurring conditions. We showed that cause of death data do not provide complete information regarding disease occurrence prior to death, even if information from underlying and secondary causes of death are considered jointly. Using additional information regarding hospital diagnoses affected the ranking of the most common conditions but did not lead to substantially different conclusions concerning which diseases are most important.

Chapter 3 presents two studies investigating the occurrence of disability in relationship with age and time to death using six annual waves of the Dutch GLOBE longitudinal study and a subsequent 12-year mortality follow-up. In the first study we showed that within the last ten years of life, and particularly within the last five years, the prevalence and incidence of disability increased substantially, but also the severity of disability increased, as time to death decreased. The occurrence of ADL disability was more strongly associated with time to death than with age, also among groups in presence of various diseases (chronic non-specific lung disease, heart disease and diabetes) and among various age groups. The association with time to death was stronger towards older ages. OECD disability was more strongly related to age. In the second study, relationships of ADL disabilities with age and time to death were assessed for three levels of disability with the aim to test the key assumption of the theory of a dynamic equilibrium. This assumption is that mild disability is most strongly associated with age and severe disability most strongly with time to death. Severe ADL disability, defined as major difficulty with one (or more) out of ten ADL activities, was particularly associated with approaching death, whereas mild disability, defined as minor difficulty with at least one activity was not at all related with time to death. As was shown in a calculation example, these associations are in accordance with the hypothesis of dynamic equilibrium. This implies that particularly the years lived with mild disability may increase substantially when the life expectancy continues to increase, whereas the years with severe disability are expected to increase to a smaller extent.

Part II Explaining the burden of disability

Chapter 4 comprises a study assessing the contribution of chronic disease to the burden of ADL disability using data from the Dutch POLS survey 2001-2007. In the research presented, the disabling impact, which refers to the extent a disease leads to disability, was calculated for a variety of diseases using an additive regression model. This model accounted for possible disability without any disease reported and for competing causes of disability. Musculoskeletal and cardiovascular diseases contributed most to the burden of ADL disability, but also chronic non-specific lung disease (males) and diabetes (females) contributed much. Within the musculoskeletal and cardiovascular disease groups, back pain, peripheral vascular disease and stroke contributed particularly by their high disabling impact. Arthritis and heart disease were less disabling but contributed substantially because of their high prevalence. The disabling impact of diseases was particularly high among persons older than 80.

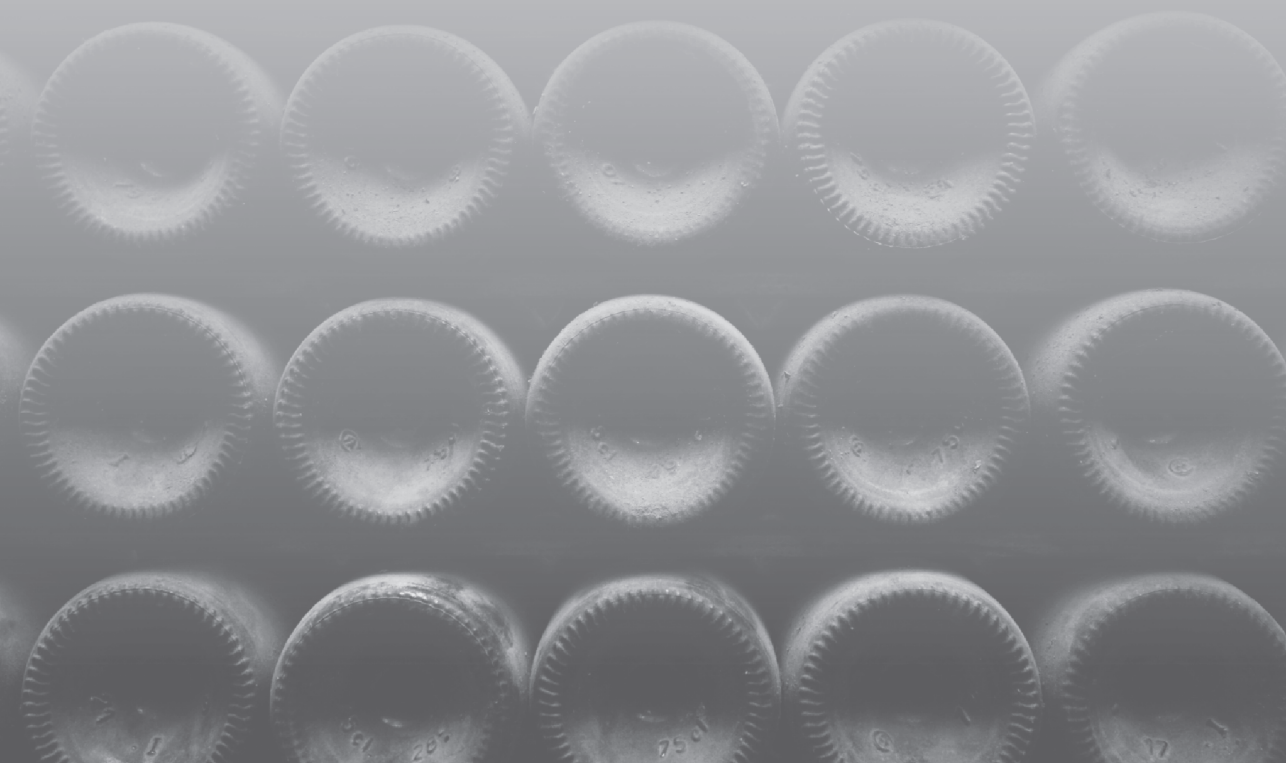
In **chapter 5** a study is presented investigating to what extent diseases contribute to educational inequalities in the prevalence of OECD disabilities. A method similar to that in chapter 4 was used. In this analysis in chapter 5, however, disease contributions to the prevalence of OECD disability were estimated for groups differing according to the highest obtained level of education. Furthermore, it was investigated to what extent disease contributions to inequalities in disability are due to differences in the disabling impact. Large absolute differences in the prevalence of OECD disability of 18% (points) in males and 15% in females existed between groups with the highest and lowest level of education. 64% of the inequalities in males and 69% in females were due to the diseases included. For mobility limitations only, these percentages were 90% and 84%. In males, diseases that contributed most to the inequalities were back pain (17 %), disorder neck/arm (13%), other (11%) and peripheral vascular disease (7%). In females, arthritis (18%), other (17%), back pain (13%) and chronic non-specific lung disease (7%) contributed most. In males and females, 49% and 51% of the total inequality in disability prevalence was explained by diseases' disabling impacts.

Chapter 6 presents a study that aimed to resolve which lifestyle factor (obesity, smoking or heavy drinking) is associated most with living many years with ADL disability, using a Sullivan life table approach. A secondary aim of the study was to assess whether Sullivan life table estimates could be improved by stratification according to age at death. Data from the Dutch POLS Survey, 1997-1999, with mortality follow-up until 2006 were used. Particularly smoking was associated with a high mortality, whereas mortality risks for obesity and heavy drinking were only slightly elevated. The odds for ADL disability were high for obese persons, moderate for heavy drinkers and low for smokers. Using the estimated mortality and disability risks, Sullivan life tables were constructed. It was estimated that the years lived with disability differed most according to BMI, least according to smoke status, and in between according to alcohol consumption. Obese persons could expect to live at least two years more with

disability than smokers and heavy drinkers. Employing information on time to death led to lower estimates of years lived with disability, and to smaller differences in these years according to BMI, alcohol, and smoking. Conclusions regarding which risk factor is most important, however, remained unchanged.

In **chapter 7** the main findings of this thesis are summarized, the data and methods used are discussed, the results are compared to previous studies and new findings are highlighted. The chapter is concluded with recommendations for practice and research. The main conclusions of this thesis are as follows. Multiple causes of death, including underlying and secondary causes of death, provide underestimates of the end of life prevalence of some diseases. Using additional information regarding hospital diagnoses affects the ranking of the most common conditions but does not lead to substantially different conclusions concerning which diseases are most important. Mild disability is most strongly associated with age, whereas severe disability is particularly associated with time to death. Therefore, the years lived with mild disability will most likely expand when the life expectancy further increases. The years lived with severe disability, however, are less likely to expand due to an expected increase in the age of onset of severe disability. Given that diseases contribute to the burden of disability by high prevalences as well as by high disabling impacts, policy aimed at reducing the burden of disability should aim at preventing the onset of disabling conditions, as well as at reducing their disabling impact. Reductions in the prevalence and disabling impact of diseases among groups with a low education could lead to substantial reductions in the social inequality in the burden of disability. If the inequality in the prevalence of diseases would remain unchanged, eliminating the inequality in disabling impacts would still reduce the disability inequality by 50%. Reducing obesity, smoking and heavy drinking all three will increase the life expectancy and the disability free life expectancy, but only reducing obesity in the population will reduce the years lived with disability.

Samenvatting



SAMENVATTING

Vergrijzing is de opwaartse verschuiving in de leeftijdsverdeling van een populatie. Dit fenomeen vindt momenteel plaats in bijna alle landen ter wereld en plaatst huidige samenlevingen voor grote uitdagingen. Deze uitdagingen zijn in essentie gerelateerd aan een groter wordende groep ouderen die sociaal en financieel afhankelijk is van een kleiner wordende groep jongere personen. Belangrijke financiële uitdagingen zijn onder andere hoe de uitgaven voor gezondheidszorg binnen acceptabele grenzen kunnen worden gehouden en hoe het voortbestaan van het publieke pensioenstelsel kan worden gegarandeerd op de lange termijn. Belangrijke sociale uitdagingen betreffen het behoud van een goede gezondheid van een toenemende groep ouderen en het voorkomen van een sterke afname in de kwaliteit van leven in de bevolking. Als kader voor een aanpak van de uitdagingen van vergrijzing zijn "actief ouder worden" en "participatie" voorgesteld. Echter, om actief te blijven en te kunnen participeren tot op hoge leeftijd is het behoud van een goede gezondheid essentieel. Verder is het van groot belang dat wanneer de levensverwachting blijft stijgen, zoals wordt verwacht, de gewonnen levensjaren jaren zijn in goede gezondheid.

Om toekomstige samenlevingen in staat te stellen zich voor te bereiden op een verwachte toename van de ziektelast is het essentieel de huidige last van ziekten en beperkingen te kwantificeren en om inzicht te krijgen in mogelijke ontwikkelingen in de toekomst. Voor het ontwikkelen van interventies die op een effectieve manier de beperkingenlast kunnen terugdringen en kunnen bijdragen aan een compressie van morbiditeit is het noodzakelijk inzicht te krijgen in welke factoren, zoals ziekten en leefstijl, het meest bijdragen aan de huidige beperkingenlast. De onderzoeksvragen van dit proefschrift waren:

1. Wat is de huidige last van ziekten en beperkingen?
2. Welke determinanten verklaren de huidige beperkingenlast?

Dit proefschrift bestaat uit twee delen die samenhangen met deze onderzoeksvragen en een algemene discussie die beide vragen betreft. Het eerste deel betreft de last van ziekten en beperkingen, in het bijzonder in relatie met het levenseinde. Het tweede deel betreft de bijdragen van ziekten en leefstijlfactoren aan de beperkingenlast en aan opleidingsverschillen in de beperkingenlast. In de studies die worden beschreven werden twee maten van beperkingen gebruikt: ADL (en mobiliteits) beperkingen, en beperkingen vastgesteld op basis van de OESO vragenlijst (OESO beperkingen). OESO beperkingen zijn in het algemeen minder ernstig dan ADL beperkingen en omvatten functionele beperkingen in mobiliteit, horen en zien. In ieder hoofdstuk waarin beperkingen worden onderzocht zijn deze onderzocht als ADL beperkingen (of als beide maten), behalve in hoofdstuk 5.

Deel I: Optreden van ziekten en beperkingen

In **hoofdstuk 2** wordt een studie gepresenteerd waarin de prevalentie van de meest voorkomende ziekten aan het einde van het leven werd onderzocht, evenals de prevalentie van de bij deze ziekten meest voorkomende co-morbiditeiten. In deze studie werd gebruik gemaakt van informatie over ziekten aanwezig aan het einde van het leven, beschikbaar uit de Nederlandse doodsoorzakenregistratie, en informatie over ontslagdiagnoses uit ziekenhuizen van 86.987 personen in de leeftijd van 50-84 jaar. Bij mannen kwamen respectievelijk pneumonie, kanker van de trachea, bronchus en long, acuut hartinfarct, COPD en bronchiëctasieën, en cerebrovasculaire ziekten het meest voor aan het einde van het leven. Bij vrouwen waren dit cerebrovasculaire ziekten, pneumonie, dementie, diabetes en hartfalen. Het overgrote deel van de sterfgevallen had één of meer co-morbiditeiten. We lieten zien dat doodsoorzaken geen compleet beeld geven van het voorkomen van ziekten aan het einde van het leven, zelfs niet als onderliggende en secundaire doodsoorzaken samen worden genomen. Het gebruik van aanvullende informatie over ziekenhuisdiagnoses had invloed op de rangorde van meest voorkomende ziekten maar leidde niet tot een substantieel andere conclusie over welke ziekten het belangrijkst zijn.

In **hoofdstuk 3** worden twee studies gepresenteerd waarin het optreden van beperkingen in relatie tot leeftijd en tijd tot sterven werd onderzocht. Hierbij werd gebruik gemaakt van zes jaargangen van de Nederlandse longitudinale GLOBE studie met een sterfte follow-up van 12 jaar. In de eerste studie lieten we zien dat de prevalentie en incidentie van beperkingen in de laatste 10 levensjaar, maar vooral in de laatste vijf jaar, aanzienlijk toeneemt. Maar ook de ernst van beperkingen was hoger naarmate de tijd tot sterven korter was. Het optreden van ADL beperkingen hing sterker samen met tijd tot sterven dan met leeftijd, ook binnen verschillende ziektegroepen (chronische aspecifieke respiratoire aandoeningen, hartziekten en diabetes) en leeftijdsgroepen. De relatie met tijd tot sterven was sterker op hogere leeftijd. OESO beperkingen hingen sterker samen met leeftijd. In een tweede studie werden relaties van ADL beperkingen met leeftijd en tijd tot sterven onderzocht waarbij drie niveaus van ernst van beperkingen werden onderscheiden. Het doel was te onderzoeken of de relaties van milde, matige en ernstige beperkingen met tijd tot sterven in overeenstemming zijn met de theorie van het dynamisch equilibrium. Deze theorie stelt dat bij een stijgende levensverwachting vooral de jaren met minder ernstige morbiditeit zullen stijgen, terwijl de jaren met ernstige morbiditeit gelijk blijven. Dit impliceert dat ernstige beperkingen sterk gerelateerd zullen zijn aan tijd tot sterven, maar dat milde beperkingen meer gerelateerd zijn aan leeftijd. Uit ons onderzoek bleek dat ernstige beperkingen, gedefinieerd als grote moeite met één (of meer) van tien ADL activiteiten, vooral samenhangen met tijd tot sterven, terwijl milde beperkingen, gedefinieerd als enige moeite met tenminste één activiteit, in het geheel niet samenhangen met tijd tot sterven. Zoals werd gedemonstreerd met een rekenvoorbeeld zijn deze relaties in overeenstemming met de hypothese van dynamisch equilibrium. Dit onder-

schrijft de hypothese dat bij een verdere toename van de levensverwachting met name de jaren geleefd met een milde beperking zullen toenemen, terwijl de jaren met een ernstige beperking gelijk blijven.

Deel II: Verklaring van de beperkingenlast

Hoofdstuk 4 omvat een studie waarin de bijdragen van chronische ziekten aan de last van ADL beperkingen werd onderzocht, waarbij gebruik werd gemaakt van gegevens van de Nederlandse POLS survey, 2001-2007. De beperkende impact, dit is de mate waarin een ziekte leidt tot beperkingen, werd berekend voor een verscheidenheid aan ziekten. Hierbij werd gebruik gemaakt van een additief regressie model. Aandoeningen van het bewegingsapparaat en hart- en vaatziekten droegen het meeste bij aan de last van ADL beperkingen, maar ook chronische aspecifieke respiratoire aandoeningen (mannen) en diabetes (vrouwen) hadden een grote bijdrage. Van de aandoeningen van het bewegingsapparaat en hart- en vaatziekten droegen rugpijn, perifere vaataandoeningen en cerebrovasculaire aandoeningen (CVA) veel bij, met name door hun hoge beperkende impact. Artrose/artritis en hartziekten hadden een kleinere beperkende impact maar droegen nog steeds aanzienlijk bij door hun hoge prevalentie. De beperkende impact van ziekten was vooral hoog onder personen ouder dan 80 jaar.

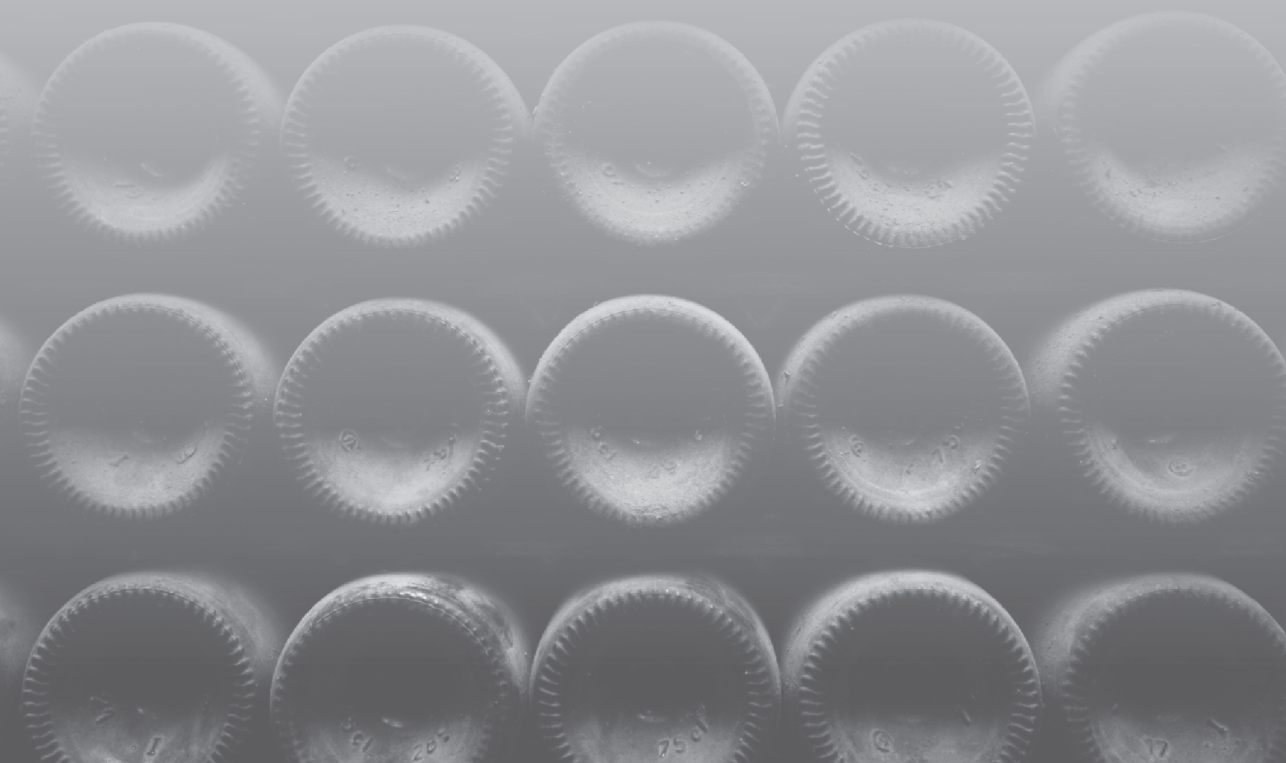
In **hoofdstuk 5** wordt een studie gepresenteerd waarin werd onderzocht in welke mate ziekten bijdragen aan opleidingsverschillen in de prevalentie van OESO beperkingen. Hierbij werd gebruik gemaakt van een methode vergelijkbaar met die uit hoofdstuk 4. In de analyse in hoofdstuk 5 werden echter bijdragen geschat voor groepen met een verschillend opleidingsniveau. Verder werd onderzocht in hoeverre bijdragen van ziekten aan verschillen in de beperkingenlast werden veroorzaakt door verschillen in beperkende impact. Er waren grote absolute verschillen in de prevalentie van OESO beperkingen van 18%(punten) voor mannen en 15% voor vrouwen tussen groepen met het hoogste en het laagste opleidingsniveau. 64% van het verschil bij mannen en 69% bij vrouwen werd veroorzaakt door de geïncludeerde ziekten. Voor mobiliteitsbeperkingen alleen waren deze percentages 90% en 84%. Ziekten die het meest bijdroegen aan de opleidingsverschillen voor mannen waren rugpijn (17%), nek/arm aandoeningen (13%), overige (11%) en perifere vaataandoeningen (7%). Voor vrouwen waren dit artrose/artritis (18%), overige (17%), rugpijn (13%) en chronische aspecifieke respiratoire aandoeningen (7%). Voor mannen en vrouwen werd 49% en 51% van het totale opleidingsverschil in de prevalentie van beperkingen verklaard door verschillen in de beperkende impact van ziekten.

Hoofdstuk 6 omvat een studie met als doel helder te krijgen welke leefstijlfactor (obesitas, roken of zwaar drinken) het meest gerelateerd is aan een groot aantal levensjaren met een ADL beperking. Hierbij werd gebruik gemaakt van Sullivan overlevingstafels. Een tweede doel

van de studie was te onderzoeken of schattingen op basis van de Sullivan overlevingstafel verbeterd kunnen worden door stratificatie naar tijd tot sterven. Er werd gebruik gemaakt van gegevens van de Nederlandse POLS survey, 1997-1999, met een sterfte follow-up tot 2006. Met name roken hing samen met een hoge sterfte, terwijl sterfte bij obesitas en zwaar drinken matig was verhoogd. De kans op een ADL beperking was hoog voor personen met obesitas, matig verhoogd voor zware drinkers en laag voor rokers. Op basis van de geschatte kansen op sterfte en beperkingen werden Sullivan overlevingstafels geconstrueerd. De schattingen wezen uit dat de jaren geleefd met een beperking het meest varieerden naar BMI, het minst naar rookstatus en ertussenin naar alcohol consumptie. Naar verwachting leven personen met obesitas minstens twee jaar meer met een beperking dan rokers of zware drinkers. Het gebruik van informatie over tijd tot sterven resulteerde in lagere schattingen van de jaren met een beperking en in kleinere verschillen in deze jaren naar BMI, alcohol consumptie en rookstatus. De conclusie welke factor het belangrijkst is bleef echter onveranderd.

In **hoofdstuk 7** worden de belangrijkste bevindingen samengevat, de gebruikte data en methoden worden bediscussieerd, de resultaten worden vergeleken met eerdere studies en nieuwe bevindingen worden uitgelicht. Het hoofdstuk wordt afgesloten met aanbevelingen voor praktijk en onderzoek. De hoofdconclusies van dit proefschrift zijn als volgt. Meervoudige doodsoorzaken bestaande uit onderliggende en secundaire doodsoorzaken geven een onderschatting van de prevalentie van sommige ziekten aan het einde van het leven. Het gebruik van aanvullende informatie uit ziekenhuisdiagnoses beïnvloed de rangorde van de meest voorkomende ziekten, maar leidt niet tot substantieel andere conclusies over welke ziekten het belangrijkst zijn. Milde beperkingen zijn het sterkst gerelateerd met leeftijd, terwijl ernstige beperkingen met name gerelateerd zijn met tijd tot sterven. Dit onderschrijft de veronderstelling dat de jaren geleefd met milde beperkingen zullen toenemen bij een verdere stijging van de levensverwachting, maar dat de jaren met ernstige beperkingen minder sterk zullen toenemen doordat de leeftijd waarop de eerste (ernstige) beperking optreedt zal stijgen. Aangezien ziekten zowel door een hoge prevalentie als door een hoge beperkende impact bijdragen aan de beperkingenlast, zal beleid met als doel het terugdringen van de beperkingenlast zich moeten richten op zowel het voorkómen van ziekten als het terugdringen van de beperkende impact van ziekten. Reducties in de prevalentie en beperkende impact van ziekten onder laagopgeleiden kan leiden tot een aanzienlijke vermindering van de sociale ongelijkheid in de beperkingenlast. Wanneer wordt aangenomen dat het opleidingsverschil in de prevalentie van ziekten onveranderd blijft, kan het opheffen van het verschil in de beperkende impact van ziekten nog steeds leiden tot een vermindering van de ongelijkheid in de beperkingenlast van 50%. Het terugdringen van obesitas, roken en zwaar drinken zullen alle drie de levensverwachting en de levensverwachting zonder beperkingen verhogen, maar alleen het terugdringen van obesitas zal de jaren met één of meerdere beperkingen verminderen.

Dankwoord



DANKWOORD

Als je aan het dankwoord kan beginnen weet je dat het goed zit. De arbeid is gedaan en al dat rest is het bedanken van mensen. Dat bedanken doe ik graag, ik kijk namelijk met veel plezier terug op mijn tijd bij MGZ en de samenwerking met de verschillende mensen tijdens mijn promotie onderzoek.

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Suzanne Polinder, bedankt voor je co-auteurschap bij het Nederlandstalige artikel over compressie van morbiditeit en, Istvan Majer en Irina Stirbu, bedankt dat ik bij jullie co-auteur kon zijn en op die manier van jullie heb kunnen leren. Istvan, gaan we nog eens naar Sparta, of heb je tegenwoordig een seizoenskaart voor ADO? Harry en Suzie, ook jullie wil ik bedanken voor de samenwerking bij het schrijven van het 'diabetes artikel', een klus die voor mijn promotie begon en 'enige' uitloop heeft gehad. Collega's van Netspar, bedankt voor de leerzame discussies tijdens onze meetings en andere contactmomenten.

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Naast mijn kamergenoten wil ik ook alle andere collega's bedanken. Bedankt voor werkinhoudelijke praatjes, de gezelligheid, de meer serieuze gesprekken en de lunchwandelingen die het hoofd weer leegmaakten voor het tweede deel van de dag. Heren van de helpdesk, bedankt voor de assistentie op computer gebied. Dames van het secretariaat, in het bijzonder Anja, bedankt voor het maken van afspraken en andere hulp.

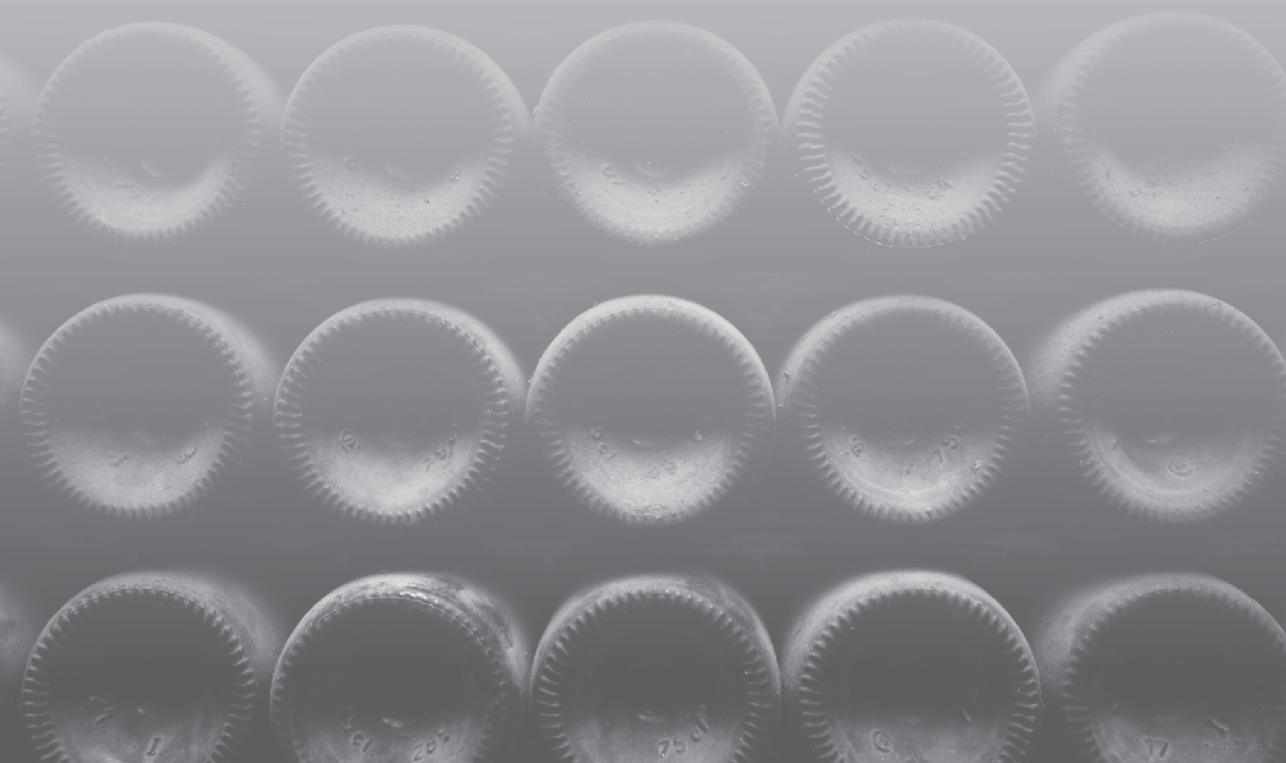
Wat ben ik blij met vrienden, dichtbij en verder weg. Vrienden van de Bethelkerk, top om met elkaar te lachen, mee te leven en muziek te maken. Mupputs, idem, zou ik zeggen, zij het op een wat grotere afstand. Wanneer gaan we weer de man uithangen in de Ardennen? En mannen van Zestienhoven H_3, het was na een goede dag werken altijd heerlijk om weer eens flink te kunnen beuken. Over de resultaten zullen we het maar niet hebben.

Walter en Huub, ik twijfelde even of ik jullie beide schoonbroers (ik blijf Zeeuws-Vlaming) wel zou moeten vragen als paranimf. Ik was even bang dat de flauwe grappen niet van de lucht zouden zijn in het zweetkamertje. Ach ja, een beetje luchtigheid is ook wel lekker op zo'n moment. Bedankt voor de bijstand!

En dan, lieve familie, bedankt voor alles, zou ik bijna zeggen. Waar ik jullie voor wil bedanken gaat veel verder dan het schrijven van een proefschrift. Bedankt dat jullie er zijn en dat we het leven delen. Pa en ma, bedankt dat de deur altijd open staat bij jullie en dat jullie altijd voor ons klaar staan. Pa en ma Waalewijn, jullie zijn een tweede familie geworden, bedankt daarvoor. Broers en zussen, het is een groot goed deel te zijn van een breed familieverband, het begint nu cliché te klinken maar, dank jullie wel.

Ada, bedankt dat jij mijn lieve vrouw bent. Wat is het fijn om samen met jou door het leven te gaan. Laten we er nog maar wat jaren aan vast plakken zo, samen met onze lieve kinderen. Wout, bedankt dat je zo'n lieve, stoere knul bent en Julie, bedankt dat je zo'n mooie meid bent. Ada, bedankt voor alle vrijheid en ondersteuning die je me de laatste tijd hebt gegeven bij het schrijven van mijn proefschrift. Maar nu Wout ook op zaterdag en zondag "papa werken" gaat zeggen, is het misschien toch tijd voor wat meer family-time.

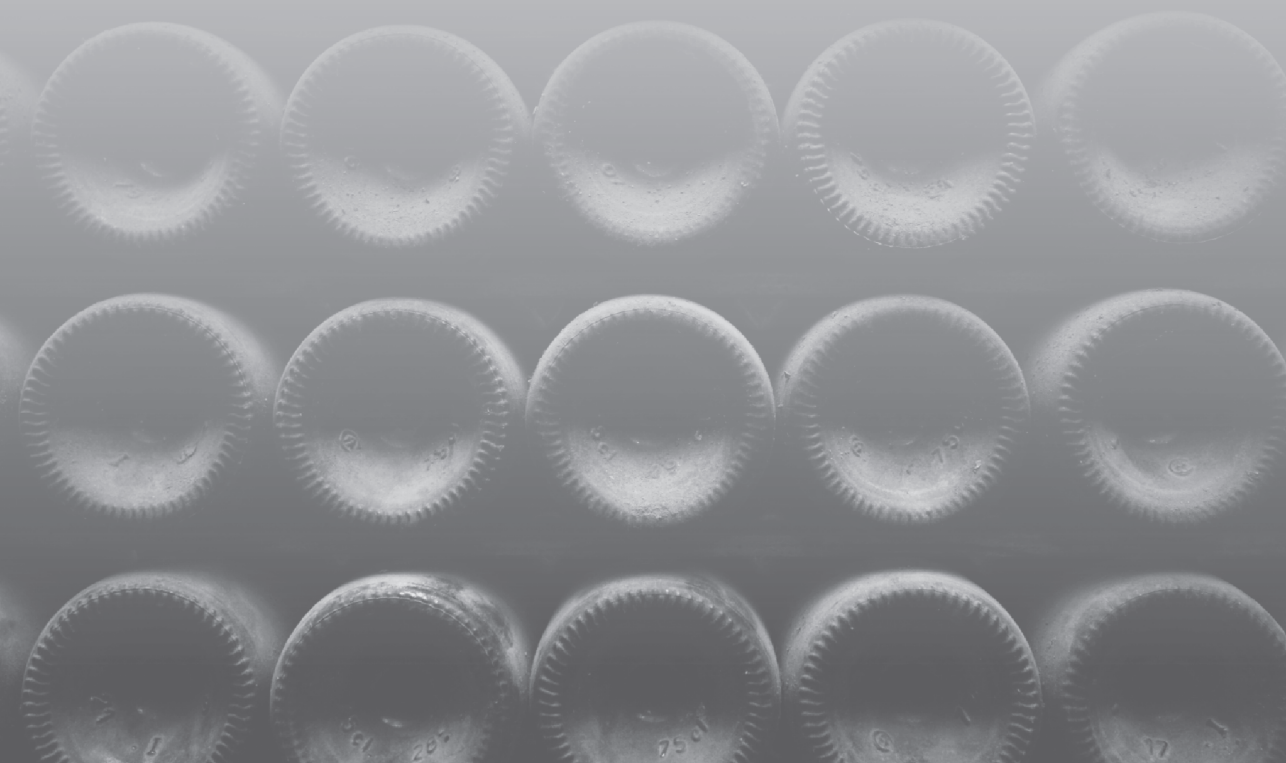
About the author



ABOUT THE AUTHOR

Bart Klijs was born on October 10, 1978 in Terneuzen, the Netherlands. After completing secondary school in 1998, he studied Physiotherapy at Fontys Hogescholen, Eindhoven. He received his Bachelor degree in 2002 and started a Master of Health Sciences (Human Movement Sciences), at Maastricht University. In 2005, Bart graduated and started working as a physiotherapist at Zorggroep Rijnmond, Rotterdam. Between 2006-2007, he worked as a Junior Researcher at the Department of Public Health, Erasmus MC, University Medical Centre, Rotterdam where he was involved in a pilot study on the effectiveness of population based screening for type 2 diabetes. Having shortly experienced working as a Youth Monitor researcher at the Municipal Health Service, Rotterdam, in 2007 he returned to the Department of Public Health, where he started as a PhD student within the Netspar theme "Living Longer in Good Health", which resulted in this thesis. During his PhD project, Bart obtained a Master of Science degree in Public Health at the Netherlands Institute for Health Sciences.

List of Publications



LIST OF PUBLICATIONS

Klijs B, Nusselder WJ, Looman CW, Mackenbach JP. Contribution of chronic disease to the burden of disability. PLoS One. 2011, 6(9):e25325.

Majer IM, Nusselder WJ, Mackenbach JP, Klijs B, van Baal PHM. Mortality risk associated with disability: a population-based record linkage study. Am J Pub Health. 2011, 101(12):e9-e15.

Klijs B, Mackenbach JP, Kunst AE. Obesity, smoking, alcohol consumption and years lived with disability: a Sullivan life table approach. BMC Public Health. 2011, 24;11:378.

Klijs B, Mackenbach JP, Kunst AE. Future disability projections could be improved by connecting to the theory of a dynamic equilibrium. J Clin Epidemiol. 2011, 64(4):436-43.

Klijs B, Mackenbach JP, Kunst AE. Disability occurrence and proximity to death. Disabil Rehabil. 2010, 32(21):1733-41.

Inspectie voor de Gezondheidszorg. Ongelijkheid in gezondheid, is gezondheidszorg van belang? - Sociaaleconomische en etnische verschillen in gezondheidszorguitkomsten op het terrein van hart- en vaatziekten in Nederland. 2010.

Klijs B, Nusselder WJ, Mackenbach JP. Compressie van morbiditeit: een veelbelovende benadering om maatschappelijke consequenties van vergrijzing te verlichten? Tijdschr Gerontol Geriatr 2009, 40: 228-236.

GGD Rotterdam Rijnmond. Jeugdmonitor gemeente Albrandswaard. 2007

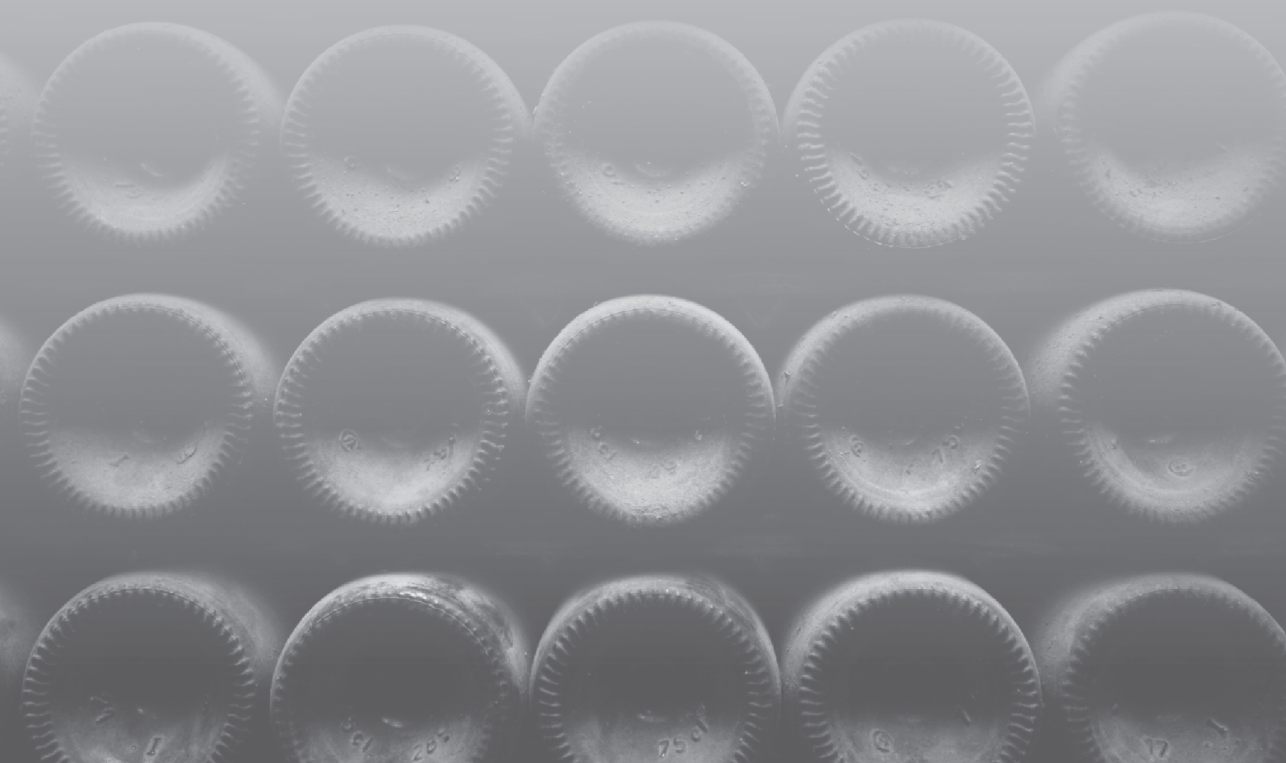
Klijs B, Otto SJ, Heine RJ, van der Graaf Y, Lous J, de Koning HJ. Screening for type 2 diabetes in a high-risk population: study design and feasibility results of a population-based randomized controlled trial. Submitted for publication.

Willems JI, Otto SJ, Klijs B, Looman CWN, de Koning HJ. Screening for diabetes in the general population: The long-term effects of a negative screening test. Submitted for publication.

Klijs B, Nusselder WJ, Looman CW, Mackenbach JP. Contribution of chronic disease to educational inequalities in the burden of disability. Manuscript.

Klijs B, Nusselder WJ, Mackenbach JP. Disease presence among decedents: a nationwide study using combined information from death certificates and hospital discharge records. Manuscript.

PhD Portfolio



PHD PORTFOLIO

Bart Klijs	PhD period: 2007-2011
Erasmus MC, Department of Public Health	Promotor: Prof. Dr. J.P. Mackenbach
	Supervisor: Dr. W.J. Nusselder

	Year	Workload
General academic skills		
- Biomedical English writing and communication	2009	112 hrs.
In-depth courses (e.g. Research school, Medical Training)		
- Master of Public Health, Netherlands Institute for Health Sciences (NIHES), Rotterdam, the Netherlands.	2007-2009	
o Erasmus Summer Programme		
· History of epidemiologic ideas		
· Principles of research in medicine	2008	20 hrs.
· Introduction to public health	2008	20 hrs.
· Methods of public health research	2008	20 hrs.
· Methods of health services research	2008	20 hrs.
· Prevention research	2008	20 hrs.
· Health economics	2008	20 hrs.
· Conceptual foundation of epidemiologic study design	2008	20 hrs.
· Cohort studies	2009	20 hrs.
· Case-control studies	2009	20 hrs.
· Principles of genetic epidemiology	2009	20 hrs.
· Topics of health and diseases in the elderly	2009	20 hrs.
· Demography of ageing	2009	20 hrs.
	2009	20 hrs.
o Core Curriculum		
· Study design		
· Classical methods for data-analysis	2007	120 hrs.
· Public health research	2007	160 hrs.
· International comparison of health care systems	2007	120 hrs.
· Modern Statistical Methods	2008	40 hrs.
	2007	120 hrs.
o Advanced short courses		
· Planning and evaluation of screening		
· Major determinants and major disease	2006	40 hrs.
· Medical demography	2008	40 hrs.
· Analysis of time-varying exposures	2008	40 hrs.
· Ethnicity health and healthcare	2009	20 hrs.
	2009	30 hrs.

Presentations

- Oral presentation "disability and mortality among the elderly" at the Netspar kick-off meeting 'living longer in good health' in Rotterdam, the Netherlands.	2007	15 hrs.
- Oral presentation "Association between disability and proximity to death" at a research meeting at the Department of Public Health Erasmus Medical Center in Rotterdam, the Netherlands.	2008	25 hrs.
- Oral presentation "Disability and proximity to death" at the 16th annual conference of the European Public Health Association in Lisbon, Portugal.	2008	25 hrs.
- Oral presentation "Contribution of chronic diseases to the burden of disability in the Netherlands" at the 21st annual meeting of the REVES Network on Health Expectancy in Copenhagen, Denmark.	2009	25 hrs.
- Oral poster presentation "Disability occurrence and proximity to death" at the 33rd annual meeting of 'werkgroep epidemiologisch onderzoek Nederland (WEON) in Amsterdam, the Netherlands.	2009	25 hrs.
- Oral presentation "Contribution of chronic diseases to the burden of disability in the Netherlands" at a Netspar klankbordgroep meeting at Tilburg University, the Netherlands.	2009	25 hrs.
- Oral presentation "The contribution of chronic disease to educational inequalities in the burden of disability" at the 22nd annual meeting of the REVES Network on Health Expectancy in Havana, Cuba.	2010	25 hrs.
- Oral presentation "Contribution of diseases to old age mortality in the Netherlands" at a research meeting at the Department of Public Health Erasmus Medical Center in Rotterdam, the Netherlands.	2010	25 hrs.
- Oral presentation "Contribution of chronic disease to educational inequalities in the burden of disability" at the Dutch Congress for Public Health (Nederlands Congres Volksgezondheid)	2011	25 hrs.
- Oral presentation "Contribution of chronic disease to educational inequalities in the burden of disability" at a lunch seminar at the Department of Public Health and Healthcare (V&Z) at the National Institute for Public Health and the Environment (RIVM).	2011	25 hrs.

International conferences		
- 16th annual conference of the European Public Health Association in Lisbon, Portugal.	2008	25 hrs.
- 21st annual meeting of the REVES Network on Health Expectancy in Copenhagen, Denmark.	2009	25 hrs.
- 22nd annual meeting of the REVES Network on Health Expectancy in Havana, Cuba.	2010	25 hrs.
Seminars and workshops		
- Attending seminars of the department of Public Health.	2007-2011	50 hrs.
- Microdata middag at Statistics Netherlands in Voorburg, the Netherlands.	2007	5 hrs.
- Onderzoekersmiddag doodsoorzaken at Statistics Netherlands in Voorburg, the Netherlands.	2007	5 hrs.
- Symposium of Research institute for diseases in the elderly (RIDE) in the Hague, the Netherlands	2008	10 hrs.
- Epar introduction and careerplanning day for Ph.D.'s, workshop time management at the Erasmus University in Rotterdam, the Netherlands	2009	4 hrs.
- Symposium gezonde tijdsreeksen at Statistics Netherlands in Voorburg, the Netherlands	2009	8 hrs.
- Netspar panel at Tilburg, presentation panel paper "Health disability and work at Tilburg University in Tilburg, the Netherlands	2009	3 hrs.
- Netspar theme conference "Longevity risk" at Tilburg University, in Tilburg, the Netherlands		4 hrs.
Didactic skills		
- Teaching module "Population ageing and disability" within Nihes course "Analysis of population health" by Anton Kunst	2010	25 hrs.